Summer 2022

Cognitive Consequences of COVID-19 Infection and Quarantine-Induced Social Isolation: Hope for the Young and Mildly Infected

Kristin Nickole Kirchner

Cognitive Consequences of COVID-19 Infection and Quarantine-Induced Social Isolation: Hope for the Young and Mildly Infected

by

Kristin Nickole Kirchner

Bachelor of Science
The University of South Carolina Upstate, 2017

Master of Arts
The University of South Carolina, 2020

Submitted in Partial Fulfillment of the Requirements

For the Degree of Doctor of Philosophy in

Experimental Psychology

College of Arts and Sciences

University of South Carolina

2022

Accepted by:

Jessica Green, Major Professor

Doug Wedell, Committee Member

Kate Flory, Committee Member

Susan Steck, Committee Member

Tracey L. Weldon, Vice Provost and Dean of the Graduate School

DEDICATION

“No one is born into this world to be alone.” (Eiichiro Oda). I dedicate this dissertation to every individual who has helped me become the person I am today. To my family: Mom and Dad, Grandma and Bebop, Memaw and Pawpaw. I thank you for everything. Thank you for your time and your sacrifices. Thank you for showing me what it means to share both knowledge and love. I am proud to be your daughter and granddaughter. To Austin, Chris, Colin, Erica, Katherine, Kyle, Mackenzie, Matthew, Nick, Nolan, and Rachel: from both near and far, their dedication to me has been unwavering throughout the years. I thank them sincerely for being the brightest parts of my days. To Alec, Andrew, Casey, Dakota, Drake, Ky, Nian, Nick, and Ron: our time spent together has been irreplaceable and I would not trade it for the bluest hat in the world. I thank Dr. Jessica Green for her mentorship during the final years of my degree. I also would like to thank Neil Cicierega, for the music, and Charlie, Dennis, Ian, and Vinny for their entertainment during the writing process. I also specially thank F.D.H. for his unconditional love.

ACKNOWLEDGEMENTS

I would like to acknowledge Dr. Jessica Green, my primary mentor, for her guidance. I would also like the acknowledge the other members of my committee, Dr. Doug Wedell, Dr. Kate Flory, and Dr. Susan Steck, for their contributions to the present project. I thank Austin Hughes for his assistance with data extraction. Acknowledgement and thanks to fellow lab members Sori Kim and Jonathan Conrady. I also thank my participants for their time and willingness to participate. This research was supported in part by the National Institute of Health T32 Training Grant 5T32GM081740.

ABSTRACT

Coronavirus disease 2019 (COVID-19) has infected over 539 million individuals worldwide, and initial research supports the possibility that COVID-19 may damage the central nervous system either directly or indirectly. Neurological signs and noted cognitive deficits observed in even mildly infected patients are a cause for concern for those infected by COVID-19; the effect of social isolation on the central nervous system is also of interest. The present study sought to determine the extent of these potential cognitive deficits in a young and mildly infected sample of college students. Participants completed an extensive survey assessing their experience with COVID-19 and any pandemic-induced social isolation. Participants then completed a battery of cognitive assessments to evaluate attention, memory, and executive functioning. Results largely suggested that mild infection did not cause lasting cognitive deficits. While social isolation largely did not influence cognition, it had an effect on non-diagnostic measures of certain mental health disorders. Overall, the present data suggest no evidence of current Long-COVID related cognitive deficits in a young and mildly infected sample, despite participants reporting perceived deficits in their cognition. This perceived lack will be important for clinicians and researchers to consider as the COVID-19 pandemic continues to develop.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

ACE2 ..... Angiotensin-Converting Enzyme 2

COVID-19 ..... Coronavirus Disease 2019

CNS ..... Central Nervous System

HIV-1..... Human Immunodeficiency Virus Type 1

PCC ..... Post-COVID Conditions

SARS ..... Severe Acute Respiratory Syndrome

WNV ..... West Nile Virus

CHAPTER 1

INTRODUCTION

1.1 BACKGROUND

Coronavirus disease 2019 (SARS-CoV-2, COVID-19) has infected over 566 million individuals worldwide, leading to 6.3 million COVID-19 linked deaths (WHO “COVID-19 Dashboard”, obtained July 26th, 2022). COVID-19 has since been declared the sixth public health emergency of international concern (Williams et al., 2021). Official identification of the novel coronavirus occurred in early January 2020. During this initial period, important aspects about SARS-CoV-2 were discovered, including its interaction with angiotensin-converting enzyme 2 (ACE2), its ability to replicate in many species, and its initial symptoms of infection. Fever, cough, fatigue, pneumonia, increased plasma cytokines and chemokines, and its extreme transmissibility were identified in the early patients of COVID-19 in Wuhan, China (Huang et al., 2020; Jotz et al., 2020). Six weeks after declaring COVID-19 a Public Health Emergency, on March 11th, 2020, the World Health Organization declared COVID-19 a pandemic. In March of 2020, it was first identified that SARS-CoV-2 induces increased levels of pro-inflammatory cytokines and chemokines without triggering a host’s immune response (Blanco-Melo, 2020). Also during March, worldwide “stay at home” orders and mandatory quarantine and social-distancing measures were put into place. In April of 2020, unemployment increased, mostly in low-wage industries

(CBPP, 2022). Drastic increases in mental health issues (namely anxiety and depression) in the general population were observed as early as July of 2020 (CDC “Anxiety and Depression”). In December of 2020, the first variant was identified, and since then at least five major variants have been discovered. It was not until the beginning of 2021 that vaccines were readily available, but as of May of 2022, only 66% of the United States population is considered fully vaccinated (CDC “COVID Data Tracker”). Treatments and “cures” for COVID-19 are still limited, and vaccination is currently considered the top way to protect oneself from COVID-19 (Cai et al., 2020).

1.2 COVID-19 OVERVIEW

COVID-19 is the seventh of the coronaviruses known to infect humans. Four of the coronaviruses lead to mild illness while the remaining three (SARS-CoV-1, MERS-CoV, SARS-CoV-2/COVID-19) can lead to more severe and potentially deadly illness (Williams et al., 2021; Bougakov et al., 2021). SARS-CoV-1 infected more than 8000 people worldwide during the 2002-2004 outbreak, and MERS-CoV had a mortality rate of almost 35% (Guadarrama-Ortiz et al., 2020). SARS-CoV-2 has a higher transmission rate than both (Williams et al., 2021).

Common symptoms of COVID-19 include fever, cough, fatigue, difficulty breathing, and in more severe cases respiratory failure or pneumonia (Almeria et al., 2020; Guadarrama-Ortiz et al., 2020). One of the more unique symptoms of COVID-19 displayed is loss of smell (anosmia); this symptom was often one of the first, and most salient, signs that someone had contracted COVID-19

(Almeria et al., 2020; Bougakov et al., 2021; Guadarrama-Ortiz et al., 2020; Graham et al., 2021). However, with more recent variants of COVID-19, anosmia is not always present (CDC “What You Need to Know About Variants”).

COVID-19, similar to SARS-CoV-1, enters cells using angiotensin 2 (ACE2) (Almeria et al., 2020; Boldrini et al., 2021). SARS-CoV-2 attaches to ACE2 using its spike protein, allowing its RNA to enter the cell (Shang et al., 2020). ACE2 receptors are present in bronchial epithelial cells, endothelial cells, on the surface of other organs (lungs, kidneys, heart, etc.), and in neurons (Li et al., 2020). SARS-CoV-2 mainly affects the lower respiratory tract, causing respiratory symptoms in 85% of patients with COVID-19 (Guadarrama-Ortiz et al., 2020).

While many fully recover from COVID-19 within 2 weeks, others experience symptoms of COVID-19 for an extended period. “Long-COVID,” “long-haul COVID,” or “post-COVID conditions” (PCC) is defined by the CDC as “signs or symptoms that develop during or after infection consistent with COVID-19, continue for more than 12 weeks and are not explained by an alternative diagnosis” (“COVID-19 Rapid Guideline”, 2020). However, definitions for Long-COVID, PCC, and long-haul COVID are mixed, sometimes with these terms being used to describe different conditions rather than being used interchangeably (Stefanou et al., 2022; Garg et al., 2021a). Other definitions for PCC include: having recovered from the acute phase of COVID-19 but displaying either lingering symptoms or new symptoms months after infection (Williams et al., 2021), ongoing symptomology that persist for more than 12 weeks (NHS

“Long-term effects of coronavirus (long COVID)”), having one persisting physical symptom for a minimum duration of 12 weeks (Stephenson et al., 2022), new or persistent symptoms occurring 4 weeks after acute infection (Walker et al., 2021), the “time lag between microbiological recovery and clinical recovery” (Raveendran et al., 2021), a “multi-organ disorder with a wide spectrum of clinical manifestations” (Stefanou et al., 2022), and “signs and symptoms that emerge during or after an infection consistent with COVID-19, persist for more than 12 weeks, and are not explained by an alternative diagnosis” (NICE).

The current literature does not always describe later observed deficits or symptomology as being a part of PCC, which creates an artificial divide in the current research. In brief, even when deficits are observed at a later date in a certain sample or population, these deficits are not always attributed to being a part of a “Post-COVID Condition.” Even clinically, PCC is not always correctly or consistently diagnosed (Walker et al., 2021). Many of the symptoms associated with PCC are nonspecific and are present in the never-infected general population, with controls and previously infected individuals reporting “symptoms of PCC” at similar rates (Amin-Chowdhury et al., 2021).

Many of the cases thus far associated with PCC have been self-reported and broadly defined, as currently no official diagnostic tools exist to diagnose an individual with PCC (Hampshire et al., 2021). According to the CDC, “Post-COVID Conditions” encompass a wide range of symptoms, such as fatigue, difficulty thinking or concentrating (brain fog), malaise, shortness of breath, heart palpitations, headache, dizziness, depression, anxiety, diarrhea, skin changes, or

changes in menstrual cycles (CDC “Long COVID or Post-COVID Conditions”). The research cited herein are a blend of data specifically designated as contributing to the literature for “Long-COVID” or PCC and data that have not been specifically designated by their primary researchers as contributing to the literature on PCC, due in part to the lack of a clear consensus on a definition for what constitutes a PCC.

It is estimated that anywhere between 10-25% of COVID-19 infected individuals may suffer from some form of PCC (Guo et al., 2022). A recent meta-analysis revealed that 3-6 months post-infection, fatigue was present in 30%, breathing difficulties in 25%, sleep disturbances in 24%, and difficulty concentrating in 22%. For those who were 6-9 months post infection, “effort intolerance” was the most frequent symptom, at 45%, followed by fatigue at 36%, sleep disturbances at 29%, and difficulty breathing at 25%. For those 9-12 months post infection, fatigue was the most commonly found symptom at 37% prevalence, followed by difficulty breathing at 21%. Only fatigue persisted as a common symptom at 12 months post infection, at 41% prevalence (Alkodaymi et al., 2022). Cognitive disorders were only found in 14% of those 3-6 months post infection and in 15% of those 6-9 months post infection (Alkodaymi et al., 2022). However, the rate of cognitive difficulties was higher in a different meta-analysis, with rates of 20-30% in a non-hospitalized population and 30% in a hospitalized population (Ceban et al., 2022). In children, the most frequently endorsed symptoms were headache and fatigue (Molteni et al., 2021). PCC are more likely to develop when an individual has experienced more severe COVID-19 infection

or in individuals who required hospitalization for COVID-19, but PCC can still occur in individuals who have not been hospitalized (Ziauddeen et al., 2022; Townsend et al., 2021; Chen et al., 2022; Del Corral et al., 2022), who were mildly infected (Townsend et al., 2021), and who are young (Zimmermann et al., 2022; Stephenson et al., 2022; Molteni et al., 2021).

1.3 NEUROLOGICAL AND PSYCHIATRIC SYMPTOMOLOGY

Neurological symptoms of COVID-19 were first noted in late March 2020, presenting in the form of loss of taste and/or smell (Carvalho et al., 2021). Neurological symptomology associated with the COVID-19 virus is present in around 30-80% of positive cases (Rogers et al., 2021; Bougakov et al., 2021). Neurological symptoms can occur independently of respiratory symptoms and can continue to occur months after respiratory symptoms have resolved, indicating independent and ongoing nervous system involvement (Boldrini et al., 2021).

Further evidence to support neural damage relating to the COVID-19 virus is found in the host of neurological and psychiatric symptoms associated with the virus. Neurological symptoms seem to occur early in the disease (Romero-Sanchez et al., 2020; Bougakov et al., 2021). The proportion of patients affected by neurological symptoms varies. Thus far, presence of neurological symptoms and complications have been found in varying proportions of COVID-19 patients: 36% of middle-aged, hospitalized, mixed severity patients (Mao et al., 2020), 54.8% of all ages, hospitalized patients (Cai et al., 2020), 21% of intensive care unit admitted, older adults (Kandemirli et al., 2020), and 57% of hospitalized,

older adults (Romero-Sanchez et al., 2020), for example. A meta-analysis to determine the frequency of neurological manifestations in COVID-19 patients published in late 2021 analyzed 350 studies. Interestingly, only 11% of the studies contained non-hospitalized participants. This meta-analysis estimates about 30% of COVID-19 patients will display some kind of neurological symptomology, with older populations and those more severely infected displaying more neurological symptoms (Misra et al., 2021). Another recent literature review estimates the prevalence of neurological symptoms at 21.3% for hospitalized COVID-19 patients (Cagnazzo et al., 2021). For non-hospitalized patients, prevalence of neurological manifestations has also been mixed: 46.7% prevalence for CNS specific manifestations (Ding et al., 2020), 52% for home-isolated young adults (Blomberg et al., 2021), 38.2% for middle aged adults (Pérez-González et al., 2022), and even up to 81% for middle aged adults (Hugon, 2022) to name a few. Fatigue has also been shown to be more frequently endorsed by non-hospitalized COVID-19 infected individuals (20.9% prevalence as compared to 5.3%) (Pérez-González et al., 2022). Uniquely, one study showed that both COVID-19 positive and never infected COVID-19 groups showed relatively equal prevalence of brain fog, fatigue, and impaired cognition, suggesting that factors other than infection could also be at play (Graham et al., 2021).

It has been found that neurological symptoms seem to correlate to disease severity, where patients who are more severely affected by the COVID-19 virus are more likely to experience neurological symptoms (Whittaker et al.,

2020; Majolo et al., 2021; Misra et al., 2021). The neurological symptoms observed in clinical COVID-19 populations include stroke (Nannoni et al., 2021), encephalopathies (Garg et al., 2021b), inflammatory syndrome (Hoste et al., 2021), elevated cerebrospinal fluid antibodies (Tandon et al., 2021), headache (Almeria et al., 2020; Bougakov et al., 2021, Mao et al., 2020; Graham et al., 2021), microbleeds (Hampshire et al., 2021), seizures (Boldrini et al., 2021; Bougakov et al., 2021), hypoxia (Hampshire et al., 2021), and brain fog (Hygon et al., 2022; Graham et al., 2021).

Psychological and psychiatric consequences have also been observed (Mendez et al., 2022; Hampshire 2021; Cai et al., 2020; Guadarrama-Ortiz et al., 2020; Pennix et al., 2021; Mendez et al., 2021), some of which persisted for months after hospital discharge. Specifically, anxiety and depression are acutely present (Maley et al., 2022; Hao et al., 2020; Vannorsdall et al., 2022; Dondaine et al., 2022; Boldrini et al., 2021; Cai et al., 2020; Mazza et al., 2021; Graham et al., 2021; Mendez et al., 2021; Kujawa et al., 2020; Luo et al., 2020). During the COVID-19 pandemic, rates of depression and anxiety have increased within many populations, as seen in citizens from Denmark, (Sønderskov et al., 2020), Ireland (Hyland et al., 2020), Istanbul (Özdin et al., 2020), Hong Kong (Choi et al., 2020), and the United States (Kujawa et al., 2020). Potential comorbid interactions of depression and anxiety with the COVID-19 virus cannot be ignored (Cai et al., 2020; Méndez et al., 2021; Mazza et al., 2020). Worldwide, anxiety and depression are the highest in patients either with COVID-19 or at high risk for COVID-19 (Luo et al., 2020). Women have been found to be more

psychologically affected than men in several studies of anxiety and depression in the context of COVID-19 (Özdin et al., 2020; Sønderskov et al., 2020; Hyland et al., 2020; Elbay et al., 2020; Lebel et al., 2020). SARS-CoV-1 survivors similarly experienced psychiatric complaints after hospital discharge (Cai et la., 2020). Cognitive impairment in survivors of acute respiratory distress syndrome has been found to still have a 20% prevalence rate up to 5 years after hospital discharge (Herridge et al., 2016).

Neuropsychiatric symptoms have been found to persist in anywhere between 20-79% of patients up to several months past the recovery from viral symptoms (Mendez et al., 2022; Boldrini et al., 2021; Majolo et al., 2021; Poletti et al., 2021). However, some studies have found resolution of these symptoms with time, with a range from 6 weeks to 9 months before full resolution (Guo et al., 2022; Williams et al., 2021; Zhao et al., 2022; Mazza et al., 2021; Ferrucci et al., 2021; Kujawa et al., 2020). Other studies have suggested that the neuropsychiatric symptoms associated with hospitalized COVID-19 survivors is due more to hospitalization rather than the infection itself (Nersesjan et al., 2022). The presence of neurological and psychiatric symptoms in COVID-19 patients supports the theory that COVID-19 can affect the central nervous system.

1.4 CNS INVOLVEMENT OF COVID-19

Although it is clear that COVID-19 can affect nervous system function, the specific mechanisms by which it does so are still under investigation. At present, there is substantial evidence that COVID-19 is neurovirulent (i.e., able to cause

changes in the nervous system that lead to disease), some evidence that it is neuroinvasive (i.e., able to enter the nervous system), and minimal evidence that it is neurotropic (i.e., able to infect and replicate within cells of the nervous system), but exact mechanisms are still unknown and require further investigation; few firm conclusions can be drawn at this time.

To be neuroinvasive, SARS-CoV-2 would need to enter the nervous system. It is hypothesized that SARS-CoV-2 may be able to enter the central nervous system directly through the nasal mucosa and olfactory tract, vagal nerve, or trigeminal pathway (Krasemann et al., 2022; Orsini et al., 2020; Bougakov et al., 2021; Boldrini et al., 2021; Guadarrama-Ortiz et al., 2020). The proposed method of entry by SARS-CoV-2 begins in the nasal cavity, and continues through the olfactory nerve, olfactory bulb, piriform cortex, and eventually the brainstem. This same route of entry has been observed in 229E and OC43, other coronaviruses (Arbour et al., 2000).

ACE2 is expressed in neurons and glial cells (Li et al., 2020; Bougakov et al., 2021; Williams et al., 2021). If SARS-CoV-2 can gain entry to the CNS, through the olfactory nerve or a damaged blood-brain barrier, then the virus could potentially directly infect neurons. SARS-CoV-1 has previously been detected in neurons of the hypothalamus and cerebral cortex, with a heavy viral load detected in the brainstem (Gu et al., 2005; Williams et al., 2021). Mice transgenic for human ACE2 displayed brain invasion of SARS-CoV-2, which resulted in death within days (Orsini et al., 2020). In these mice, the piriform

cortex and olfactory regions were the first to become infected (Orsini et al., 2020). Other mice models have shown similar neuroinvasion (Song et al., 2021).

Another possible entryway into the CNS might be through the blood-brain barrier with the assistance of inflammatory cytokines or monocytes due to the instability of the barrier caused by inflammation; SARS-CoV-2 is able to directly damage endothelial cells, and entry of SARS-CoV-2 into the CNS via endothelial cells has been observed (Boldrini et al., 2021; Varga et al., 2020; Hang et al., 2021; Krasemann et al., 2022). SARS-Cov S protein has also been observed in the cytoplasm of endothelial cells (Meinhardt et al., 2021). SARS-CoV-2 RNA has been observed in the cerebellum, trigeminal ganglion, olfactory bulb, and olfactory mucosa (Meinhardt et al., 2021; Molina-Gil et al., 2021). SARS-CoV-2 proteins have been detected via immunohistochemistry in vagus nerve fibers and the choroid plexus epithelium (Bulfamente et al., 2021; Gomes et al., 2021; Pellegrini et al., 2020). SARS-CoV-2 RNA has also been detected in blood serum; detection of this RNA occurs in 90% of patients who develop “critical disease,” and is found in only 50% of patients who develop moderate or severe disease (Jacobs et al., 2022; van Riel et al., 2021). In general, SARS-CoV-2 RNA has been detected in 2.5% of sampled brain regions in only 20% of cases (Serrano et al., 2022), in 71.4% of cases using PCR, immunohistochemistry, electron microscopy, and in situ hybridization (Meinhardt et al., 2021), in brain tissue of a case study of a child infected with COVID-19 (Gomes et al., 2021), and in brain organoids (Song et al., 2021; Zhang et al., 2020; Bullen et al., 2020). While much of this work suggests that SARS-CoV-2 may be able to enter the

nervous system directly, through either the cranial nerves or by passing through the blood brain barrier, it is largely still hypothetical at this point and it remains unclear what role, if any, such direct infection of the CNS plays in COVID-19 symptoms and PCC.

To be neurotropic, SARS-Cov-2 would need to be able to infect and replicate in cells of the nervous system. SARS-CoV-2 has also been detected in cortical neurons of autopsied individuals and in human cortical astrocytes of human stem-cell-derived organoids (Song et al., 2021; Andrews et al., 2022). Neurotropism has been detected in the olfactory mucosa and in olfactory sensory neurons (de Melo et al., 2021). Stem cell derived midbrain dopaminergic neurons have also been found to be selectively permissive to SARS-CoV-2 infection *in vitro* and *in vivo* (Han et al., 2021). However, others have found no evidence of productive infection or CNS involvement (Bauer et al., 2021; Schaller et al., 2020; Solomon et al., 2020).

To be neurovirulent, SARS-CoV-2 would need to be able to cause pathology in the CNS that contributes to disease of the nervous system; this pathology can be independent of neuroinvasiveness or neurotropism. That is, SARS-CoV-2 could indirectly lead to changes in nervous system function by affecting other systems in the body.

COVID-19 infection has been shown to increase levels of inflammatory cytokines, which can activate glial cells once crossing over the blood-brain barrier and even weaken the blood-brain barrier itself (Boldrini et al., 2021; Almutairi et al., 2016; Erickson et al., 2012). Increased serum levels of

proinflammatory cytokines (such as interleukins 1, 4, 6, 10, and tumor necrosis factor alpha) have been observed in patients with severe COVID-19 (Luporini et al., 2021; van Riel et al., 2021; Boldrini et al., 2021; Pennix et al., 2021; Mazza et al., 2021; Guo et al., 2020). Proinflammatory cytokines, chemokines, and macrophages seem to have a significant role in the advancement and severity of COVID-19 (Andrews et al., 2022; Sodagar et al., 2022; Williams et al., 2021). SARS-CoV-2 induces systemic inflammation, which can in turn induce activation of microglia in the CNS (Bulfamante et al., 2021; Boldrini et al., 2021; Pennix et al., 2021; Han et al., 2021). Direct evidence of activated microglia, microglial clusters, astrogliosis, and extensive inflammation have been observed in COVID-19 patients (Lee et al., 2021; Schurink et al., 2020; Matschke et al., 2020). Elevated levels of these chemicals can lead to dysregulation of neurotransmitter release, decreased neurogenesis, neurodegeneration, or even to cytokine storm syndrome (Boldrini et al., 2021; Williams et al., 2021; Orsini et al., 2020). Post-mortem studies of individuals who died from COVID-19 indicate evidence of ischemic lesions and neuroinflammation (Guo et al., 2022). The effects of chronic neuroinflammation through activated glial cells are detrimental, and well-studied (Schain et al., 2017; Streit et al., 2004).

Higher levels of bilateral grey matter volume have been detected in the hippocampi of COVID-19 patients, while loss of grey matter has been observed in areas connecting to the olfactory cortex; white matter changes have also been observed (Majolo et al., 2021; Guo et al., 2022; Hampshire et al., 2021; Bougakov et al., 2021). Neuroimaging data shows that the medial temporal lobe

is the most vulnerable to COVID-19 (Moriguchi et al., 2020; Poyiadji et al., 2020). MRI findings from COVID-19 patients in the intensive care unit showed abnormalities in the frontal, parietal, occipital, and temporal lobes, in addition to the insular cortex and cingulate gyrus (Kandemirli et al., 2020). Hemorrhagic lesions have also been observed in many of these areas, specifically the orbitofrontal cortex, the medial temporal lobe, hippocampus, thalamus, and insular cortex (Guo et al., 2022). Microglial nodules and neuronophagia has been detected in the brain stem, cortex, and limbic structures (Boldrini et al., 2021). It has even been proposed that respiratory issues observed in COVID-19 patients may be caused by SARS-CoV-2 infecting the respiratory centers of the medulla and pons (Li et al., 2020). Viral RNA from SARS-CoV-2 has been detected in the medulla, cerebellum, the area postrema, the olfactory cortex, and in cerebral spinal fluid (Boldrini et al., 2021; Meinhardt et al., 2020; Bougakov et al., 2021). Hospitalized COVID-19 patients showed levels of neurodegenerative biomarkers (such as tau, GFAP, and NfL) at levels higher than Alzheimer's patients (Frontera et al., 2021 at NIH convention). However, other studies have shown no detection of SARS-CoV-2 in cerebral spinal fluid (Pezzini et al., 2020).

Secondary mechanisms of brain damage, such as through hypoxia or blood clotting, are also possible (Bougakov et al., 2021; Orsini et al., 2020; Pennix et al., 2021). Those more seriously infected with COVID-19 might be at risk for strokes, hypoxia, or encephalitis, which alone can cause neurocognitive impairment. The overall effects of stress stemming from excessive worries about COVID-19 such as fears surrounding misinformation or confusing information,

employment uncertainties, stigma surrounding infection, or fear of infecting others cannot be understated, as sustained stress is capable of dysregulating the hypothalamic-pituitary-adrenal (HPA) axis (Cai et al., 2020). Dysregulation of the HPA axis leads to body-wide dysregulation of hormones and neurotransmitters, which could serve as an unforeseen consequence of COVID-19 related stress.

1.5 COGNITIVE COMPARISONS BETWEEN OTHER VIRUSES

Several other viruses have neuronal consequences, are neuroinvasive, or otherwise affect the CNS. Evidence of neuronal consequences and cognitive outcomes from other viruses can provide a basis for what can be expected from COVID-19 infection.

Herpes simplex virus type 1 (HSV-1) is capable of infecting nerve tissue; upon activation of the virus, it can infect the CNS (De Chiara et al., 2019). It is believed that HSV-1 infects the CNS through the bloodstream or the trigeminal nerve (Gnann and Whitley, 2017). In HSV-1 infected mice, higher levels of neuroinflammatory biomarkers were detected in conjunction with cognitive impairment (De Chiara et al., 2019). In humans, HSV-1 DNA was detected in the temporal cortex and hippocampus (Jamieson et al., 1992). In serious cases, HSV-1 can cause encephalitis, which in turn can lead to cognitive impairment, specifically impairments of memory (Gnann and Whitley, 2017; Bougakov et al., 2021).

Human immunodeficiency virus type 1 (HIV-1) is a highly virulent and infectious lentivirus. HIV-1 can gain access to the nervous system as soon as two weeks after primary infection (Atwood et al., 1993). HIV-1 gains access to

the CNS through infected monocyte-derived macrophages, where it crosses the blood-brain barrier (Atwood et al., 1993; McArthur et al., 2005; Sanmarti et al., 2014; Rao et al., 2014). Once established in the CNS, infected cells secrete chemokines which recruit additional monocytes from the periphery as part of an inflammatory response (Sanmarti et al., 2014; Rao et al., 2014; Woods et al., 2009). The virus itself can infect other monocytic cells within the CNS, such as perivascular macrophages, microglia, or astrocytes (Atwood et al., 1993; Rao et al., 2014, Swanstrom et al., 2012, Woods et al., 2009).

Within 60 days, some HIV-1 positive individuals display neuroinflammation (Lentz et al., 2009; He et al., 2014). Within 100 days, structural brain changes such as decreased brain volume and decreases in white matter have been identified (Saylor et al., 2016). Damage worsens with time, and HIV-1 damages both macro (frontal, temporal, and parietal cortices, white matter tracts), and micro (neuronal apoptosis, loss of dendrites and synapses) processes in the brain directly through the release of viral proteins, and indirectly through inflammatory cascades (Woods et al., 2009; Rao et al., 2014). Despite antiretroviral treatment, the virus's presence in the CNS does not diminish (Saylor et al., 2016). In fact, compartmentalized versions of the virus have been found in brain tissue at autopsy, indicating that the virus is capable of independent replication in the CNS despite lack of replication in the periphery (Swanstrom et al., 2012). After 10 years of antiretroviral therapy, low levels of HIV-1 RNA were still able to be detected in cerebrospinal fluid (Carroll et al., 2017). The virus can be detected in brain tissue at autopsy, brain tissue being

the second most infected tissue after the lungs (Swanstrom et al., 2012, Woods et al., 2009). It is theorized that the virus can enter a state of latency after first entering the CNS, since most clinically relevant signs of neurocognitive disease do not appear until years after primary infection (He et al., 2014). Unchecked virus in the CNS can lead to acute meningitis, meningoencephalitis, or AIDS dementia complex; even with combined antiretroviral therapy, complications such as HIV-1 associated neurocognitive disorders (HAND) can arise. HAND is an example of an after-effect of a virus that can occur from months to years to decades after initial infection, and its existence prompts potential cause for concern that COVID-19 may be capable of the same.

West Nile Virus (WNV) is a neurotropic flavivirus. It is hypothesized that WNV enters the central nervous system either through direct infection of endothelial cells or through the olfactory nerve, where it is then able to directly infect neurons and glial cells (Davis et al., 2006). More serious forms of WNV can lead to encephalitis and meningitis, but even mild forms of WNV are associated with neurological symptomology (Davis et al., 2006). Cognitive deficits in multiple domains and neuropsychiatric issues were observed up to a year past onset of symptoms (Hughes et al., 2007; Hart et al., 2014; Hawkes et al., 2018; Sadek et al., 2010; Davis et al., 2006).

Three other coronaviruses (SARS-CoV-1, 229E, and OC43) are neuroinvasive and neurotropic (Pezzini et al., 2020). Other coronaviruses have been shown to cause direct damage to the CNS, such as through peripheral demyelinating illness (Bougakov et al., 2021). MERS specifically has shown

increased rates of depression and PTSD in survivors (Park et al., 2020). The hippocampus, a brain structure heavily involved with learning and memory, is a target of viral encephalopathies for SARS-CoV-1, HSV encephalopathy, HIV-1 encephalopathy, and potentially SARS-CoV-2.

1.6 COGNITIVE OUTCOMES

In general, cognitive deficits have been found to persist for months up to a year past COVID-19 infection (Crivelli et al., 2022; Vannorsdall et al., 2022; Dondaine et al., 2022; Ferrucci et al., 2022; Liu et al., 2022; Ziauddeen et al., 2022; Nersesjan et al., 2022; Del Corral et al., 2022). Based on the symptoms associated with the aforementioned neurotropic viruses, and the current evidence for COVID-19, the following domains of cognition were selected for analyses for the present study: attention, memory, and executive functioning (as assessed by cognitive flexibility and decision making).

There are many components of attention, which is the aspect of cognition that allows the collection and initial organization of information from the environment. Properly functioning attention is characterized by one's ability to focus selectively on a stimulus, hold focus on that stimulus, and shift to focusing on other stimuli as necessary. Deficits in attention can lead to the inability to tune out unimportant details or the inability to focus on details important the task at hand.

In both SARS-CoV-1 and MERS, survivors saw impairment of attention up to 39 months after recovery (Mazza et al., 2021). In HIV-1 associated neurocognitive disorder, attention is one of the main cognitive domains affected,

with symptoms including reduced ability to shift attention, change focus, divide attention, concentrate, and sustain attention to stimuli (Atwood et al., 1993, Hinkin et al., 2000, Antinori et al., 2007; Chang et al., 2014). Attentional deficits can cause difficulty in all areas of a patient's daily life (Sanmarti et al., 2014). Specifically, deficits in sustained attention have been shown to have a negative effect on medication adherence, and even driving ability, in HIV-1 positive individuals (Woods et al., 2009, Marcotte et al., 2006).

Deficits in attention have been observed in hospitalized COVID-19 patients requiring rehabilitation and oxygen treatments (Jaywant et al., 2021; Almeria et al., 2020). Deficits in attention seem to become greater with disease severity for COVID-19, wherein hospitalized patients have greater deficits than those with milder symptoms (Hampshire et al., 2021). Patients presenting neurological symptoms during COVID-19 infection also showed greater deficits in attention 3 months after recovery than patients who did not present neurological symptoms (Almeria et al., 2020). Even non-severely infected individuals saw deficits in attention at a later time period (Dondaine et al., 2022). Patients diagnosed with PCC, even if they have not been hospitalized, show significant deficits in attention (Graham et al., 2021). Research specific to COVID-19 suggests that brain stem involvement of the COVID-19 virus may lead to deficits in attention (Gandhi et al., 2020). There is also evidence to support that simply the fear of the COVID-19 virus is enough to induce deficits in attention (Ismail et al., 2021).

For the present study, assessments of sustained attention and selective attention were chosen. Sustained attention is a component of cognitive capacity that allows maintenance of the ability to detect infrequent, weak, or unpredictable stimuli over a long period of time (Levine et al., 2006; Sarter et al., 2001). Continuous performance tasks often involve a participant attending to continuous stimuli (such as presentation of images or tones) for a long period of time; the participant is expected to attend to all stimuli and correctly respond to only the target stimulus as quickly as possible (Roebuck et al., 2016). Deficits in sustained attention have been observed in those infected with the neuroinvasive West Nile virus (Fromm et al., 2015). Preliminary data has also shown that vigilance deficits occur in COVID-19 survivors (do Carmo Filho et al., 2022; Zhao et al., 2022).

To assess sustained attention in the present study, a vigilance task was used. Alertness is an important component of vigilance, and alertness is known to be modulated by norepinephrine and metabolic chemicals such as glucose, oxygen, and thyroid hormones (Oken et al., 2006). Stress, sleep, and apathy are other factors that can influence vigilance ability (Oken et al., 2006). Sustained attention is thought to be modulated by the right middle frontal gyrus, the right parietal lobe, the amygdala, and the HPA axis (Lewin et al., 1996; Oken et al., 2006).

Selective attention reflects the process of attending to a particular object or stimulus. Those with deficits in selective attention may be unable to tune out unimportant details and may have difficulty focusing on the task at hand. HIV-1

positive patients exhibit selective attention deficits (Lew et al., 2018). Selective attention deficits have also been observed in patients with West Nile virus (Lambert et al., 2016). Unpublished data also suggests a deficit in selective attention in COVID-19 survivors as assessed by the Eriksen Flanker Task (Kao, 2021). The Flanker Task was used for the present study. The Flanker Task is used to assess visual attention and the ability to filter out distracting information to focus on relevant information. Flanker Task performance is thought to be modulated by the left middle frontal gyrus, the inferior parietal and frontal cortices, anterior cingulate cortex, dorsolateral prefrontal cortex, and orbitofrontal cortex (Salo et al., 2017; Luks et al., 2010; Rusnáková et al., 2011; vel Grajewska et al., 2011).

Similar to attention, there are many facets of memory. Deficits in memory are associated with difficulty in important aspects of everyday functioning, such as decision making or reasoning, which can lead to a loss of independence. The aspects of memory that will be discussed will be working memory, spatial working memory, and memory capacity.

Working memory reflects the ability to create a temporary (or “working”) memory for short-term processing and information storage (Schouten et al., 2011). Working memory is also defined as the cognitive skill that allows an individual to retain and manipulate information over a brief period of time; thus, working memory is an essential process for the maintenance of concentration, reasoning, learning, and planning. A commonly used assessment for verbal working memory is the forward and reverse digit span memory task, which is

used as part of the WAIS assessment for working memory. Digit Span performance is thought to be mediated by the dorsolateral prefrontal cortex, inferior parietal lobe, anterior cingulate cortex, and basal ganglia; of note, the backward portion of the task is thought to rely more on visuospatial imagery than the forward portion of the task, and additionally the backward portion activates the dorsolateral prefrontal cortex more than the forward portion does (Aleman et al., 2008; Geva et al., 2021; Hoshi et al., 2000). It is worth noting that working memory and attention are often considered intermingled processes, with attention serving as a “gatekeeper” for the information that is permitted to occupy one’s working memory (Awh et al., 2006).

A subset of working memory is visuospatial working memory. Visuospatial working memory represents the ability to temporarily retain visuospatial information. A Delayed Match to Sample task is a commonly used assessment for maintenance ability of visual information (Daniel et al., 2016). This task is thought to be mediated by the dorsolateral prefrontal cortex, fusiform gyrus, parietal cortex, and anterior cingulate cortex (Daniel et al., 2016; Habeck et al., 2004; Cirillo et al., 1989). Working memory capacity reflects the amount of information that can be reliably held for manipulation in one’s working memory. Working memory capacity is important for completing any cognitive task because of the need to hold information while it is being processed. Working memory capacity can be a reflection of one’s processing ability, their ability to combine new and old information, or their ability to use attention to maintain or suppress certain information (Cowan, 2010; Engle, 2002). Working memory capacity,

which is thought to be mediated by the parietal lobe and dorsolateral prefrontal cortex, was assessed using a Change Detection task (Beck et a., 2001).

The effect of emotional valence on memory consolidation was also a focus of the present study. It is known that negative and positive stimuli are encoded in different ways and utilize different brain structures (Bowen et al., 2018). The left superior prefrontal cortex, right fusiform gyrus, and ventral striatum are more active when consolidating positive stimuli (Kuchinke et al., 2005; Lewis et al., 2003; Wittmann et al., 2008) while the amygdala, sensory-processing regions, and left inferior prefrontal cortex are more active when consolidating negative stimuli (Bowen et al., 2018; Lewis et al., 2003). Regardless of valence, consolidation of emotional information can be attributed in part to the left orbitofrontal gyrus, bilateral inferior frontal gyrus, and hippocampus (Kuchinke et al., 2005; Bowen et al., 2018). An emotional memory task was used to assess any unique interactions that valence may have on memory for COVID-19 survivors. It has previously been found in socially isolated COVID-19 survivors that positive bias in emotion recognition was reduced when compared to those who had not been as socially isolated, regardless of infection status (Bland et al., 2021).

In other neuroinvasive diseases, working memory dysfunction has been identified as a predictor of poor medication adherence, unemployment, and low independence (Chang et al., 2016; Woods et al., 2009). HIV-1 positive individuals perform worse in measures of working memory and spatial memory than HIV-1 negative controls; poorer working memory in these populations has

been associated with elevated levels of inflammatory cytokines (Walker et al., 2018; Wilson et al., 2017; Morales et al., 2012). Visual working memory has also been shown to be impaired in West Nile Virus; HSV-1 encephalitis can also lead to impairments in memory (Fromm et al., 2015; Bougakov et al., 2021). In both SARS-CoV-1 and MERS, survivors saw impairment of memory up to 39 months after recovery (Mazza et al., 2021). Deficits in memory have been observed in recovered COVID-19 patients, and those with neurological symptoms had even lower scores in working memory than those without neurological symptoms (Vannorsdall et al., 2022; Alemanno et al., 2021; Becker et al., 2021; Graham et al., 2021; Mendez et al., 2021; Hampshire et al., 2021; Jaywant et al., 2021; Almeria et al., 2020). However, other studies in COVID-19 positive populations indicated the lack of long-term working memory and emotional processing deficits (Guo et al., 2022; Hampshire et al., 2021; Mattioli et al., 2021; Zhao et al., 2022).

Cognitive flexibility is an aspect of executive functioning that reflects the ability to adapt ones thinking or behavior to achieve a certain outcome; in other words, if a certain pattern or response is not leading to success, proper cognitive flexibility will allow the adaptation to a response that does allow for success. The Wisconsin Card Sorting Task (or Berg's Card Sorting Task) are assessments of cognitive flexibility. They are also thought to assess set-shifting, which is an important aspect of executive functioning that gives the ability to disengage from familiar or relevant stimuli and actively engage with, or shift attention to, new, previously irrelevant stimuli (Pennington & Ozonoff, 1996; Walker et al., 2018).

Card Sorting Task performance is thought to be mediated by the ventrolateral and dorsolateral prefrontal cortex, anterior cingulate cortex, and inferior parietal lobe (Buchsbaum et al., 2005; Nagahama et al., 1996; Lie et al., 2006). Severity of COVID-19 infection has been associated with Wisconsin Card Sorting Task performance, wherein more severely infected individuals perform worse (Guo et al., 2022). Deficits in executive function have been observed in COVID-19 recovered individuals, with those displaying neurological symptoms having even greater deficits (Becker et al., 2021; Alemanno et al., 2021; Mazza et al., 2021; Helms et al., 2020; Almeria et al., 2020). However, there is also some evidence to support that executive functioning deficits may recover over time in COVID-19 recovered individuals (Guo et al., 2022; Mattioli et al., 2021; Zhao et al., 2022).

Decision making is an associated domain which involves the process of selecting an option or belief based upon previously gathered information, perception of possible outcomes, and/or the current situation. The Iowa Gambling Task is a commonly used task to assess decision making and risk-taking behavior. Brain regions thought to be involved in this task are the insula, basal ganglia, the ventral and dorsal prefrontal cortex, the frontal gyrus, and the lateral orbitofrontal cortex (Lin et al., 2008; Lawrence et al., 2009). In HIV-1, decision making as assessed by the Iowa Gambling Task is found to be impaired (Nakao et al., 2020). During the COVID-19 pandemic, it was found that selections on the Iowa Gambling Task improved as lockdown restrictions were eased, indicating the possible influence that social isolation may have on decision making (Ingram et al., 2021).

The social aspects of the COVID-19 pandemic could be just as impactful as viral infection. Specifically, social isolation necessitated by mandated quarantining was a shared experience despite COVID-19 viral status. Social isolation can be defined as a deprivation of social connectedness (Zavaleta et al., 2017). A positive social experience comes not only from the quality of one's social relations, but also through the frequency and quantity of these interactions (Zavaleta et al., 2017). One could assume that individuals who are more technologically literate and adjusted to online communication (such as young adults) may not be as affected by the restriction of in-person socialization activities. However, CDC data from June 2020 showed that young adults (i.e., those aged 18-24) were more likely to suffer from mental health problems than other age groups; similar results were found by the Harvard Graduate School of Education, wherein 61% of young adults reported feeling lonely as compared to 24% of adults aged 55-56 (Czeisler et al., 2020; Weissbourd et al., 2021). Young adults who are pursuing higher education have additional unique stressors. These can include the unexpected cancelling or format changes of coursework, unknown living situations, instability of funding, or even feelings of "unjustness" due to experiencing a different college experience than was expected (Zurlo et al., 2020).

Social isolation is associated with a host of negative health outcomes, such as poor cardiovascular health, worse mental health, impaired executive functioning, impaired ability to focus, and poor sleep quality (Somma et al., 2021; Pfefferbaum and North, 2020; Luo et al., 2020; Zovetti et al., 2022). Social

isolation can cause stress, which activates the HPA axis; this can cause cognitive deficits, increased psychological distress, and body-wide hormonal dysfunctions. An early study showed that 31% of their sample of COVID-19 survivors met criteria for “excessive stress,” which has further been corroborated by similar research (Ismail et al., 2021; Cai et al., 2020, Hao et al., 2020). In addition, quarantining and “lockdowns” may also have led to sedentary behavior, which is known to result in negative health outcomes (Stranahan et al., 2006; Cal et al., 2020; Galea et al., 2020). Specific to the COVID-19 pandemic, following long-term quarantine, rates of perceived stress rose, and cortisol was found to be dysregulated (Baliyan et al., 2021).

Much of the research on social isolation in humans is in the elderly; in this population, isolation is significantly associated with decreases in verbal fluency and both delayed and immediate recall (Shankar et al., 2013). Loneliness has also been found to negatively impact decision making and working memory in older adults with pre-existing cognitive issues (Stewart et al., 2020). However, social isolation has been found to be detrimental to neuronal health, memory, and emotional regulation during development as well (Ibi et al., 2008; Cinini et al., 2014; Ingram et al., 2021; Liu et al., 2020; Fone et al., 2008; Stranaham et al., 2006). Social isolation may also disproportionately negatively affect adolescents with ADHD (Navarro-Soria et al., 2021). Social interaction can be considered a protective factor against cognitive decline, or even as a restorative to help enhance cognition (Ingram et al., 2021; Zovetti et al., 2022; Evans et al., 2018).

In non-human primates, it has been found that social deprivation specifically during the transition between adolescence to adulthood lead to increased cortisol and decreased neurogenesis (Cinini et al., 2014). In mice, adolescent isolation led to decreased survival of new neurons and decreased object recognition when combined with pro-inflammatory cytokines (Hueston et al., 2017). Functional and structural changes in the pre-frontal, temporal cortex, parietal cortex, the limbic system, the cerebellum, and the striatum have been found to be associated with loneliness and social isolation (Zovetti et al., 2022). In the context of the COVID-19 pandemic and subsequence social isolation, it was found that selections on the Iowa Gambling Task improved as lockdown restrictions were eased (Ingram et al., 2021). It was also found that Flanker Task reaction time improved as lockdown restrictions were eased (Ingram et al., 2021). Thus, while the virus itself could be harmful to the brain and its functioning in isolation, the social aspects of living through a pandemic may be just as damaging.

The 2016 National Institute of Health's "Sex as a Biological Variable" policy serves as an important call to action to include biological sex as a factor in research. There is evidence from other neuroinvasive viruses and diseases to support that there may be sex differences within COVID-19 infection as well. For example, HIV-1 positive women show impairments in memory, learning, and information processing speed (Rubin et al., 2019). Impairments in attention and calculation speed also were higher in women with HIV-1 than in men with HIV-1 (Qiao et al., 2019). While not a virus, in Alzheimer's disease, women have shown

greater cognitive deterioration than men in the domains of episodic, semantic, verbal, and visuospatial memory (Laws et al., 2018).

Already, some sex differences have been observed for COVID-19. Males with COVID-19 have higher levels of plasma immune cytokines than females, while females have a more robust T-cell activation (Takahashi et al., 2020). Specifically, pro-inflammatory cytokines such as interleukins 10, 15, and 8 were higher in males; markers of brain injury were also found to be higher in males with COVID-19 than in females with COVID-19 (Savarraj et al., 2021). In general, it's been found that males have less favorable outcomes for COVID-19 infection. However, females show a higher prevalence of changes in smell and taste, which may indicate increased neuroinvasiveness (Santos et al., 2021). Females also show significantly more PCC symptoms than males (Fernández-de-Las-Peñas et al., 2022).

Men more frequently presented with severe COVID-19 infection than women, and they are at a higher risk of death (Bunders et al., 2020). Females typically have a stronger immune response against viruses than males, perhaps due to a stronger expression of antiviral mechanisms coded by the X chromosome (Bunders et al., 2020). Specific to COVID-19, it has been hypothesized that estrogen may downregulate the expression of ACE2, which may account for some of the sex differences observed (Liu et al., 2010). Previously hospitalized COVID-19 female patients were more likely to report subjective declines in cognitive functioning than males (Ferrucci et al., 2021). While not related to COVID-19 infection directly, it has also been found that

female health care workers have been disproportionately negatively affected in the domains of depression and anxiety during the COVID-19 pandemic (Pappa et al., 2020).

It is presently unknown what the long-term effects of COVID-19 infection may be on overall health and cognition. It is also unknown the effect that COVID-19 infection, or quarantine and mass shut-down events caused by COVID-19, may have specifically to those still in development. The present study seeks to determine the potential cognitive deficits that may have been caused by COVID-19 infection, social isolation because of widespread quarantining, or a combination of both. Since the majority of individuals that were infected with COVID-19 were not seriously affected by the infection (i.e., to the point of hospitalization), it is also of increased clinical relevance to sample from a population that experienced more mild illness with COVID-19. In the present study, several aspects of attention, memory, and executive functioning found to be impaired in other viruses known to be neuroinvasive or neurovirulent were assessed in young adults who were previously infected with COVID-19 compared to those who were previously uninfected. The impact of the social aspects of COVID-19 (such as social isolation) were studied to determine their influence on cognitive functioning. The present study is designed to build upon prior research in neuroinvasive viruses by assessing the neurocognitive profiles of those who have had COVID-19 and lived through the beginning of the COVID-19 pandemic.

1.7 SPECIFIC AIMS

The present study has three aims. Given that cognitive deficits are a common symptom of PCC, the first aim is to determine the potential cognitive consequences of COVID-19 infection in a young-adult sample that has fully recovered from viral infection. Since social isolation can lead to changes in cognition, the second aim is to determine the potential cognitive consequences of social isolation induced by widespread quarantine measures. Given the evidence for sex differences in the prevalence of PCC, the third aim is to determine the potential interactions between COVID-19 and biological sex, and their potential influence on cognition. These aims will be addressed through the analysis of an extensive pre-experiment survey and cognitive battery

CHAPTER 2

MATERIALS AND METHODS

2.1 ETHICS STATEMENT

The present research was conducted in accordance with the University of South Carolina's Institutional Review Board. The present study was exempt from full review (ID: Pro00114536).

2.2 PARTICIPANTS

Based on an *a priori* power analysis, it was determined that approximately 84 participants were needed for 95% power to detect a large effect, 210 participants to detect a medium effect, and 1302 participants to detect a small effect for the difference between COVID-19 infected and COVID-19 uninfected groups, and the interaction between COVID-19 infection status and sex. In an attempt to achieve the number of participants required for a medium effect size, the study was made available on SONA (UofSC's Department of Psychology's online participant pool) for students to participate between September 2021 and April 2022, with an average of 10-12 available participation time slots per week (for a total of ~330 available slots over 2 semesters). Informal communication in the classroom and online was also used to inform students of study availability. Participants received course credit through the SONA system for participation in the study. Unfortunately, the required number of participants could not be recruited with time to be included in the present research. Thus, although

analyses were completed as planned with the participants obtained, results should be interpreted with caution as the estimated power to detect a medium effect was only 81.7% for the number of participants we obtained data from, and less than 60% for any smaller effects.

A total of 81 participants completed both the online assessment and in-person cognitive assessment. If participants did not participate in both the online assessment and the in-person cognitive assessment, their data were not used for any further analyses. All participants were between the ages of 18 and 30 years, with a mean age of 20.71 years. Participants were students enrolled at UofSC who were fluent in English and had normal or corrected-to-normal vision and hearing, with no individuals reporting color-blindness. The sample was 70.4% female, 69.1% white/Caucasian (participants were allowed to select as many races as they deemed fit), and 87.7% non-Hispanic or Latino. Participants were tested between the hours of 10AM and 5PM. Additional demographic information, COVID-19 experience, and psychiatric assessment information can be found in Table 2.1. Information on severity of infection is based on the answers for “Which of the following best describes your experience with COVID-19,” a question from the Google Form (see Appendix A).

Consent to participate was obtained by the researcher, and all questionnaires and screening questions were framed as requiring voluntary responses only. Data collection and analyses were conducted at the Institute for Mind and Brain building affiliated with the University of South Carolina’s Psychology Department.

2.3 STIMULI AND APPARATUS

The study consisted of two parts: an online survey and an in-person cognitive assessment. After registering for the study, participants received a link to a Google Form. The survey consisted of 190 questions and took approximately 20 minutes to complete. The first portion of the survey assessed previous COVID-19 infection status, vaccination status, and the symptoms experienced by those who had previously been infected with COVID-19. Participants were prompted to indicate whether they were officially diagnosed with COVID-19 via nasal swab, blood test, or saliva test. Eight participants indicated that they thought they had COVID-19 at some point but had not been officially diagnosed. Only participants who indicated that they had also experienced a loss of taste and smell were included in the “previously COVID-19 infected” group, as these symptoms are salient and unique to COVID-19 infection (Almeria et al., 2020; Bougakov et al., 2021; Guadarrama-Ortiz et al., 2020; Graham et al., 2021). Of the eight participants, four had experienced loss of smell and taste and were placed in the “previously infected” group, while the remaining four were placed in the “COVID-19 uninfected” group. All statistical analyses were conducted both with these four individuals placed in the “previously infected” and “uninfected” groups; the inclusion of these individuals in either group did not alter the outcome any of the statistical tests.

All participants, regardless of previous COVID-19 infection status, completed the UCLA Loneliness scale (version 3, Russel 1996). This 20-item scale had participants indicating how often a particular statement was descriptive

of themselves, with the options being “never,” “rarely,” “sometimes,” or “often,” with values for each item ranging from 1-4. Scores range from 20-80 and interpretation is continuous, with no categorical cutoffs. The online survey also had participants complete several non-diagnostic screening questionnaires to assess the presence of symptoms common to Autism Spectrum Disorder, dyslexia, Attention-Deficit Disorder (ADD), depression, and anxiety, as many of these are commonly comorbid with deficits in attention, memory, and executive functioning. To measure the expression of Autism-Spectrum traits, the Autism-Spectrum Quotient Test was used (Baron-Cohen et al., 2001). Options for each item were “definitely agree,” “slightly agree,” “slightly disagree,” and definitely disagree.” In this 50-item, self-administered screening questionnaire for use in adults within a normal IQ range, the possible scores range from 0-50, with a score above 26 indicating a higher likelihood of having autism. The “Revised Dyslexia Checklist” was used to assess symptoms of dyslexia (Vinegard, 1994). This non-diagnostic screening questionnaire has 20 items that the participant endorses as true of themselves with a “yes” or a “no.” Scores range from 0-20, with a score above 8 indicating potential dyslexia or reading difficulties. ADHD was assessed using the 24-item Jasper-Goldberg Adult ADHD Questionnaire (Jasper et al., 1993). This non-diagnostic screening questionnaire has individuals rating 24 items from 0 (“Not at all”) to 5 (“Very much); scores range from 0-120, with scores over 70 associated with a high likelihood of ADHD. The Beck Depression Inventory-II (BDI-II) was used to assess symptoms of depression based on the raw score scale for non-clinical settings (Jackson-Koku, 2016). This

21-item inventory has 4 different statements for each item, and the participant endorses whichever of the 4 statements best describes themselves. Each statement has a score from 0-3; scores range from 0-63, with scores over 21 indicating a high likelihood of clinical depression. The Beck Anxiety Inventory (BAI) questionnaire was used to assess participants' level of anxiety (Beck et al., 1988). This inventory has 21 common symptoms of anxiety, and the participant rates how often they have been bothered by that particular symptom in the past month, with scores for each item ranging from 0-3; total scores range from 0-63, with scores between 22-35 indicating moderate levels of anxiety and scores over 35 indicating "concerning levels of anxiety." The online portion of the survey, along with all questions and all options for each question, can be found in Appendix A.

Stimuli for the in-person portion of the cognitive assessments were presented on a 23-inch computer monitor. The in-person portion of the experiment took approximately one hour to complete. Not all participants were able to complete all cognitive assessments due to occasional time constraints, but all participants completed at least 7 of the 8 tasks. As previously described, eight different cognitive assessment tasks were used: Vigilance, Flanker Compatibility, Digit Span, Berg's Card Sorting Task, Emotional Memory, Match to Sample, Iowa Gambling Task, and a Change Detection Task. Seven of the assessments were adapted from existing experiments provided by Neurobehavioral Systems for use with their Presentation software, and one assessment (the Change Detection task) was obtained from an outside source

(see Fukuda and Vogel et al., 2019). Representative stimuli for all cognitive tasks can be found in Appendix B

Vigilance: Participants were instructed to click the left mouse button when a white square appeared within the top half of a larger dark navy square in the middle of the screen and to not take any action if the white square appeared within the bottom half of the navy square. The vigilance task had 2 blocks, with one block having more frequently appearing targets than the other block. For the infrequent block, correct targets appeared on 43 out of the total 193 trials. For the frequent block, correct targets appeared on 150 of the total 193 trials. There were 20 practice trials before the first block. The target stimuli appeared for 250ms. Immediately following the display of the target stimuli, the participants had 1750ms to respond using the left mouse button if the target stimuli was in the upper half of the target area. If the stimuli appeared in the bottom half, the participants were instructed to not respond. Reaction time, accuracy, number of missed targets, and the number of false alarms were recorded.

Flanker Compatibility Task: Participants were asked to indicate whether a square or diamond appeared on the screen within one of four circle outlines (positioned in the four cardinal directions in relation to the center of the screen). The shapes could appear in the presence of either zero or three non-target shapes (crowding shapes) which would also appear within one of the circle outlines. During some trials, a large distractor shape (always a diamond or square) would appear to the either the right or left of the 4 circles at the same time as the target stimuli. Distractor shapes were present on 64 trials, and 64

trials had no distractor shape. For each trial, the 4 rings would first be displayed empty for 500ms. After, the rings, target shape, crowding shapes, and distractor shape (if during a distractor trial) would appear and remain onscreen for 2000ms. Following this, the participant had 2050ms to respond with either the left mouse button for a square or the right mouse button for a diamond to indicate which target shape appeared within the circle outline. Reaction time and error rates were recorded.

Digit Span: Participants began with the forward-span task. The number span began at 3 digits. Numbers were presented via a speaker delivered in a neutral, male voice. Each digit took approximately 500ms to be delivered, and a 500ms pause occurred between each digit delivery. Immediately after the delivery, participants were asked to type the number string from memory; this free-response portion was not timed. Once the participant responded with two correct answers at a given length, the length of the digit span would increase by one digit until the participant failed both trials for a given digit span length. Immediately following the forward-span task was the backward-span task, which proceeded in the same way with the exception that the starting string for the Backward span began with 2 digits instead of 3. Digit span capacity was estimated by finding the last list length at which a number string was recalled correctly.

Berg's Card Sorting Task: The participant was presented with 4 playing cards that vary in suit (diamond, triangle, circle, or plus), color (yellow, blue, green, or red), and number of items on the card (1, 2, 3, or 4). They were then

given a 5th card to sort into one of the 4 existing card piles. The participant was not told the criteria to sort by (whether it be suit, color, or number), and determined through trial and error how to correctly sort the cards. The first sort was always considered “correct” as long as the card pulled matched at least one attribute of the sorting pile chosen. The sorting criteria changed after 5 correct sorts were made in a row; there were 64 total trials. The number of incorrect sorts following a “rule change” was recorded.

Emotional Memory: This task involves the presentation of words with a positive (examples: freedom, trust, victory, safe), negative (examples: abuse, violent, misery, murder), or neutral (examples: wood, circle, corn, board) valence. Fifteen words of each valence were presented at 1000ms during the encoding phase as black text upon a white background. After all the words were presented, participants were then asked to indicate via clicking their mouse whether a presented word had previously appeared during the experiment. “Target” words were words that appeared in the initial list of 45 words and were shown during this recognition phase; “distractor” words were words that were shown during this recognition phase that did not appear in the initial list of 45 words. Distractor words were also of positive, negative, or neutral valence. During this recognition phase, words were presented for 5000ms, and participants had this time and an additional 5000ms to indicate whether they had previously seen that word or not. The dependent variable for this task is memory accuracy.

Match to Sample: A 4x4 grid was presented with squares either shaded in or unshaded. The number of shaded squares was either 7, 8, or 9. A fixation point was present for 500ms before the grid was presented. The grid was presented for 1000ms. After a delay of either 1000ms or 5000ms, two possible grids were presented: one with the same pattern as before and one with a different pattern. There was a delay where no objects were on the screen. Then, participants were asked to select from two different grids which grid was the one they previously saw. Accuracy and reaction time were measured.

Iowa Gambling Task: Four decks of cards were presented to the participant. The participant was told in the instructions to draw cards from whichever deck they want and to attempt to make a "profit." The trial consisted of 100 trials. Each card drawn tells the participant that they either gained or lost "money" for that draw. The deck draw for each trial was recorded. If participants attempted to draw too quickly from a single (i.e., they were not paying attention to how much money they were gaining or losing), the task ended. The probabilities for each deck were as follows. Two decks (in this case, Decks 1 and 3) always yield $100 and two decks (Decks 2 and 4) always yield $50. Ten draws from Decks 1 or 3 will result in a total loss of $1250, and ten draws from decks 2 and 4 will result in a total loss of $250. This leads to a net loss of $250 for Decks 1 and 3 and a net gain of $250 for Decks 2 and 4. Therefore, Decks 1 and 3 are considered disadvantageous decks and Decks 2 and 4 are considered advantageous decks. Deck 3's loss occurs all at once, with a single $1250 penalty, while Deck 1's losses occur with penalties ranging from $150-350.

Similarly, Deck 2's losses occur with penalties ranging from $25-$75, while Deck 4's losses occur all at once in the amount of $250. Decks 1 and 3 are both high-risk/high-reward decks, but for different reasons. Deck 3 has a severe but infrequent risk while Deck 1 has a more consistent risk.

Change Detection Task: 2, 4, 6, or 8 squares of 9 varying, vivid colors appeared on a light grey background screen for 150ms. After a delay of 900ms where no squares were present on the screen, a single square appeared on screen in one of the original locations where a square had appeared previously. The participant was tasked with determining whether the square was the same color and in the same position as the previous array of shapes. There were 120 total arrays presented. Accuracy for each of the 4 array sizes was recorded.

2.4 PROCEDURE

Prior to the participant's appointment for the cognitive assessment, the participant completed the Google Form portion of the study online. Upon arrival, the participant was seated in front of the computer and provided with a description of the nature of the experiment. The participant was instructed to let the researcher know if they had any questions at any point during the task. The participant was also made aware that they were allowed to take breaks between assessments if they desired. Task order was different for each participant and was determined via an 8-sided die at the time of participation. Participants completed as many of the 8 tasks as they were willing to; some participants who arrived late to their appointment did not stay over their allotted time to complete an 8th task while others chose to fully complete the experiment.

2.5 HYPOTHESES

It was hypothesized that former COVID-19 infection would have an impact on cognitive functioning in the following domains: sustained attention, selective attention, attention shifting, verbal short-term memory, emotionally valence memory, spatial working memory, and decision making.

It was also hypothesized that increased social isolation (as assessed by the UCLA Loneliness Scale v3) would have an impact on cognitive functioning in the same domains mentioned previously. As previously stated, correlations were calculated to determine whether social isolation scores may be related to any of the cognitive or self-report measures.

It was also hypothesized that changes in cognitive functioning consistent with PCC would interact with biological sex. Sex differences and subsequent cognitive deficits are prevalent in HIV-1 (Rubin et al., 2019; Scully 2018; Qiao et al., 2019) and Alzheimer's disease (Laws et al., 2018). However, the sex differences observed are not consistent across disease or domain. In COVID-19, more severe symptomology and increased mortality for males has been observed, in addition to increased cytokines compared to females (Bunders & Altfeld, 2020; Takahashi et al., 2020). If severity during the acute phase is the primary determinant of PCC symptoms, it would be expected that biological males would show more signs of PCC related deficits than females; however, given that females may have greater neuroinvasiveness and have a higher prevalence of PCC in general, it may be that prior COVID-19 infection leads to poorer cognitive outcomes for biological females than biological males

2.6 DATA ANALYSIS

Cognitive data were collected from Neurobehavioral Systems' Presentation software. Survey data were collected using Google Forms. All data analyses were performed using IBM's SPSS v20.

First, several correlations were conducted between the measure from a cognitive assessment and the following: social isolation scores, depression scores, anxiety scores, ADHD scores, and autism scores. If a correlation with a significance of $p < 0.05$ existed between these variables, that factor was added as a cofactor into the analysis. This was to ensure that all potential covariates and influencing variables could be accounted for during analysis. It should be noted that analyses including covariates were also conducted without the covariates to determine whether there were any discrepancies in the results; there were no discrepancies found, so covariates remained included in the relevant analyses to ensure a more accurate portrayal of the results. A full correlation matrix can be found in Appendix C.

Sex differences were explored for each dependent variable. It should be assumed that all assumptions were met for all relevant statistical tests unless otherwise stated. All means have been adjusted to account for any mentioned covariates, when relevant.

Table 2.1: Demographic information for the 81 participants who completed both the online and in-person assessments.

	Total Sample (n=81)	COVID-19 Uninfected (n=35)	Previously COVID-19 Infected (n=46)
Age (mean, standard deviation)	20.7 (1.6)	21.12 (2.1)	20.4 (1.1)
Biological sex (frequency, percent)			
Male	24 (29.6)	12	12
Female	57 (70.4)	23	34
Race (freq., %)			
American Indian/Alaskan Native	3 (3.7)	3	0
Asian	10 (12.3)	4	6
Black/African American	5 (6.2)	4	1
White/Caucasian	67 (82.7)	28	39
Unknown/Do not wish to say	4 (4.9)	1	3
Ethnicity (freq., %)			
Hispanic or Latino	9 (11.1)	4	5
Non-Hispanic or Latino	71 (87.7)	31	40
Do not wish to say	1 (1.2)	0	1
Vaccine Status (freq., %)			
Vaccinated fully	66 (81.5)	30	36
Would prefer not to say	3 (3.7)	0	3
Not vaccinated	12 (14.8)	5	7
Vaccine (freq., %)			
Pfizer	41 (50.6)	15	26
Moderna	19 (23.5)	14	5
J&J	5 (6.2)	1	4
Unvaccinated/Unknown/prefer not to say	16 (19.8)	5	11
Severity (Previously infected only)			
“Asymptomatic”			7
“Mildly infected”			37
“Evidence of lower respiratory disease”			2
Measures (mean, SD)			
UCLA Loneliness Scale V3	45.1 (10.14)	45.6 (9.84)	44.6 (10.46)
Beck’s Depression Inventory	13.0 (8.80)	11.8 (7.78)	14.0 (9.48)
Beck’s Anxiety Inventory	19.8 (14.1)	19.9 (15.39)	19.8 (13.16)
Jasper/Goldberg’s Adult ADHD Self-Test	49.3 (27.20)	47.7 (25.42)	50.6 (28.72)
Baron-Cohen’s Autism Quotient	19.8 (6.09)	19.6 (5.36)	19.9 (6.65)
Vinegrad’s Revised Dyslexia Checklist	5.2 (3.9)	5.74 (3.97)	4.8 (3.90)

CHAPTER 3

RESULTS

3.1 BERG'S CARD SORTING TASK

For the Berg's Card Sorting task, "average number of sorts until a correct sort" was used as the dependent variable. This average significantly correlated with the measure for dyslexia (p=0.004, r=0.319) and autism (p=0.043, r=0.227), so they were added as covariates into the analysis. One participant was excluded from the analyses because they did not provide enough information to accurately calculate their dyslexia and autism scores. There was no significant difference between those who had previously had COVID-19 (M=2.3831, SE=0.174) and those who did not (M=2.3642, SE=0.241), F(1,76)=0.126, p = 0.724 (Figure 3.1). However, there was a significant interaction between previous COVID-19 infection status and biological sex (F(1,74)=4.737, p=0.033, partial eta squared=0.060), despite biological sex not being significant on its own (F(1,74)=0.836, p = 0.363) (Figure 3.1).

3.2 DIGIT SPAN TASK

For the Digit Span task, "highest span of digits correctly remembered" was used as the dependent variable for both the forward-span and backward-span task. The forward-span number did not significantly correlate with any other pre-existing factors, but the backward-span number significantly correlated with isolation and dyslexia scores, so these two were added as covariates into the

analysis for the backward-span analysis. Two participants were excluded from the analyses because they did not provide enough information to accurately calculate their social isolation and dyslexia scores. A Welch's t-test was used to determine whether there were any differences between previously COVID-19 infected (N=46, M=7.087, SE=0.222) and COVID-19 uninfected groups (N=35, M=6.6857, SE=0.196) on forward digit-span ability; there was no significant difference Welch's t(78.981)=1.843, p=0.179) (Figure 3.2A). In the corrected model, there was no significant effect of COVID-19 infection; there was no difference between previously COVID-19 infected (N=45, M=5.84, SE=0.198) and COVID-19 uninfected (N=34, M=5.58, SE=0.321) groups on backward digit-span ability (F(1,75)=0.150, p=0.7) (Figure 3B). There were no significant interactions between COVID-19 status and sex for either forward (F(1,77)=0.015, p=0.904) (Figure 3.2A) or backward (F(1,74)=0.017, p=0.896) digit span (Figure 3.2B). The significant correlation between backward digit span ability and social isolation prompted analysis via linear regression. The regression equation including social isolation and dyslexia scores was significant, F(2,76)=4.535, R^2=0.107, p=0.014, but the overall contribution of social isolation scores to the model was minimal (F-change significance= 0.240), and added only 0.017 to R^2. (Figure 3.2C)

3.3 CHANGE DETECTION TASK

For the Change Detection task, short-term memory capacity was estimated using the accuracy rates from the 2, 4, 6, and 8 set sizes as previously described (Cowan, 2001). This estimated short-term memory capacity

significantly correlated with the measure for dyslexia (p=0.044; r = -0.227), so dyslexia was added as a covariate into the analyses. One participant was excluded from the analyses because they did not provide enough information to calculate their dyslexia scores; one participant was excluded because they did not complete the task. There was no significant difference between those who had previously had COVID-19 (N=44, M=3.841, SE=0.070) and those who did not (N=35, M=3.735, SE=0.078), F(1, 76)=1.014, p=0.317 (Figure 3.3). There was also no significant interaction between biological sex and COVID-19 infection status (F(1,74)=0.679, p=0.414) (Figure 3.3).

3.4 EMOTIONAL MEMORY TASK

For the Emotional Memory task, accuracy for remembered words was obtained for positive, negative, neutral, and distractor words. Average accuracy for positive, negative, neutral, or distractor words was not significantly different between COVID-19 uninfected and previously COVID-19 infected groups. One participant was excluded from the analyses because they did not complete the task. For positively valanced words, there was no significant difference of accuracy between COVID-19 uninfected (N=35, M=0.743, SE=0.026) and previously COVID-19 infected (N=45, M=0.726, SE=0.029) groups (t(78)=-0.418, p=0.677) (Figure 3.4A). For negatively valanced words, there was no significant difference of accuracy between COVID-19 uninfected (N=35, M=0.76, SE=0.029) and previously COVID-19 infected (N=45, M=0.776, SE=0.024) groups (t(78)=0.432, p=0.667) (Figure 3.4B). For neutral words, there was no significant difference of accuracy between COVID-19 uninfected (N=35, M=0.73, SE=0.028)

and previously COVID-19 infected (N=45, M=0.708, SE=0.027) groups (t(78)=-0.54, *p*=0.591) (Figure 3.4C). For distractor words, there was no significant difference of accuracy between COVID-19 uninfected (N=35, M=0.789, SE=0.03) and previously COVID-19 infected (N=45, M=0.782, SE=0.022) groups (t(78)=-0.192, *p*=0.848) (Figure 3.4D). A significant interaction between COVID-19 infection status and biological sex was found only for distractor word accuracy (*F*(1,76)=4.992, *p*=0.028, partial eta squared=0.062) (Figure 3.4D). There was no significant difference between COVID-19 uninfected (N=35, M=0.751, SE=0.025) and previously COVID-19 infected (N=45, M=0.7511, SE=0.024) groups on accuracy for emotional words (t(78)=-0.008, *p*=0.994) (Figure 3.4E). There was no significant difference between COVID-19 uninfected (N=35, M=0.759, SE=0.023) and previously COVID-19 infected (N=45, M=0.75, SE=0.019) groups on accuracy for non-emotional words (t(78)=-0.484, *p*=0.63) (Figure 3.4F). There was no significant interaction between COVID-19 infection status and biological sex on accuracy for emotional words (*F*(1,76)=0.199, *p*=0.657; Figure 3.4E) or non-emotional words (*F*(1,76)=1.122, *p*=0.293; Figure 3.4F). It should be noted that the total sample reflected the expected difference in accuracy for emotional (M=0.74, SE=0.01621) words versus non-emotional (M=0.7174, SE= 0.1953) words (Paired sample t test: t(79)=2.049, *p*=0.044); in addition, negative (M=0.7692, SE=0.0186) words were remembered significantly more than positive (M=0.7333, SE=0.0198) words (Paired sample t test: t(79)=2.061, *p*=0.043).

3.5 VIGILANCE TASK

For the Vigilance task, overall accuracy, number of false alarms, number of misses, and an accuracy comparison between the first and second block were the dependent variables analyzed. Five participants were excluded from the analyses because they did not complete the task. For overall accuracy, there was no significant difference between previously COVID-19 infected (N=45, M=0.991, SE=0.003) and COVID-19 uninfected (N=32, M=0.981, SE=0.007) groups (Welch's t=1.746, p=0.194) (Figure 3.5A). A 2-way ANOVA for overall accuracy between biological sex and COVID-19 infection status could not be reliably conducted due to the violation of homogeneity of variance (Levene's F=8.105, p<0.001), but regardless there was no significant interaction (F (1, 72)=3.578, p=0.063) (Figure 3.5A). For total number of false alarms, there was no significant difference between previously COVID-19 infected (N=45, M=4.4, SE=0.665) and COVID-19 uninfected (N=32, M=3.72, SE=0.514) groups (t(75)=0.757, p=0.452) (Figure 3.5B). There was no significant interaction between COVID-19 infection status and biological sex on total number of false alarms (F(1,73)=0.001, p=0.979) (Figure 3.5B). For total number of misses, there was no significant difference between previously COVID-19 infected (N=45, M=1.49, SE=0.478 and COVID-19 uninfected (N=32, M=3.41, SE=1.126) groups (Welch's t=2.456, p=0.125) (Figure 3.5C). A 2-way ANOVA between biological sex and COVID-19 infection status for total number of misses could not be reliably conducted due to the violation of homogeneity of variance (Levene's F=7.846, p<0.001), but regardless there was no significant interaction (F(1,

72)=3.461, *p*=0.067) (Figure 3.5C). The accuracy comparison value reflects the overall accuracy on the first half of the task minus the accuracy on the second half; in other words, negative values indicate an increase in performance in the second half of the task. For the accuracy comparison value, there was no significant difference between previously COVID-19 infected (N=45, M=-0.006, SE=0.004) and COVID-19 uninfected (N=32, M=-0.005, SE=0.007) groups (t(75)=-0.09, *p*=0.928) (Figure 3.5D). There was no significant interaction between COVID-19 infection status and biological sex on this accuracy comparison value (*F*(1,73)=0.606, *p*=0.439) (Figure 3.5D).

3.6 IOWA GAMBLING TASK

For the Iowa Gambling task, four dependent variables were examined. Twenty-three participants were excluded from the analyses because they either did not complete the task, or the paradigm detected that they were too quickly choosing from one deck repeatedly (thus not taking the time to consider their choices and see the consequences before choosing again). First, the proportion of high-risk-high-reward choices within the last half (draws from Deck 3 in the last 50 draws) of the task was calculated. For the high-risk-high-reward variable, there was no significant difference between previously COVID-19 infected (N=33, M=0.345, SE=0.03) and COVID-19 uninfected (N=25, M=0.375, SE=0.03) groups (t(56)=-0.699, *p*=0.488) (Figure 3.6A). There was no significant interaction between biological sex and COVID-19 infection status for the high-risk-high-reward variable (*F*(1,54)=0.001, *p*=0.970) (Figure 3.6A).

Second, the proportion of frequent-risk-high-reward choices within the last half (draws from Deck 1 in the last 50 draws) of the task was calculated. For the frequent-risk-high-reward variable, there was no significant difference between previously COVID-19 infected (N=33, M=0.1515, SE=0.015) and COVID-19 uninfected (N=25, M=0.1688, SE=0.016) groups (t(56)=-0.771, p=0.444) (Figure 3.6B). There was no significant interaction between biological sex and COVID-19 infection status for the high-risk-high-reward variable (F(1,54)=0.091, p=0.764) (Figure 3.6B).

Third, the proportion of disadvantage draws within the last half of the task was calculated. For the “proportion of disadvantageous draws in the last half” variable, there was significant correlation with isolation scores (r = -0.273, p=0.038), so that variable was added as a covariate; there was no significant difference between previously COVID-19 infected (N=33, M=0.498, SE=0.026) and COVID-19 uninfected (N=25, M=0.542, SD=0.030) groups (F(1,55)=1.264, p=0.266 (Figure 3.6C). The significant correlation with social isolation scores prompted a separate analysis. Using linear regression, social isolation scores were a significant (p=0.038) predictor of “proportion of disadvantageous draws in the last half of the task” (r=0.273), such that: % disadvantageous draws in the last half= 0.701 + (-0.004*social isolation score). (Figure 3.6D). There was no significant interaction between biological sex and COVID-19 infection status on “proportion of disadvantageous draws in the last half” (F(1,53)=0.007, p=0.936) (Figure 3.6C).

The fourth dependent variable was a proportion of the disadvantaged draws from the first half of the task to the last half of the task; values over 1 indicate that more disadvantageous choices were made earlier in the task than later in the task. For the “disadvantageous draws early vs late” variable, there was no significant difference between previously COVID-19 infected (N=33, M=1.375, SE=.255) and COVID-19 uninfected (N=25, M=1.11, SD=0.109) groups (t(56)=0.848, *p*=0.400) (Figure 3.6E). There was also no significant interaction between biological sex and COVID-19 infection status on “disadvantageous draws early vs late” (*F*(1,54)=0.938, *p*=0.337) (Figure 3.6E).

3.7 MATCH TO SAMPLE

For the Match to Sample task, 5-second-delay accuracy, 5-second-delay reaction time, 1-second-delay accuracy, and 1-second-delay reaction time were evaluated as dependent variables. Both 5-second and 1-second accuracy significantly correlated with the measure for dyslexia ($p<0.002$; *r*’s = -0.365 and -0.520, respectively); dyslexia was added as a covariate into the analyses. One participant was excluded from the analyses because they did not provide enough data to accurately calculate their dyslexia score; one participate was excluded from the analyses because they did not complete this task. For the 5-second delay accuracy, there was no significant difference between those who had previously had COVID-19 (N=45, M=0.872, SE=0.017) and those who did not (N=34, M=0.864, SE=0.02), *F*(1, 76)=0.094, *p*=0.759 (Figure 3.7A). There was also no significant interaction between biological sex and COVID-19 infection status on 5-second delay accuracy (*F*(1,74)=0.002, *p*=0.961) (Figure 3.7A). For

the 5-second delay reaction time, there was no significant difference between those who had previously had COVID-19 (N=46, M=1499.760, SE=56.049) and those who did not (N=34, M=1417.3259, SE=49.224), Welch's t=1.221, p=0.273 (Figure 3.7B). There was also no significant interaction between biological sex and COVID-19 infection status on 5-second delay reaction time (F(1,76)=0.441, p=0.508) (Figure 3.7B). For the 1-second delay accuracy, there was no significant difference between those who had previously had COVID-19 (N=45, M=0.907, SE=0.013) and those who did not (N=34, M=0.920, SE=0.015), F(1, 76)=0.434, p=0.512 (Figure 3.7C). There was also no significant interaction between biological sex and COVID-19 infection status on 1-second delay accuracy (F(1,74)=0.032, p=0.859) (Figure 3.7C). For the 1-second delay reaction time, there was no significant difference between those who had previously had COVID-19 (N=46, M=1305.646, SE=51.774) and those who did not (N=34, M=1221.780, SE=40.795), t(78)=-1.203, p=0.233 (Figure 3.7D). There was also no significant interaction between biological sex and COVID-19 infection status on 1-second delay reaction time (F(1,76)=0.623, p=0.433) (Figure 3.7D).

3.8 FLANKER TASK

For the Flanker task, a comparison value was calculated to determine to change in reaction time and accuracy between a compatible and incompatible distractor shape trials. This was calculated by subtracting the incompatible from the compatible trials; positive values represent that the participant was more accurate (or quicker, for the reaction time assessment) on the compatible trials

than on the incompatible trials. One participant was excluded from the analyses because they did not complete the task; two participants were excluded because they did not provide enough information to accurately calculate their dyslexia and anxiety scores. The comparison accuracy value correlated significantly with both dyslexia (r = -0.291, p=0.039) and anxiety (r = -0.32, p=0.004), so these were added as covariates into relevant analyses. There was no significant difference between those who had previously had COVID-19 (N=44, M=0.018, SE=0.012) and those who did not (N=34, M=0.018, SE=0.013), F(1, 74)=0.001, p=0.979 (Figure 3.8A); there was also no significant interaction between COVID-19 infection status and biological sex (F(1,72)=0.153, p=0.697) (Figure 3.8A). For the comparison reaction time value, there was no significant difference between those who had previously had COVID-19 (N=46, M=-40.438, SE=9.477) and those who did not (N=34, M=-55.561, SE=11.391), t(78)=1.093, p=0.278 (Figure 3.8B); there was also no significant interaction between COVID-19 infection status and biological sex (F(1,76)=0.660, p=0.419) (Figure 3.8B).

3.9 CONSTRUCT VALIDITY OF COGNITIVE MEASURES

To evaluate the validity of our measures for the cognitive constructs of interest (attention, working memory, cognitive flexibility, and decision making) we performed an exploratory factor analysis using variables from our cognitive tasks. The analysis was conducted using the JASP software package (JASP 2022, Macintosh version 0.16.3). Bartlett's test of sphericity (Bartlett, 1950) was used to ensure that the correlation matrix was not random and the KMO statistic (Kaiser, 1974) was required to be above a minimum of .60. Common factor analysis was

performed using a minimum residual estimation procedure with oblique rotation (promax). Parallel analysis and visual scree analysis were used to determine the number of factors to be retained. It should be noted that this study was not designed with the purpose of performing factor analysis. Although the correlation matrix was determined to meet the minimum standards for factor analysis [Bartlett's test of sphericity - $\chi 2(171)= 1037$, $p < .001$; KMO statistic= 0.64, which is considered "mediocre"] it was not ideally suited to this analysis. Coupled with the low number of participants, the results of this analysis should be interpreted with caution.

With that in mind, the cognitive tasks used did generally cluster into factors that were in line with our hypothesized cognitive constructs. Parallel analysis and visual scree plots both suggested that four factors should be retained. As can be seen in Table 3.1, Factor 1 consisted of memory-related response time measures, while Factor 2 consisted of memory-related accuracy measures. The measures from the vigilance task loaded on Factor 3, while the measures from the Flanker task loaded on Factor 4. The separation of the two attention tasks onto different factors is consistent with the idea that the Vigilance Task and Flanker Task assess different aspects of attention (sustained vs. selective attention, respectively).

Interestingly, although we conceptualized the Berg Card Sorting Task as a measure of cognitive flexibility, the number of sorts on the BCST had a negative loading on Factor 2 (memory accuracy), which is in line with the idea that card sorting tasks depend on working memory for processes like set maintenance and

rule inference (e.g., Lange et al., 2016; Lehto, 1996), with poorer working memory capacity leading to more sorts before rule learning. It is also possible that if our study included additional measures of cognitive flexibility a separate factor that included the BCST would have emerged.

The proportion of disadvantageous draws on the Iowa Gambling Task, our measure for decision making, was not included the final factor analysis because of the high proportion of missing data (58 participants included, compared to 76-81 for the other tasks). However, when included in the model IGT performance did not load on any of the factors (uniqueness= .917) and did not change the parcellation of the other tasks onto the four factors, suggesting that the IGT was measuring distinct cognitive processes from our other tasks.

3.10 OTHER FINDINGS

It was found that social isolation correlated significantly with number of symptoms endorsed for depression (r =0.495, p<0.001) (Figure 3.9A), dyslexia (r =0.361, p=0.001) (Figure 3.9B), ADHD (r =0.359, p=0.001) (Figure 3.9C), and autism spectrum disorder (r =0.571, p<0.001) (Figure 3.9D). “Days since COVID-19 infection” (Mean= 303.98, minimum= 20, maximum=639) correlated significantly with the number of symptoms endorsed for dyslexia (r = -0.380, p=0.008) (Figure 3.10A) and social isolation scores (r = -0.298, p=0.038) (Figure 3.10B).

On the Google Form survey, participants were asked “If you experienced social isolation during COVID-19, do you personally think that it has had lasting

effects on your mental wellbeing (i.e., has it heightened any depression, anxiety, etc.)?" and "If you experienced social isolation during COVID-19, do you personally think that it has had lasting effects on your mental abilities (attention span, memory, cognition)?" The potential options were: "Yes, and I think these effects will last for a long time," "Yes, but I think these effects will not last for very long," "No, my mental wellbeing/abilities has/have remained the same," "No, and my mental wellbeing/abilities is/are better than it/they were before quarantine," and "I did not experience social isolation during COVID-19."

The "effect on mental wellbeing" groups were significantly different in number of symptoms reported for anxiety ($F(4,79)=2.821$, $p=0.03$) (Figure 3.11A), depression ($F(4,80)=6.506$, $p<0.001$) (Figure 3.11B), and ADHD ($F(4,80)=3.81$, $p=0.007$) (Figure 3.11C). The "effect on mental abilities" groups were significantly different in number of symptoms reported for depression ($F(4,80)=6.078$, $p<0.001$) (Figure 3.12A), dyslexia ($F(4,80)=3.049$, $p=0.022$) (Figure 3.12B), and ADHD ($F(4,80)=3.504$, $p=0.011$) (Figure 3.12C).

Frequency data for how the pandemic has affected participants' mental wellbeing (Figure 3.13A) and how the pandemic has affected participants' mental abilities (Figure 3.13B) were also collected. Quarantining habits were assessed by totaling the number of activities that an individual was willing to do during a certain timeframe of the pandemic (Figure 3.14). Frequency data for sense loss of taste and smell were also collected for previously infected participants, where fairly equal numbers of participants either lost or did not lose their sense of taste or small, but very few showed ongoing deficits (Figure 3.15).

For the psychiatric questionnaires, previously infected and never infected groups were not significantly different on raw score as assessed by independent samples T-test for Beck's Anxiety Inventory ($t(77)= 0.035$, $p=0.972$), UCLA Social Isolation ($t(79)= 0.446$, $p=0.657$), Beck's Depression Inventory ($t(78)= -1.126$, $p=0.264$), Adult Dyslexia Checklist ($t(78)= 1.09$, $p=0.279$), Adult ADHD Self-Test ($t(78)= -0.46$, $p=0.647$), and the Autism Spectrum Quotient Test ($t(78)= -0.209$, $p=0.835$) (means found in Table 2.1). The proportion of participants in each group who met the score cutoff for moderate levels of anxiety was not significantly different between groups (previously infected= 37.78%, uninfected= 37.14%, $X^2(1, N=79)= 0.018$, $p= 0.892$); there was also no significant different in proportions for high anxiety (previously infected= 24.44%, uninfected= 14.29%, $X^2(1, N=79)= 1.143$, $p= 0.285$). The proportion of participants in each group who met the score cutoff for "high likelihood of clinical depression" was not significantly different between groups (previously infected= 24.44%, uninfected= 14.29%, $X^2(1, N=80)= 1.27$, $p= 0.260$). The proportion of participants in each group who met the score cutoff for "high likelihood of dyslexia" was not significantly different between groups (previously infected= 17.78%, uninfected= 28.56%, $X^2(1, N=80)= 1.315$, $p= 0.251$). The proportion of participants in each group who met the score cutoff for "high probability of ADHD" was not significantly different between groups (previously infected= 26.67%, uninfected= 20%, $X^2(1, N=80)= 0.483$, $p= 0.487$). The proportion of participants in each group who met the score cutoff for a "high likelihood of having autism" was not

significantly different between groups (previously infected= 17.77%, uninfected= 5.71%, $X^2(1, N=80)= 2.620$, $p= 0.106$).

Table 3.1 - Factor Loadings

	Factor 1	F2	F3	F4	Uniqueness
Match to Sample: 1 sec. RT	0.648	*0.232*	*0.118*	*0.291*	0.460
Match to Sample: 5 sec. RT	0.573	*0.275*	*0.211*	0.429	0.388
Emotional Memory: Neg. RT	0.943	*0.079*	*-0.024*	*-0.128*	0.200
Emotional Memory: Neut. RT	0.899	*-0.131*	*-0.052*	*-0.230*	0.152
Emotional Memory: Pos. RT	0.837	*-0.145*	*0.007*	*-0.136*	0.240
Match to Sample: 1 sec. Acc.	*-0.170*	0.597	*-0.102*	*0.231*	0.549
Match to Sample: 5 sec. Acc.	*0.239*	0.771	*-0.149*	*-0.112*	0.415
Emotional Memory: Neg. Acc.	*-0.339*	0.407	*0.227*	*-0.092*	0.541
Emotional Memory: Neut. Acc.	*-0.132*	0.389	*0.190*	*-0.092*	*0.739
Emotional Memory: Pos. Acc.	*-0.145*	0.404	*0.108*	*-0.253*	0.648
Forward Digit Span	*-0.158*	0.312	*-0.067*	*0.031*	*0.842
Backward Digit Span	*0.090*	0.680	*-0.116*	*0.115*	0.566
Memory Capacity Estimate	*-0.006*	0.682	*-0.120*	*-0.054*	0.493
BCST Sorts	*-0.188*	-0.560	*-0.013*	*0.184*	0.673
Vigilance: Hits	*0.060*	*0.069*	-0.841	*-0.146*	0.244
Vigilance: Misses	*-0.053*	*-0.091*	0.995	*0.054*	-0.015
Vigilance: False alarms	*0.138*	*-0.153*	0.499	*-0.065*	0.696
Flanker: Incompatible RT	*-0.125*	*-0.139*	*0.073*	0.822	0.297
Flanker: Compatible RT	*-0.096*	*-0.096*	*-0.007*	0.918	0.158

Note. Applied rotation method is promax. Factor loadings that did not meet the 0.4 salience threshold are greyed out. Variables marked with a * were high on Uniqueness and only had a salient factor loading when the threshold was reduced to 0.3.

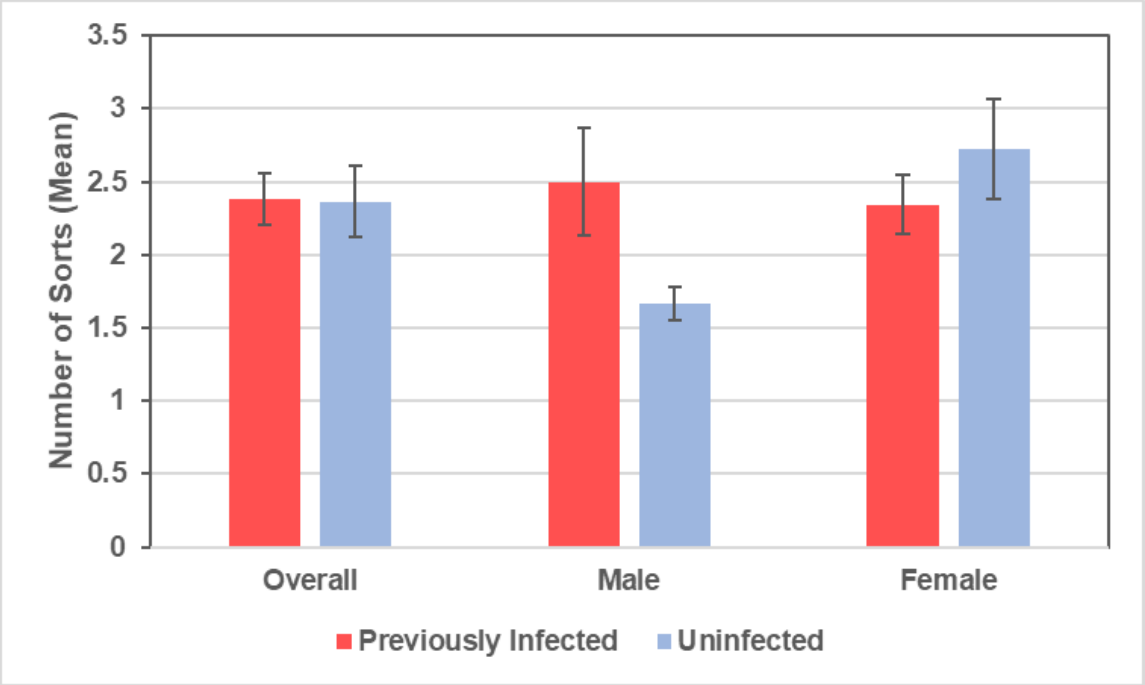

Figure 3.1: Berg's Card Sorting Task. Mean number of sorts until a correct sort for previously COVID-19 infected (N= 45, adjusted M= 2.3831, SE= 0.174), COVID-19 uninfected (N= 35, adj. M= 2.3642 , SE= 0.241), COVID-19 uninfected males (N= 12, adj. M= 1.67 , SE= 0.113), previously COVID-19 infected males (N= 11, adjusted M= 2.4995, SE= 0.366), previously COVID-19 infected females (N= 34, adj. M= 2.3455, SE= 0.2), and COVID-19 uninfected females (N= 23, adj. M= 2.7264 , SE= 0.34).

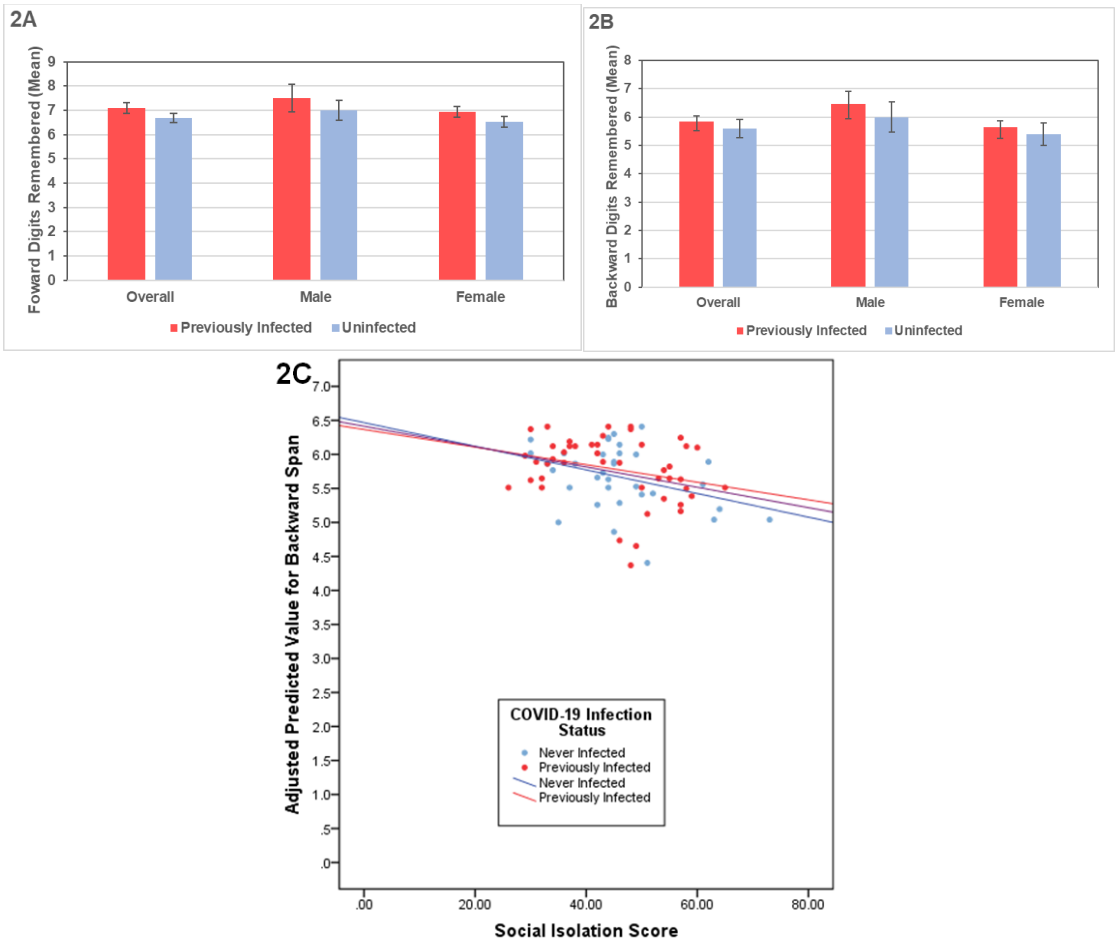

Figure 3.2: Digit Span Task. A) Mean number of digits remembered in the Forward Digit Span Task for previously COVID-19 infected (N= 46, M= 7.087, SE= 0.222), COVID-19 uninfected (N= 35, M= 6.686, SE= 0.196), previously COVID-19 infected males (N= 12, M= 7.5, SE= 0.571), COVID-19 uninfected males (N= 12, M= 7 , SE= 0.408), previously COVID-19 infected females (N= 34, M= 6.9412, SE= 0.223), and COVID-19 uninfected females (N= 23, M= 6.5217 , SE= 0.207). **B)** Mean number of digits remembered in the Backward Digit Span Task for previously COVID-19 infected (N= 45, adjusted M= 5.8444, SE= 0.198), COVID-19 uninfected (N= 34, adj. M= 5.5882 , SE= 0.322), previously COVID-19 infected males (N= 11, adjusted M= 6.4545, SE= 5, COVID-19 uninfected males (N= 11, adj. M= 6 , SE= 0.523), previously COVID-19 infected females (N= 34, adj. M= 5.647, SE= 0.211), and COVID-19 uninfected females (N= 23, adj. M= 5.391 , SE= 0.406). **C)** A scatterplot of social isolation scores plotted against the adjusted predicted values for backward digit span memory length.

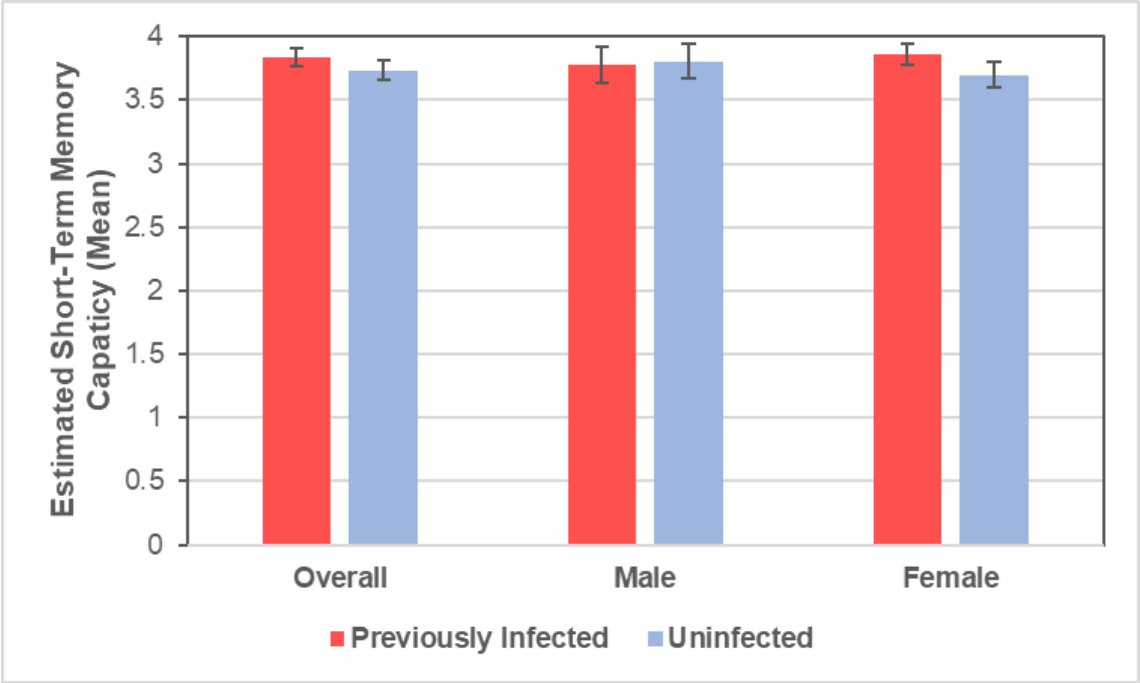

Figure 3.3: Change Detection Task. Mean estimated short-term memory capacity for previously COVID-19 infected (N= 44, adjusted M= 3.841, SE= 0.07), COVID-19 uninfected (N= 35, adj. M= 3.735 , SE= 0.078), previously COVID-19 infected males (N= 11, adjusted M= 3.777, SE= 0.143), COVID-19 uninfected males (N= 12, adj. M= 3.805 , SE= 0.135), previously COVID-19 infected females (N= 33, adj. M= 3.862, SE= 0.081), and COVID-19 uninfected females (N= 23, adj. M= 3.699 , SE= 0.098).

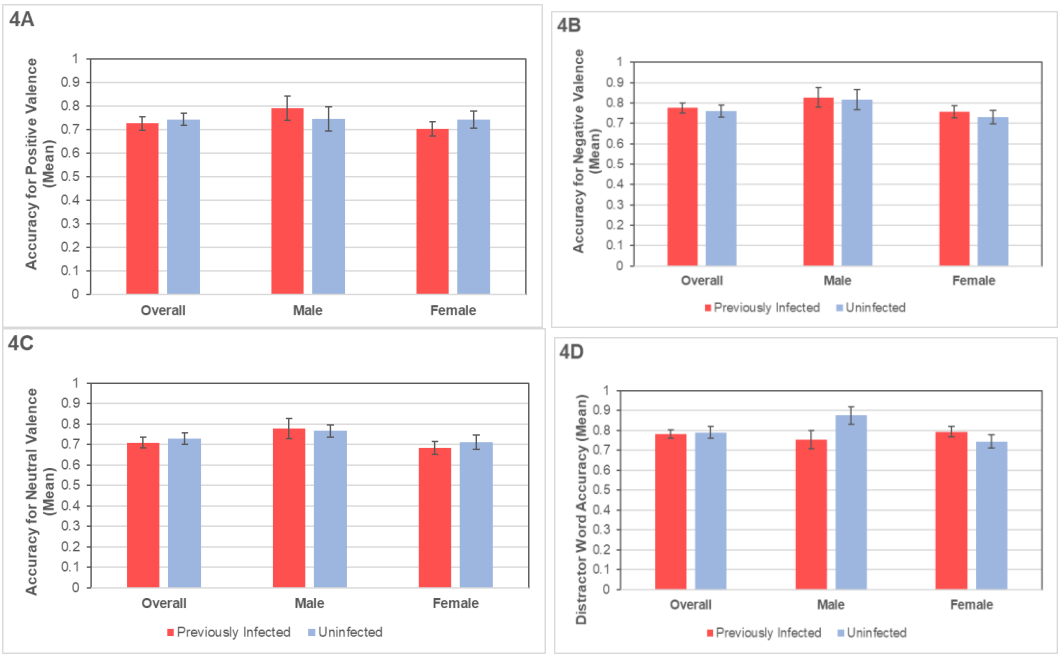

Figure 3.4: The Emotional Memory Task. A) Mean accuracy for positively valenced words for previously COVID-19 infected (N= 45, M= 0.726, SE= 0.02884), COVID-19 uninfected (N= 35, M= 0.7428 , SE= 0.02652), previously COVID-19 infected males (N= 12, M= 0.789, SE= 0.051), COVID-19 uninfected males (N= 12, M= 0.744 , SE= 0.051), previously COVID-19 infected females (N= 33, M= 0.703, SE= 0.031), and COVID-19 uninfected females (N= 23, M= 0.742 , SE= 0.037). **B)** Mean accuracy for negatively valenced words for previously COVID-19 infected (N= 45, M= 0.7763, SE= 0.02417), COVID-19 uninfected (N= 35, M= 0.76 , SE= 0.02933), previously COVID-19 infected males (N= 12, M= 0.8278, SE= 0.048), COVID-19 uninfected males (N= 12, M= 0.8167 , SE= 0.048), previously COVID-19 infected females (N= 33, M= 0.7576, SE= 0.029), and COVID-19 uninfected females (N= 23, M= 0.7304 , SE= 0.034). **C)** Mean accuracy for neutrally valenced words for previously COVID-19 infected (N= 45, M= 0.7081, SE= 0.02699), COVID-19 uninfected (N= 35, M= 0.7295 , SE= 0.02838), previously COVID-19 infected males (N= 12, M= 0.7777, SE= 0.05), COVID-19 uninfected males (N= 12, M= 0.7666 , SE= 0.03), previously COVID-19 infected females (N= 33, M= 0.6828, SE= 0.03), and COVID-19 uninfected females (N= 23, M= 0.7101 , SE= 0.036). **D)** Mean accuracy for distractor words for previously COVID-19 infected (N= 45, M= 0.7817, SE= 0.02181, COVID-19 uninfected (N= 35, M= 0.7886 , SE= 0.02978), previously COVID-19 infected males (N= 12, M= 0.7518, SE= 0.045), COVID-19 uninfected males (N= 12, M= 0.8741 , SE= 0.045), previously COVID-19 infected females (N= 33, M= 0.7925, SE= 0.027), and COVID-19 uninfected females (N= 23, M= 0.744 , SE= 0.033).

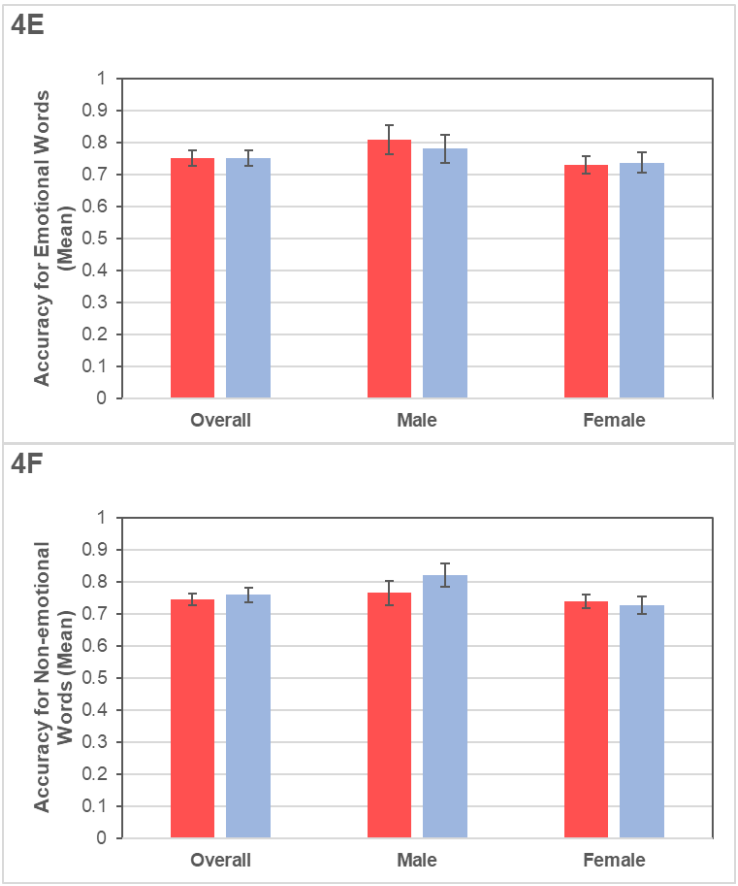

Figure 3.4 (continued): The Emotional Memory Task. **E)** Mean accuracy of emotional words for previously COVID-19 infected (N= 45, mean= 0.7511, SE= 0.02387), COVID-19 uninfected (N= 35, mean= 0.7514 , SE= 0.0248), previously COVID-19 infected males (N= 12, mean= 0.8083, SE= 0.044), COVID-19 uninfected males (N= 12, mean= 0.7805 , SE= 0.044), previously COVID-19 infected females (N= 33, mean= 0.7303, SE= 0.027), and COVID-19 uninfected females (N= 23, mean= 0.7362 , SE= 0.032). **F)** Mean accuracy of non-emotional words for previously COVID-19 infected (N= 45, mean= 0.7449, SE= 0.0186), COVID-19 uninfected (N= 35, mean= 0.759 , SE= 0.02287), previously COVID-19 infected males (N= 12, mean= 0.765, SE= 0.037), COVID-19 uninfected males (N= 12, mean= 0.82 , SE= 0.037), previously COVID-19 infected females (N= 33, mean= 0.738, SE= 0.022), and COVID-19 uninfected females (N= 23, mean= 0.727 , SE= 0.027).

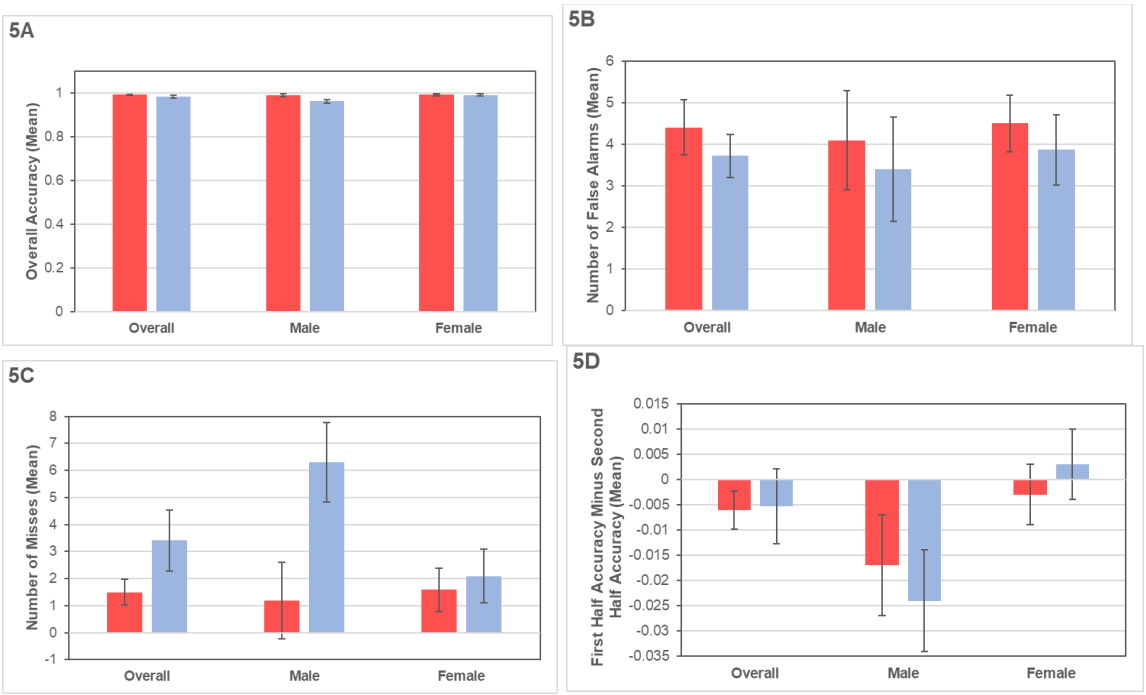

Figure 3.5: Vigilance Task. A) Mean accuracy for previously COVID-19 infected (N= 45, mean= 0.99061, SE= 0.002637), COVID-19 uninfected (N= 32, mean= 0.98087 , SE= 0.006887), previously COVID-19 infected males (N= 11, mean= 0.989, SE= 0.008), COVID-19 uninfected males (N= 10, mean= 0.961 , SE= 0.009), previously COVID-19 infected females (N= 34, mean= 0.991, SE= 0.005), and COVID-19 uninfected females (N= 22, mean= 0.99 , SE= 0.006). **B)** Mean number of false alarms for previously COVID-19 infected (N= 45, mean= 4.4, SE= 0.665), COVID-19 uninfected (N= 32, mean= 3.72 , SE= 0.514), previously COVID-19 infected males (N= 11, mean= 4.091, SE= 1.189), COVID-19 uninfected males (N= 10, mean= 3.4 , SE= 1.247), previously COVID-19 infected females (N= 34, mean= 4.5, SE= 0.676), and COVID-19 uninfected females (N= 22, mean= 3.864 , SE= 0.84). **C)** Mean number of misses for previously COVID-19 infected (N= 45, mean= 1.49, SE= 0.478), COVID-19 uninfected (N= 32, mean= 3.41 , SE= 1.126), previously COVID-19 infected males (N= 11, mean= 1.182, SE= 1.406), COVID-19 uninfected males (N= 10, mean= 6.3 , SE= 1.475), previously COVID-19 infected females (N= 34, mean= 1.588, SE= 0.8), and COVID-19 uninfected females (N= 22, mean= 2.091 , SE= 0.994). **D)** Mean accuracy comparison (accuracy on the first half of the task minus accuracy on the last half of the task) for previously COVID-19 infected (N= 45, mean= -0.0060327, SE= 0.0037875), COVID-19 uninfected (N= 32, mean= -0.005344 , SE= 0.00735559), previously COVID-19 infected males (N= 11, mean= -0.017, SE= 0.01), COVID-19 uninfected males (N= 10, mean= -0.024 , SE= 0.01), previously COVID-19 infected females (N= 34, mean= -0.003, SE= 0.006), and COVID-19 uninfected females (N= 22, mean= 0.003 , SE= 0.007).

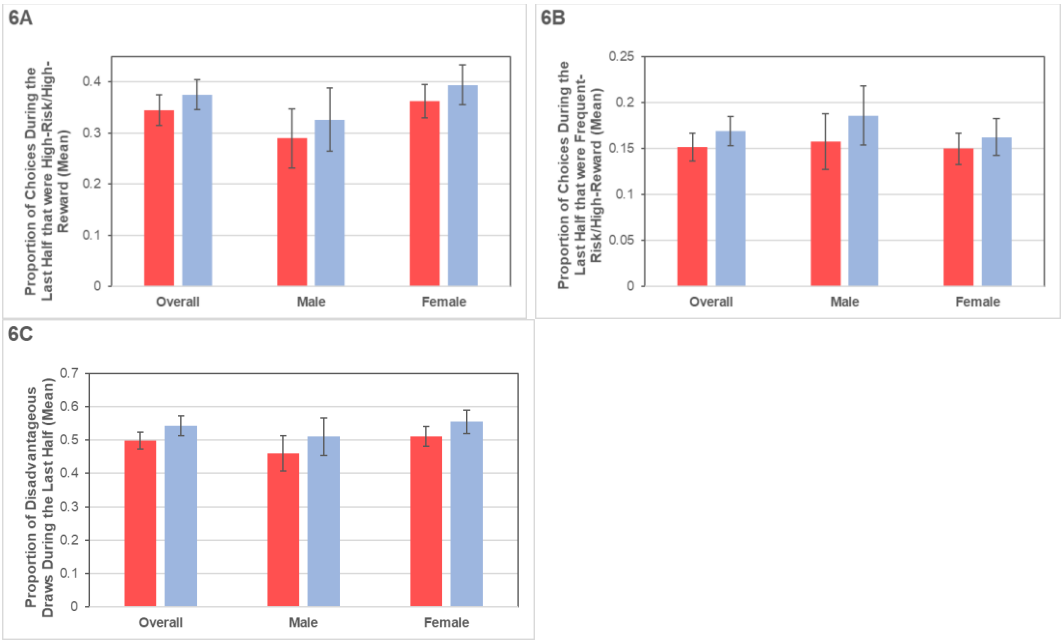

Figure 3.6: Iowa Gambling Task. A) Mean proportion of high-risk/high-reward choices that occurred during the last half of the Iowa Gambling Task for previously COVID-19 infected (N= 33, mean= 0.34485, SE= 0.030339), COVID-19 uninfected (N= 25, mean= 0.3752 , SE= 0.029738), previously COVID-19 infected males (N= 8, mean= 0.29, SE= 0.058), COVID-19 uninfected males (N= 7, mean= 0.326 , SE= 0.062), previously COVID-19 infected females (N= 25, mean= 0.362, SE= 0.033), and COVID-19 uninfected females (N= 18, mean= 0.394 , SE= 0.039). **B)** Mean proportion of frequent-risk/high-reward choices that occurred during the last half of the Iowa Gambling Task for previously COVID-19 infected (N= 33, mean= 0.1515, SE= 0.015), COVID-19 uninfected (N= 25, mean= 0.1688 , SE= 0.016), previously COVID-19 infected males (N= 8, mean= 0.1575, SE= 0.03), COVID-19 uninfected males (N= 7, mean= 0.1857 , SE= 0.032), previously COVID-19 infected females (N= 25, mean= 0.1496, SE= 0.017), and COVID-19 uninfected females (N= 18, mean= 0.1622 , SE= 0.02). **C)** Mean proportion of disadvantageous draws within the last half of the Iowa Gambling Task for previously COVID-19 infected (N= 33, adjusted mean= 0.498, SE= 0.026), COVID-19 uninfected (N= 25, adj. mean= 0.542 , SE= 0.03), previously COVID-19 infected males (N= 8, adjusted mean= 0.459, SE= 0.053), COVID-19 uninfected males (N= 7, adj. mean= 0.51 , SE= 0.056), previously COVID-19 infected females (N= 25, adj. mean= 0.51, SE= 0.03), and COVID-19 uninfected females (N= 18, adj. mean= 0.555 , SE= 0.035).

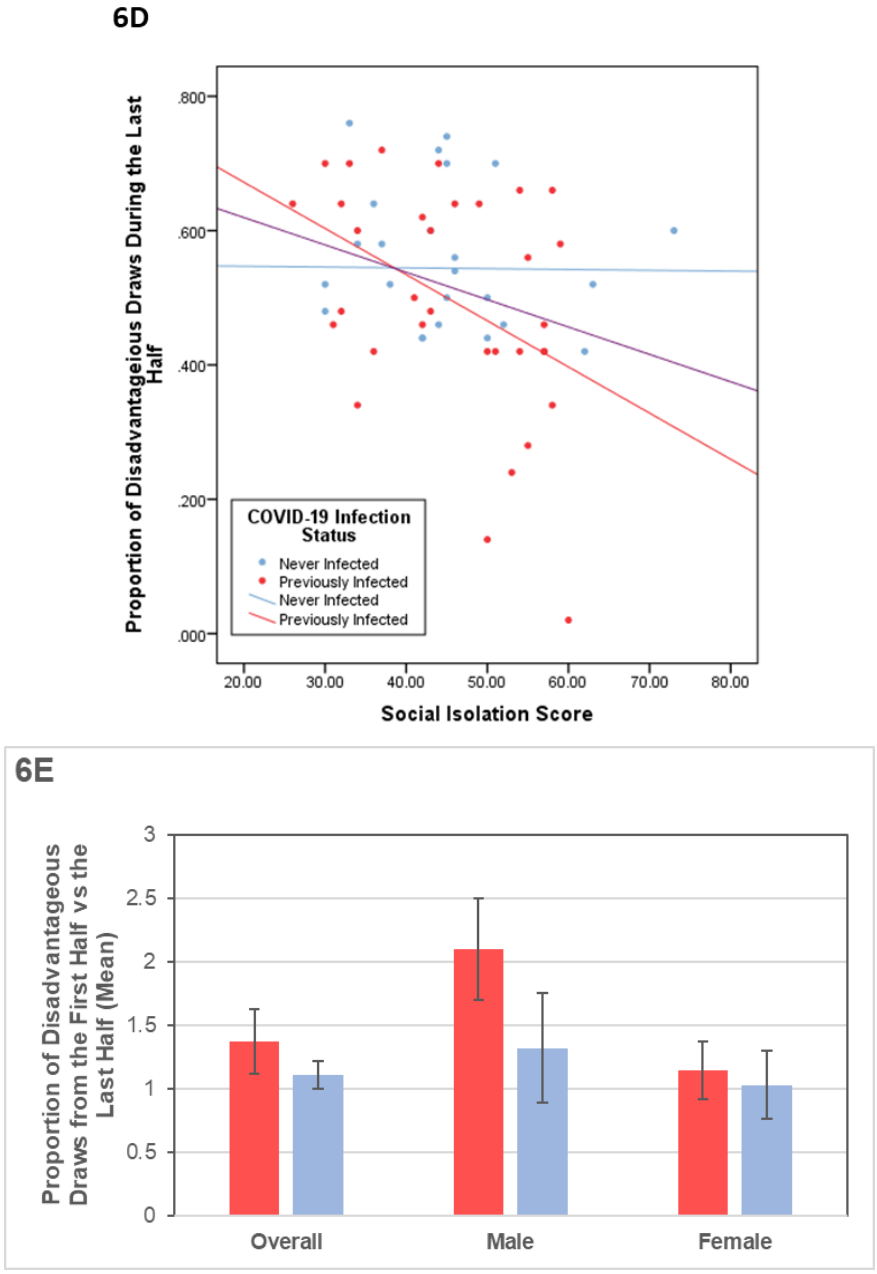

Figure 3.6 (continued): Iowa Gambling Task. D) Scatterplot displaying social isolation scores plotted against the proportion of disadvantageous draws during the last half of the task. **E)** Mean proportion of disadvantageous draws between the first and last half of the Iowa Gambling Task for previously COVID-19 infected (N= 33, mean= 1.375308, SE= 0.2551396), COVID-19 uninfected (N= 25, mean= 1.113376 , SE= 0.1093428), previously COVID-19 infected males (N= 8, mean= 2.099, SE= 0.402), COVID-19 uninfected males (N= 7, mean= 1.322 , SE= 0.43), previously COVID-19 infected females (N= 25, mean= 1.144, SE= 0.228), and COVID-19 uninfected females (N= 18, mean= 1.032 , SE= 0.268).

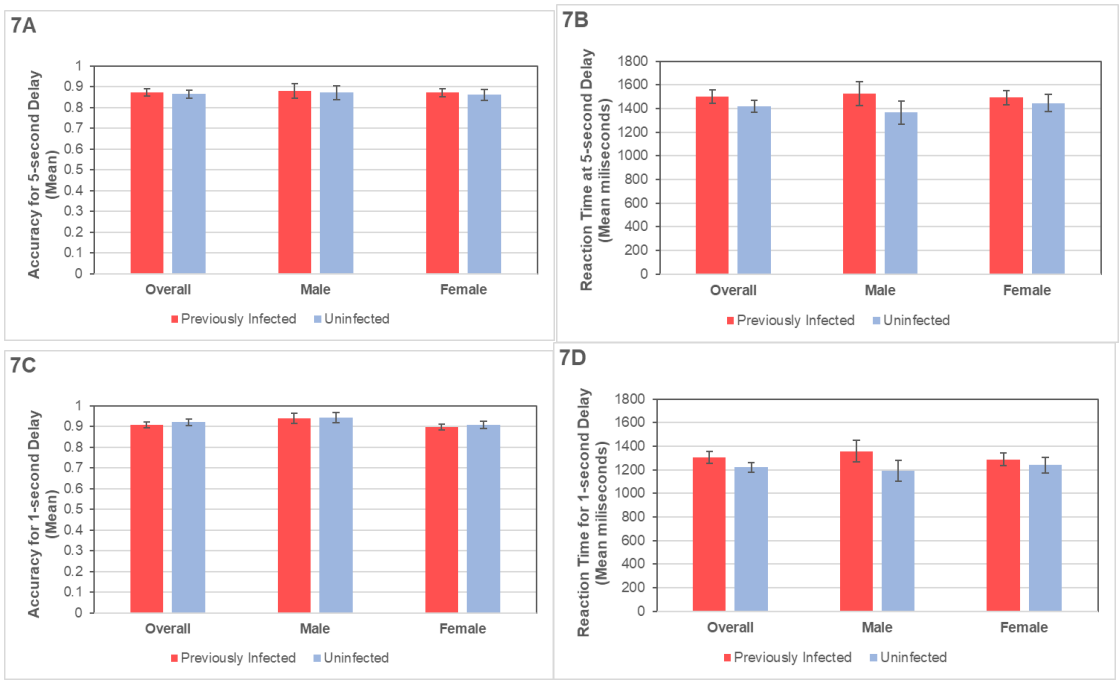

Figure 3.7: Match to Sample Task. A) Mean accuracy of the 5-second delay task for previously COVID-19 infected (N= 45, adjusted mean= 0.872, SE= 0.017), COVID-19 uninfected (N= 34, adj. mean= 0.864 , SE= 0.02), previously COVID-19 infected males (N= 11, adjusted mean= 0.879, SE= 0.035), COVID-19 uninfected males (N= 12, adj. mean= 0.871 , SE= 0.033), previously COVID-19 infected females (N= 34, adj. mean= 0.871, SE= 0.02), and COVID-19 uninfected females (N= 22, adj. mean= 0.86 , SE= 0.025). **B)** Mean reaction time for the 5-second delay task for previously COVID-19 infected (N= 46, mean= 1499.7598, SE= 56.04943), COVID-19 uninfected (N= 34, mean= 1417.3259 , SE= 49.2247), previously COVID-19 infected males (N= 12, mean= 1523.307, SE= 100.225), COVID-19 uninfected males (N= 12, mean= 1364.592 , SE= 100.225), previously COVID-19 infected females (N= 34, mean= 1491.449, SE= 59.543), and COVID-19 uninfected females (N= 22, mean= 1446.09 , SE= 74.021). **C)** Mean accuracy of the 1-second delay task for previously COVID-19 infected (N= 45, adjusted mean= 0.907, SE= 0.013), COVID-19 uninfected (N= 34, adj. mean= 0.92 , SE= 0.015), previously COVID-19 infected males (N= 11, adjusted mean= 0.939, SE= 0.026), COVID-19 uninfected males (N= 12, adj. mean= 0.942 , SE= 0.025), previously COVID-19 infected females (N= 34, adj. mean= 0.897, SE= 0.015), and COVID-19 uninfected females (N= 22, adj. mean= 0.908 , SE= 0.018). **D**) Mean reaction time for the 1-second delay task for previously COVID-19 infected (N= 46, mean= 1305.6461, SE= 51.73375), COVID-19 uninfected (N= 34, mean= 1221.7803 , SE= 40.79546), previously COVID-19 infected males (N= 12, mean= 1357.512, SE= 89.737), COVID-19 uninfected males (N= 12, mean= 1189.188 , SE= 89.737), previously COVID-19 infected females (N= 34, mean= 1287.34, SE= 53.312), and COVID-19 uninfected females (N= 22, mean= 1239.558 , SE= 66.275).

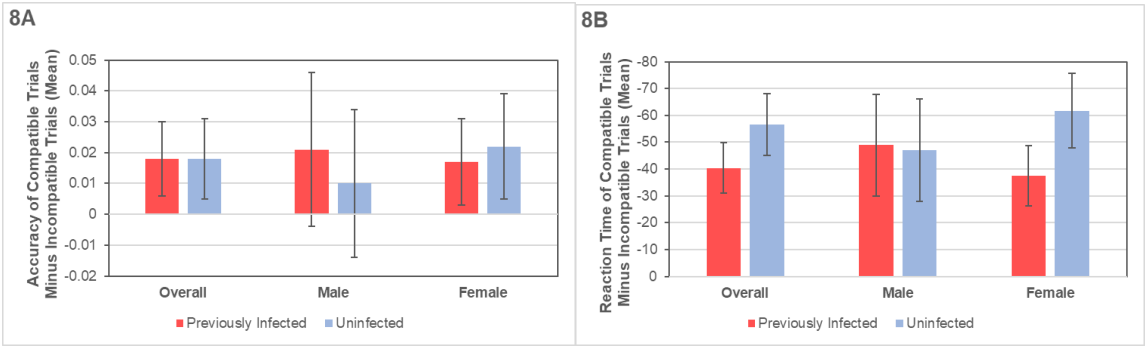

Figure 3.8: The Flanker Task. A) Mean accuracy of compatible trials minus incompatible trials during the Flanker Task for previously COVID-19 infected (N= 44, adjusted mean= 0.018, SE= 0.012), COVID-19 uninfected (N= 34, adj. mean= 0.018 , SE= 0.013), previously COVID-19 infected males (N= 11, adjusted mean= 0.021, SE= 0.025), COVID-19 uninfected males (N= 12, adj. mean= 0.01 , SE= 0.024), previously COVID-19 infected females (N= 33, adj. mean= 0.017, SE= 0.014), and COVID-19 uninfected females (N= 22, adj. mean= 0.022 , SE= 0.017). **B)** Mean reaction time of compatible trials minus incompatible trials during the Flanker Task for previously COVID-19 infected (N= 46, mean= -40.4378, SE= 9.47743), COVID-19 uninfected (N= 34, mean= -56.5608 , SE= 11.3914), previously COVID-19 infected males (N= 12, mean= -48.953, SE= 18.984), COVID-19 uninfected males (N= 12, mean= -47.024 , SE= 18.984), previously COVID-19 infected females (N= 34, mean= -37.433, SE= 11.278), and COVID-19 uninfected females (N= 22, mean= -61.763 , SE= 14.02).

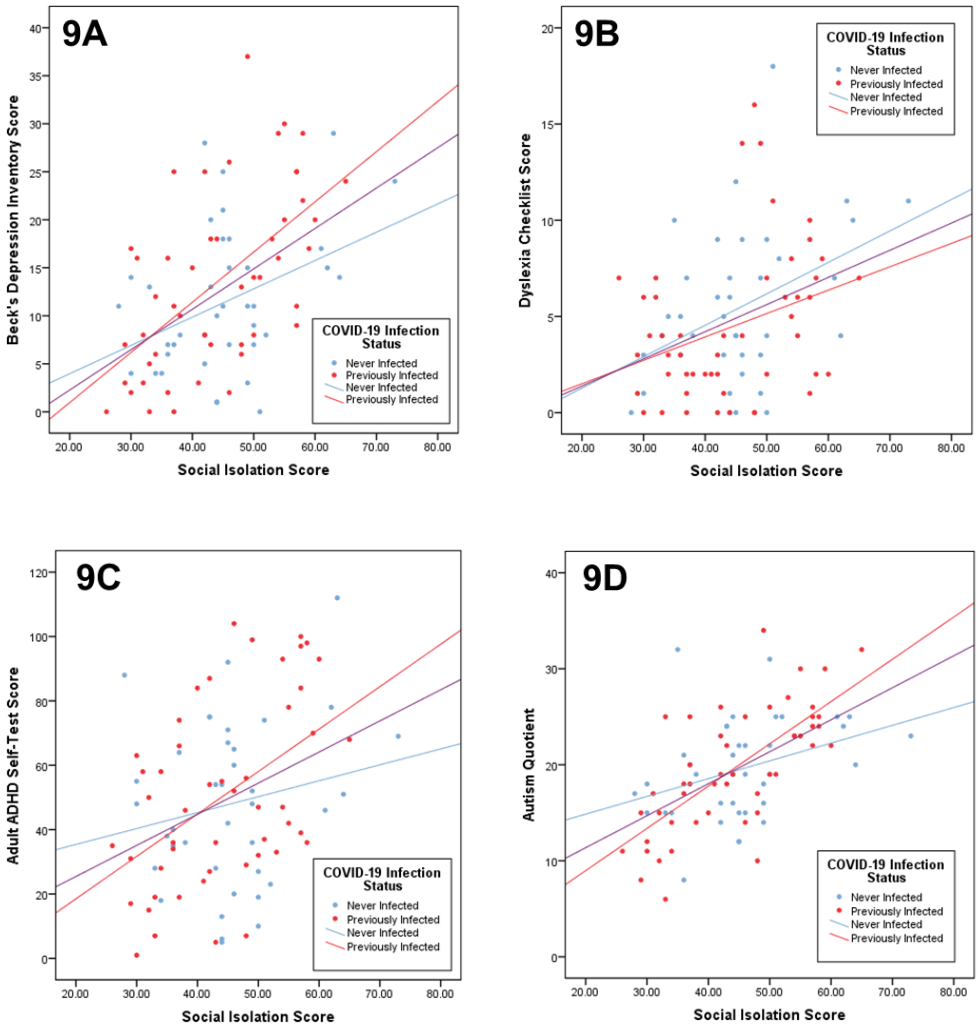

Figure 3.9: Scatterplots for Social Isolation scores. A) Social isolation scores plotted against Beck's Depression Inventory scores (N= 87, r = 0.495, p<0.001). B) Social isolation scores plotted against Dyslexia Checklist scores (N= 87, r =0.361, p=0.001). C) Social isolation scores plotted against Adult ADHD Self-Test scores (N= 87, r =0.359, p=0.001). D) Social isolation scores plotted against Autism Quotient (N= 87, r =0.571, p<0.001).

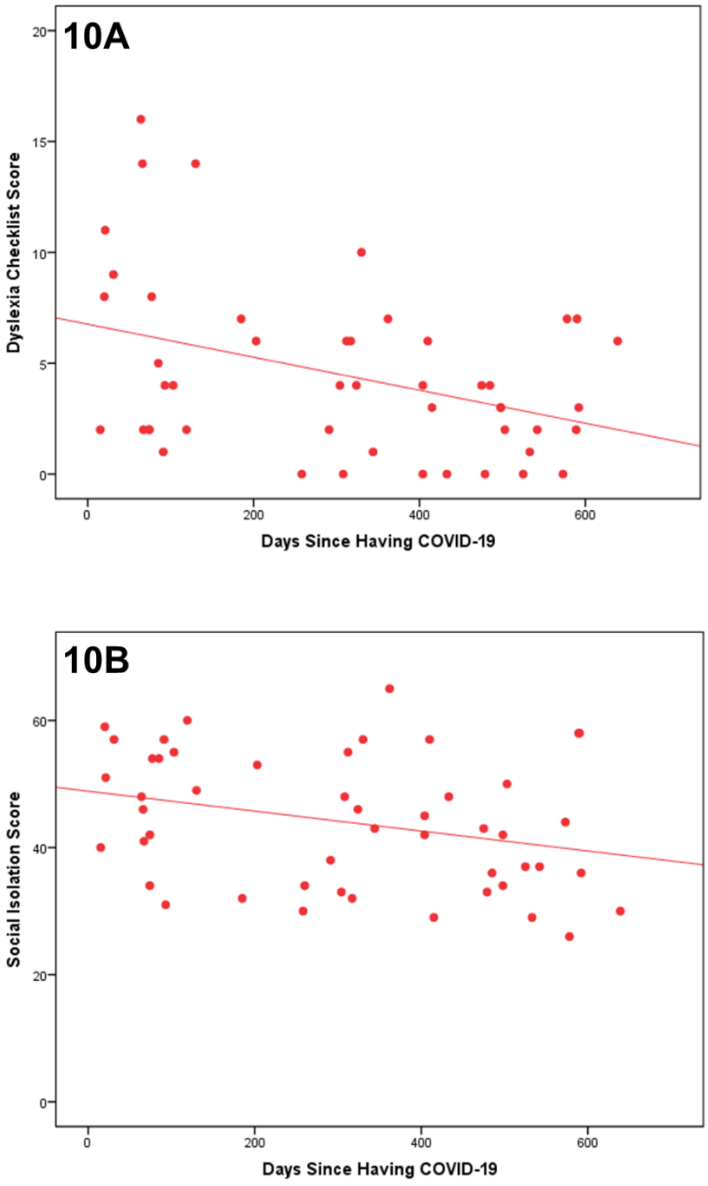

Figure 3.10: Scatterplots for “Days Since Having COVID-19.” A) Days since having COVID-19 plotted against Dyslexia Checklist scores (N= 48, *r* =-0.380, *p*=0.008). B) Days since having COVID-19 plotted against Social Isolation scores (N= 49, *r* =-0.298, *p*=0.038).

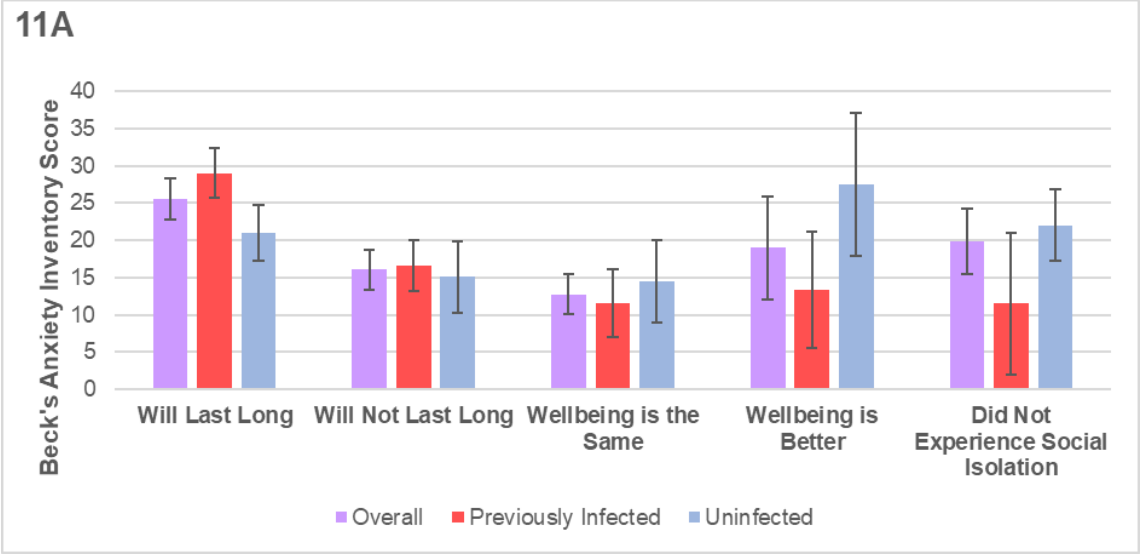

Figure 3.11: Effect on Mental Wellbeing. A) Mean Beck's Anxiety Inventory Score for participants who believe that the social isolation they experienced will have effects on their mental wellbeing that will last for a long time (Overall: N= 30, mean= 25.56, SE= 2.72; Previously infected: N= 17, mean= 29.0588, SE= 3.286; Uninfected: N= 13, mean= 21, SE= 3.757), will not last that long (Overall: N= 24, mean= 16.08, SE= 2.65; Previously infected: N= 16, mean= 16.5625, SE= 3.387; Uninfected: N= 8, mean= 15.125, SE= 4.79), will have no effect (Overall: N= 15, mean= 12.73, SE= 2.68; Previously infected: N= 9, mean= 11.555, SE= 4.516; Uninfected: N= 6, mean= 14.5, SE= 5.531), will improve their mental wellbeing (Overall: N= 5, mean= 19, SE= 6.89; Previously infected: N= 3, mean= 13.33, SE= 7.822; Uninfected: N= 2, mean= 27.5, SE= 9.579), or did not experience social isolation (Overall: N= 10, mean= 19.9, SE= 4.42; Previously infected: N= 2, mean= 11.5, SE= 9.579; Uninfected: N= 8, mean= 22, SE= 4.79).

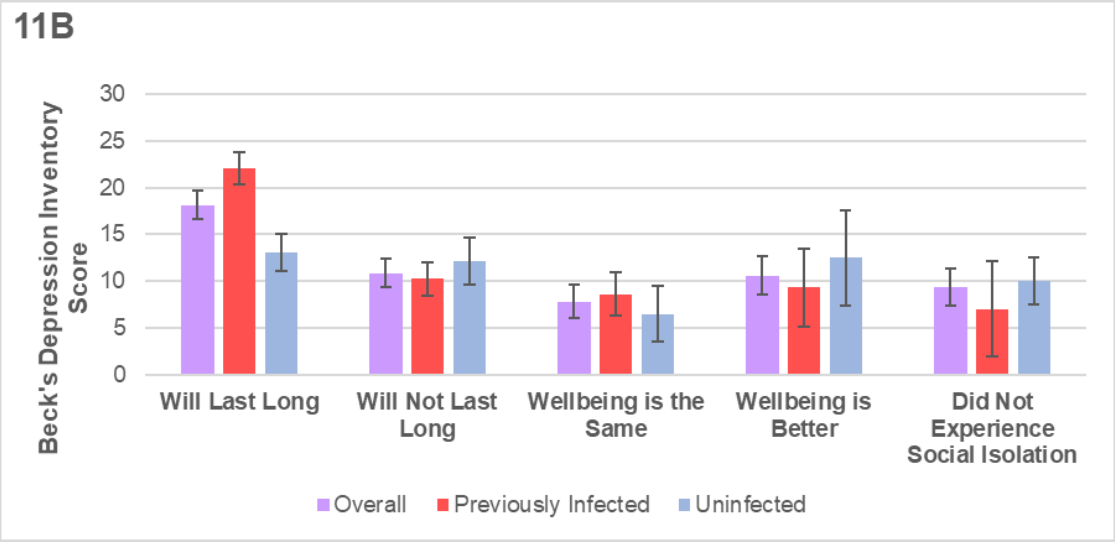

Figure 3.11 (continued): Effect on Mental Wellbeing. B) Mean Beck's Depression Inventory Score for participants who believe that the social isolation they experienced will have effects on their mental wellbeing that will last for a long time (Overall: N= 30, mean= 18.1667, SE= 1.53; Previously infected: N= 17, mean= 22.0588, SE= 1.754; Uninfected: N= 13, mean= 13.0769, SE= 2.006), will not last that long (Overall: N= 24, mean= 10.875, SE= 1.53; Previously infected: N= 16, mean= 10.25, SE= 1.808; Uninfected: N= 8, mean= 12.125, SE= 2.557), will have no effect (Overall: N= 16, mean= 7.8125, SE= 1.82; Previously infected: N= 10, mean= 8.6, SE= 2.287; Uninfected: N= 6, mean= 6.5, SE= 2.953), will improve their mental wellbeing (Overall: N= 5, mean= 10.6, SE= 2.01; Previously infected: N= 3, mean= 9.33, SE= 4.175; Uninfected: N= 2, mean= 12.5, SE= 5.114), or did not experience social isolation (Overall: N= 10, mean= 9.4, SE= 2; Previously infected: N= 2, mean= 7, SE= 5.114; Uninfected: N= 8, mean= 10, SE= 2.557).

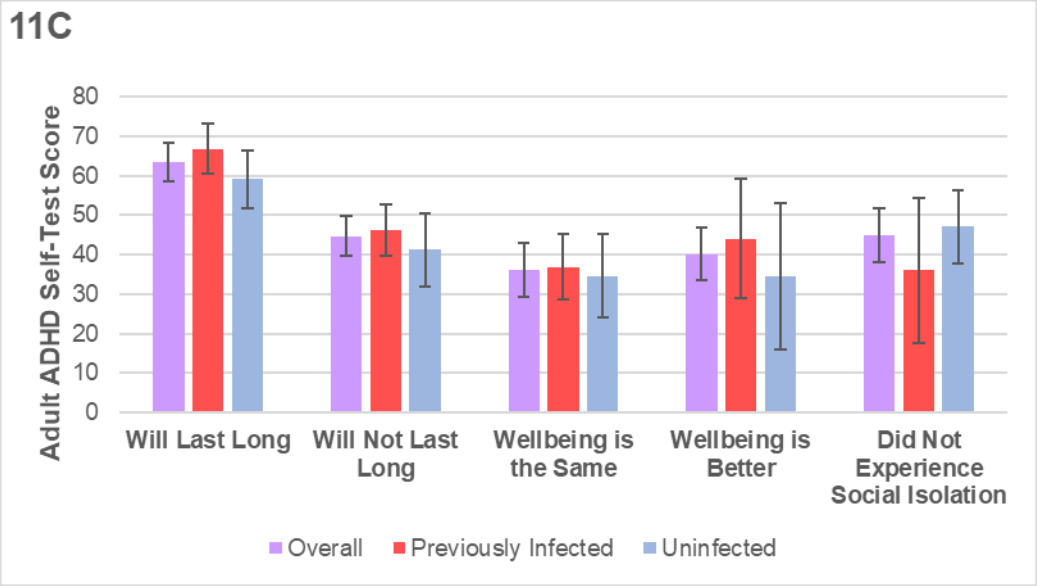

Figure 3.11 (continued): Effect on Mental Wellbeing. C) Mean Adult ADHD Self-Test scores for participants who believe that the social isolation they experienced will have effects on their mental wellbeing that will last for a long time (Overall: N= 30, mean= 63.5, SE= 4.99; Previously infected: N= 17, mean= 66.8235, SE= 6.353; Uninfected: N= 13, mean= 59.1538, SE= 7.265), will not last that long (Overall: N= 24, mean= 44.66, SE= 5.08; Previously infected: N= 16, mean= 46.375, SE= 6.548; Uninfected: N= 8, mean= 41.25, SE= 9.261), will have no effect (Overall: N= 16, mean= 36.06, SE= 6.9; Previously infected: N= 10, mean= 36.9, SE= 8.283; Uninfected: N= 6, mean= 34.66, SE= 10.693), will improve their mental wellbeing (Overall: N= 5, mean= 40.2, SE= 6.58; Previously infected: N= 3, mean= 44, SE= 15.122; Uninfected: N= 2, mean= 34.5, SE= 18.521), or did not experience social isolation (Overall: N= 10, mean= 44.9, SE= 6.78; Previously infected: N= 2, mean= 36, SE= 18.521; Uninfected: N= 8, mean= 47.125, SE= 9.261).

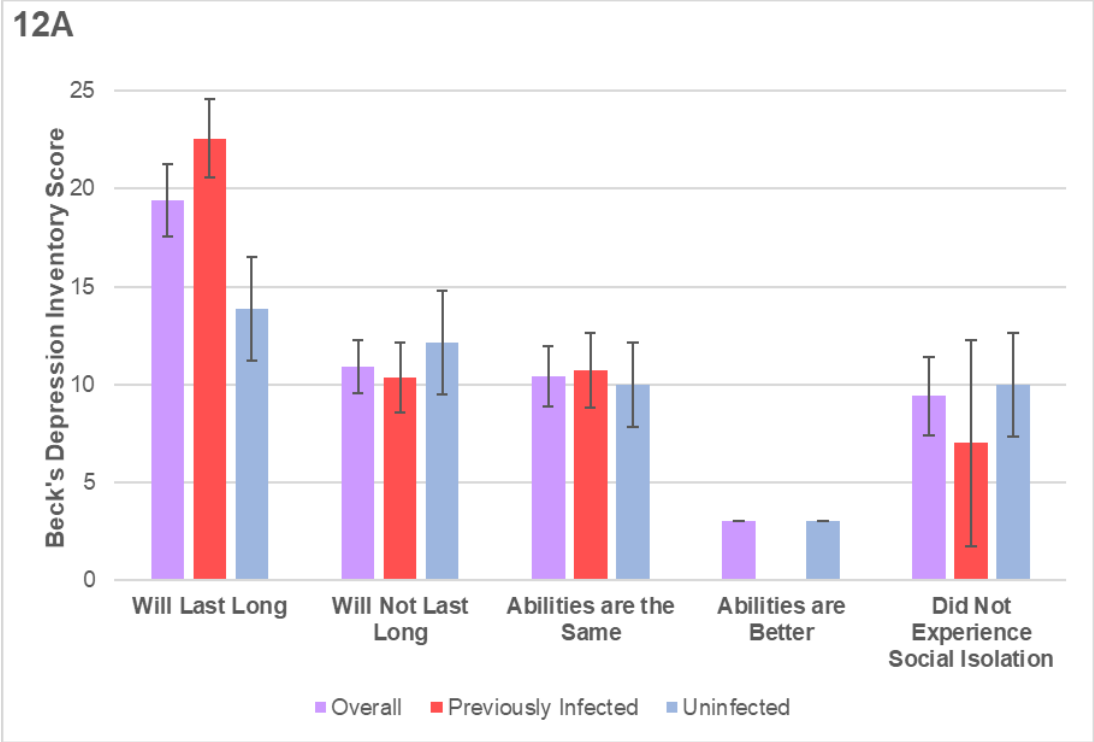

Figure 3.12: Effect on Mental Abilities. A) Mean Beck's Anxiety Inventory scores for participants who believe that the social isolation they experienced will have effects on their mental abilities that will last for a long time (Overall: N= 22, mean= 19.4091, SE= 1.83; Previously infected: N= 14, mean= 22.571, SE= 1.995; Uninfected: N= 8, mean= 13.875, SE= 2.639), will not last that long (Overall: N= 25, mean= 10.92, SE= 1.37; Previously infected: N= 17, mean= 10.353, SE= 1.81; Uninfected: N= 8, mean= 12.125, SE= 2.639), will have no effect (Overall: N= 27, mean= 10.4074, SE= 1.52; Previously infected: N= 15, mean= 10.733, SE= 1.927; Uninfected: N= 12, mean= 10, SE= 2.155), will improve their mental wellbeing (Overall: N= 1, mean= 3, SE= 0; Previously infected: N= 0, mean= , SE= ; Uninfected: N= 1, mean= 3, SE= 0), or did not experience social isolation (Overall: N= 10, mean= 9.4, SE= 1.98; Previously infected: N= 2, mean= 7, SE= 5.278; Uninfected: N= 8, mean= 10, SE= 2.639).

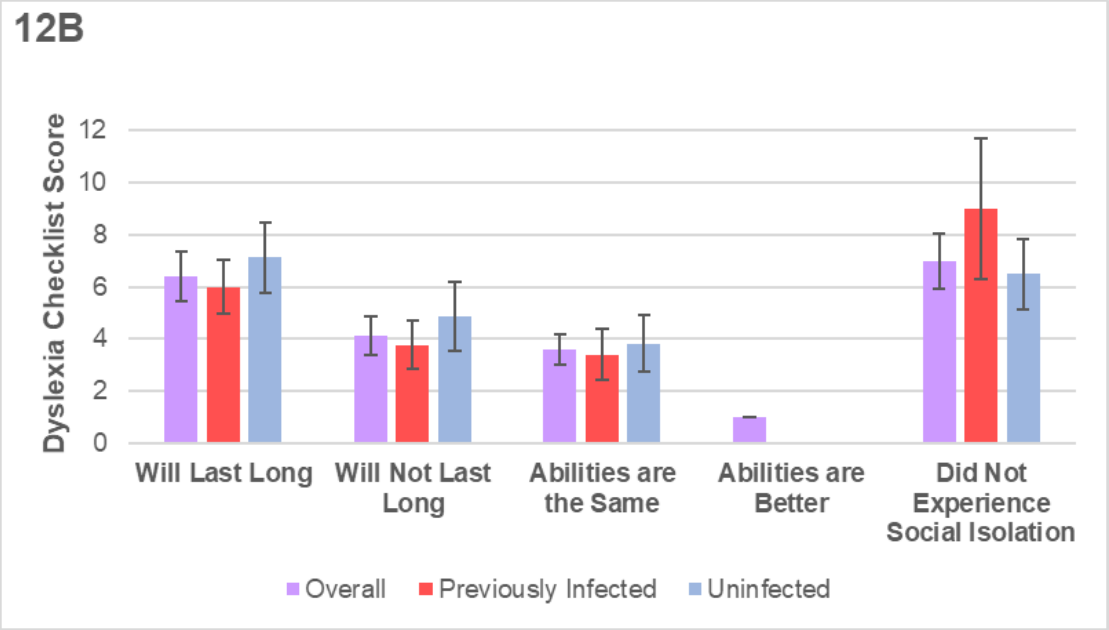

Figure 3.12 (continued): Effects on Mental Abilities. B) Mean Dyslexia Checklist scores for participants who believe that the social isolation they experienced will have effects on their mental abilities that will last for a long time (Overall: N= 22, mean= 6.4091, SE= 0.95; Previously infected: N= 14, mean= 6, SE= 1.014; Uninfected: N= 8, mean= 7.125, SE= 1.341), will not last that long (Overall: N= 25, mean= 4.12, SE= 0.757; Previously infected: N= 17, mean= 3.765, SE= 0.92; Uninfected: N= 8, mean= 4.875, SE= 1.341), will have no effect (Overall: N= 27, mean= 3.5926, SE= 0.6; Previously infected: N= 15, mean= 3.4, SE= 0.98; Uninfected: N= 12, mean= 3.833, SE= 1.095), will improve their mental wellbeing (Overall: N= 1, mean= 1, SE= 0; Previously infected: N= 0, mean= , SE= ; Uninfected: N= 1, mean= 0, SE= 0), or did not experience social isolation (Overall: N= 10, mean= 7, SE= 1.06; Previously infected: N= 2, mean= 9, SE= 2.683; Uninfected: N= 8, mean= 6.5, SE= 1.341).

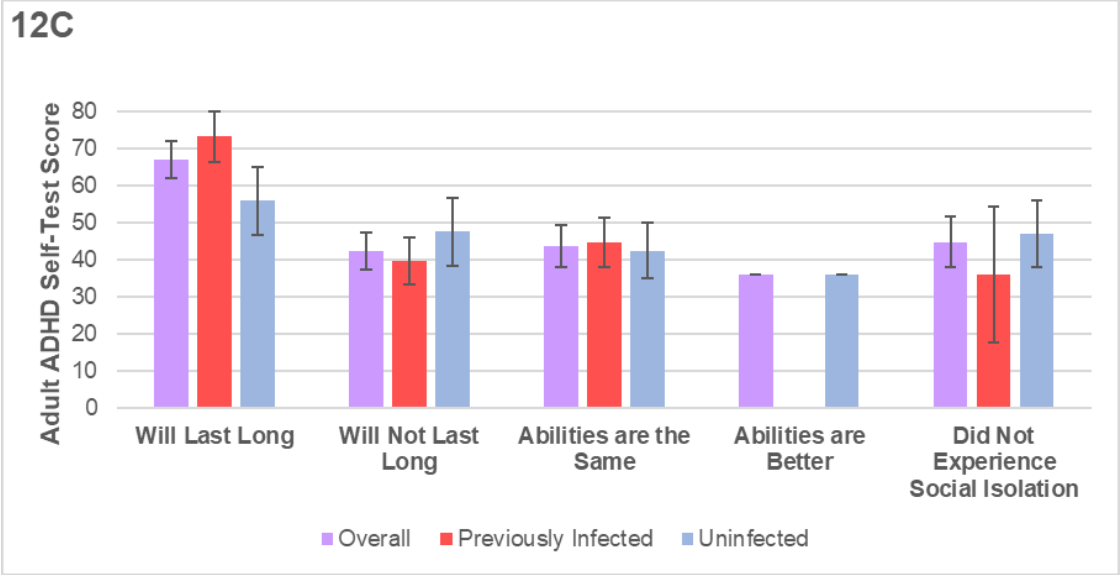

Figure 3.12 (continued): Effects on Mental Abilities. C) Mean Adult ADHD Self-Test scores for participants who believe that the social isolation they experienced will have effects on their mental abilities that will last for a long time (Overall: N= 22, mean= 67.0455, SE= 4.93; Previously infected: N= 14, mean= 73.357, SE= 6.919; Uninfected: N= 8, mean= 56, SE= 9.153), will not last that long (Overall: N= 25, mean= 42.36, SE= 5.06; Previously infected: N= 17, mean= 39.882, SE= 6.279; Uninfected: N= 8, mean= 47.625, SE= 9.153), will have no effect (Overall: N= 27, mean= 43.89, SE= 5.63; Previously infected: N= 15, mean= 44.933, SE= 6.685; Uninfected: N= 12, mean= 42.583, SE= 7.474), will improve their mental wellbeing (Overall: N= 1, mean= 36, SE= 0; Previously infected: N= 0, mean= , SE= ; Uninfected: N= 1, mean= 36, SE= 0), or did not experience social isolation (Overall: N= 10, mean= 44.9, SE= 6.78; Previously infected: N= 2, mean= 36, SE= 18.307; Uninfected: N= 8, mean= 47.125, SE= 9.153).

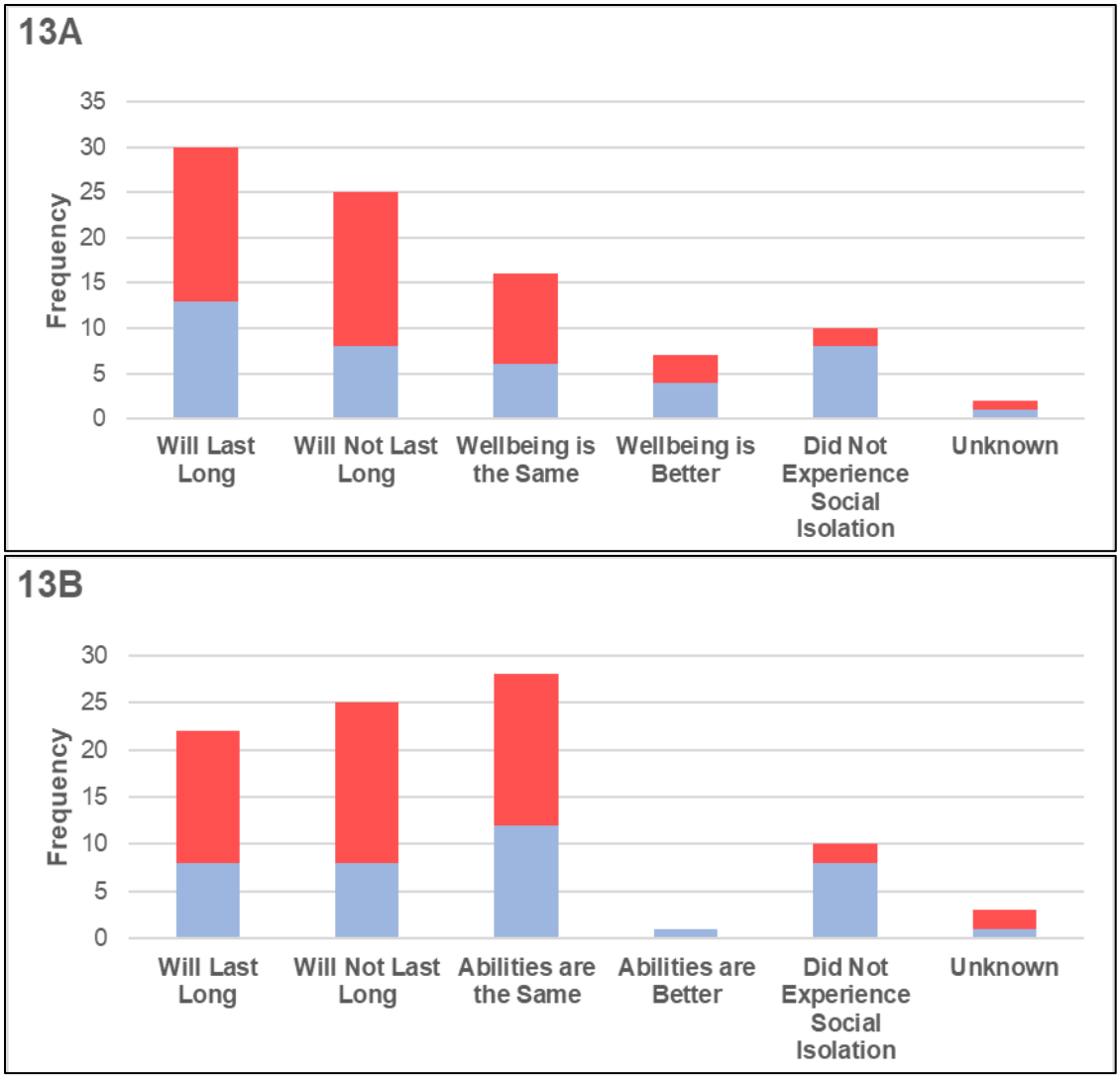

Figure 3.13: Expectancies for Social Isolation. A) Frequencies for individuals who thought that social isolation from the COVID-19 pandemic would have effects on their mental wellbeing that would last for a long time (Previously infected= 17, Uninfected= 13), would not last for a long time (Previously infected= 17, Uninfected= 8), would have no effect on their mental wellbeing (Previously infected= 10, Uninfected= 6), had improved their wellbeing (Previously infected= 3, Uninfected= 4), did not experience social isolation (Previously infected= 2, Uninfected= 8), and declined to answer (Previously infected= 1, Uninfected= 1). B) Frequencies for individuals who thought that social isolation from the COVID-19 pandemic would have effects on their mental abilities that would last for a long time (Previously infected= 14, Uninfected= 8), would not last for a long time (Previously infected= 17, Uninfected= 8), would have no effect on their mental abilities (Previously infected= 16, Uninfected= 12), had improved their mental abilities (Previously infected= 0, Uninfected= 1), did not experience social isolation (Previously infected= 2, Uninfected= 8), and declined to answer (Previously infected= 2, Uninfected= 1).

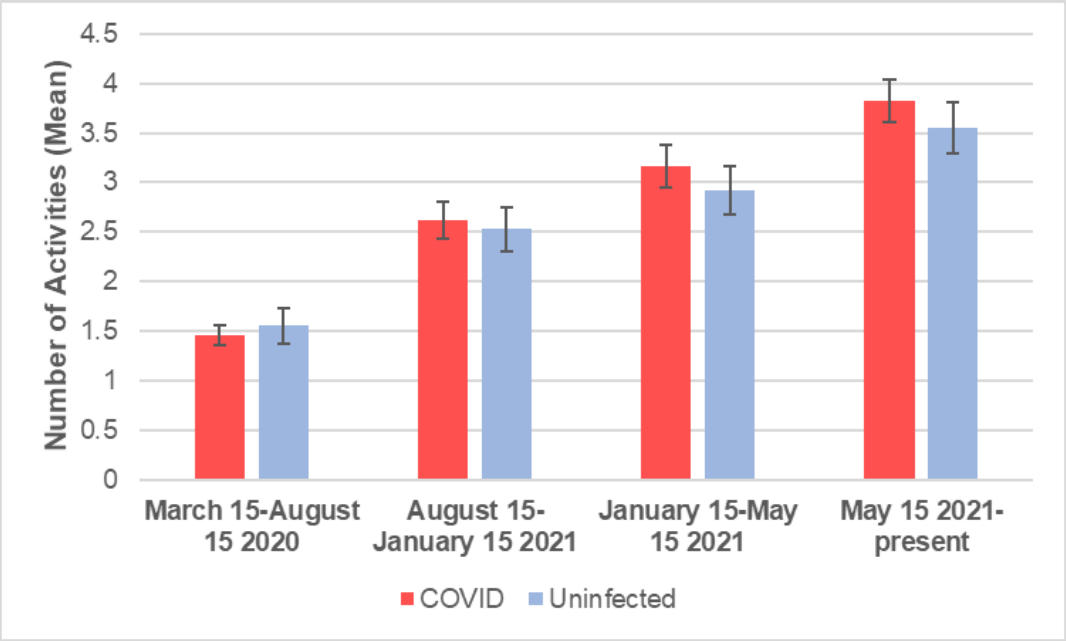

Figure 3.14: Quarantine Activities. The Mean number of activities that previously infected and COVID-19 uninfected groups participated in from March 15th-August 15th 2020 (Previously infected: M= 1.46, SE= 0.09, uninfected: M= 1.55, SE= 0.17), August 15th – January 15th, 2021 (Previously infected: M= 2.62, SE= 0.19, uninfected: M= 2.53, SE= 0.23), January 15th – May 15th 2021 (Previously infected: M= 3.16, SE= 0.22, uninfected: M=2.92, SE= 0.25), and May 15th 2021 to present (Previously infected: M= 3.82, SE= 0.21, uninfected: M= 3.55, SE= 0.26).

Figure 3.15: Sense of Taste and Smell in COVID-19 Recovered groups. Did not lose (taste= 22, smell= 26), lost, but has fully recovered (taste= 23, smell= 22), lost but has not returned to normal (taste= 4, smell= 2).

CHAPTER 4

DISCUSSION

4.1 OVERVIEW

Initial research has supported the possibility that COVID-19 may damage the CNS either directly or indirectly. The present study sought to determine the extent of these potential cognitive deficits in a young and mildly infected sample of college students who lived through the COVID-19 pandemic. Participants completed an extensive survey assessing their experience with COVID-19 and any pandemic-induced social isolation and also completed a battery of cognitive assessments to evaluate attention, memory, and executive functioning. Results largely suggested that mild infection did not cause lasting cognitive deficits. Social isolation largely did not influence cognition, but it had an effect on non-diagnostic measures of certain mental health disorders. The potential reasons for these findings will be discussed below.

4.2 ATTENTION

There were no significant findings for the vigilance task, suggesting that COVID-19 infection had no effect on sustained attention. In vigilance assessments of COVID-19 survivors thus far, deficits were only observed in recently hospitalized patients or severely infected patients; observed deficits had ameliorated after 9 months (do Carmo Filho et al., 2022; Hampshire et al., 2021; Zhao et al., 2022). It should be noted that the vigilance task in the present study

took approximately 12 minutes to complete. While it was the longest of the assessments, some assessments of vigilance and sustained attention can last for 30 minutes or longer. Remaining vigilant for a longer period of time is more difficult than for a shorter period of time, so it is possible that the length of the vigilance task used was not long enough to prove challenging for the participants.

There were no significant findings for the Flanker task, indicating that selective attention abilities were not significantly different between any of the groups. Previous research indicates deficits in attention, but these deficits have only been observed in hospitalized patients, severely infected patients, or in patients diagnosed specifically with “long-COVID” (Jaywant et al., 2021; Almeria et al., 2020; Hampshire et al., 2021; Graham et al., 2021).

Thus, using evidence from these assessments of attention, attentional processes seem to be spared in previously mildly COVID-19 infected individuals who have not been diagnosed with PCC. These findings suggest that extensive damage to the neural correlates for these processes (middle frontal gyrus, parietal lobe, prefrontal cortex, amygdala, HPA axis, orbitofrontal cortex, anterior cingulate cortex) is unlikely due to the lack of expected deficits observed (Lewin et al., 1996; Oken et al., 2006; Salo et al., 2017; Luks et al., 2010; Rusnáková et al., 2011; vel Grajewska et al., 2011).

4.3 MEMORY

There were no significant effects of COVID-19 infection, nor any interactions with biological sex, observed for the Digit Span task. Digit span tasks are meant to assess verbal working memory. In a small study of young,

previously COVID-19 infected individuals (N=10) compared to COVID-19 uninfected (N=19) individuals, verbal working memory deficits were observed using a letter span task (Yoo, 2022). However, for Yoo's study, it is unclear how long the COVID-19 group had to recover before assessment. It is likely that the present sample reflects that of previous studies wherein individuals did not display long-term working memory deficits after sufficient recovery time (Guo et al., 2022; Hampshire et al., 2021; Mattioli et al., 2021; Zhao et al., 2022).

Similarly, there were no significant effects of COVID-19 infection, nor any interactions with biological sex, observed for the Emotional Memory task aside from distractor word accuracy, wherein COVID-19 uninfected males outperformed all other groups. A recent study conducted during the first year of the COVID-19 pandemic showed that aversive emotional memories were recalled and recognized at a lower rate than expected (Leon et al., 2022). While the present sample did not have any differences between COVID-19 uninfected and previously infected COVID-19 groups, there were the expected memory differences between non-emotional and emotional words. It does not seem that COVID-19 infection nor social isolation had any extra effect on emotional memory. However, these null findings should not negate the findings of others who have found that older individuals were better at emotional regulation and were more likely to report positive memories from the pandemic than younger individuals (Carstensen et al., 2020; Ford et al., 2021). The potential long-term effects of the pandemic on younger individuals remain to be seen, but it is

possible that long-term memory (which was not assessed herein) could be affected in younger individuals more than the delayed memory task chosen.

There were no significant findings for the match to sample task, indicating that visuospatial working memory ability was not significantly different between any groups. It has previously been found that deficits in memory have been observed in recovered COVID-19 patients, and those with neurological symptoms had even lower scores in working memory than those without neurological symptoms (Alemanno et al., 2021; Becker et al., 2021; Graham et al., 2021; Mendez et al., 2021; Hampshire et al., 2021; Jaywant et al., 2021; Almeria et al., 2020). However, other studies in COVID-19 positive populations indicated the lack of long-term working memory and emotional processing deficits (Guo et al., 2022; Hampshire et al., 2021; Mattioli et al., 2021; Zhao et al., 2022). It seems that the present sample better matches the latter, especially considering that the present sample was not seriously physically affected by COVID-19 infection, nor was anyone in the sample hospitalized. Similarly, there were no significant findings for the change detection task, indicating that there were no significant differences between any groups on working memory capacity. Interestingly, it has been previously found that increased working memory capacity was a predictor of social-distancing compliance during the height of the COVID-19 pandemic in the United States (Xie et al., 2020). The aforementioned study was conducted during the first 2 weeks of the government mandated lockdowns in the United States. This finding was not replicated in the present sample; the present assessment of working memory capacity did not correlate

significantly to the assessment of quarantining for the months of March to August of 2020.

Thus, using evidence from these assessments of memory, these facets of memory seem to be spared in previously mildly COVID-19 infected individuals. These findings suggest that extensive damage to the neural correlates for these processes (dorsolateral prefrontal cortex, parietal cortex, anterior cingulate cortex, basal ganglia, fusiform gyrus, inferior frontal gyrus, orbitofrontal cortex, and hippocampus) is unlikely due to the lack of expected deficits observed (Aleman et al., 2008; Geva et al., 2021; Hoshi et al., 2000; Daniel et al., 2016; Habeck et al., 2004; Cirillo et al., 1989; Beck et a., 2001; Kuchinke et al., 2005; Bowen et al., 2018).

4.4 EXECUTIVE FUNCTIONING

There were no significant findings for Berg's Card Sorting task aside from a significant interaction between previous COVID-19 infection status and biological sex, with never infected males significantly outperforming all other categories. Card Sorting Task performance is thought to be mediated by the ventrolateral and dorsolateral prefrontal cortex, anterior cingulate cortex, and inferior parietal lobe (Buchsbaum et al., 2005; Nagahama et al., 1996; Lie et al., 2006). Overall, there were no differences between previously COVID-19 infected and COVID-19 uninfected groups on Mean number of card sorts before correctly sorting. The Card Sorting task is meant to assess cognitive flexibility, which can be considered a facet of executive functioning. It is likely that the present sample reflects that of other studies that have assessed executive functioning and found

amelioration of initial deficits in a sample that has had sufficient time to recover from COVID-19 infection (Guo et al., 2022; Mattioli et al., 2021; Zhao et al., 2022).

There were no significant findings for the Iowa Gambling task aside from the significant correlation between social isolation scores and the “proportion of disadvantageous draws in the last half of the task” measure. The Iowa Gambling Task used herein consisted of 100 draws from 4 decks. To ensure that risk-taking behavior and decision making was being assessed, and not random chance, the last 50 draws were the focus of the present assessments. It should be noted that all participants sampled from all decks at least once during the first 25 trials of the task.

Previously COVID-19 infected and COVID-19 uninfected groups were no different in the proportion of high-risk-high-reward choices nor frequent-risk-high-reward choices they made in the last half of the task. Since all participants had, and took advantage of, the opportunity to sample from all decks by the last half of the task, this lack of difference between groups indicates that one group was not more likely to engage in risk-taking behavior than the other.

Previously COVID-19 infected and COVID-19 uninfected groups were also no different in the proportion of disadvantageous draws they made in the last half of the task. Previous literature suggests that Iowa Gambling Task selections improved consistently as “lockdown” restrictions were reduced; in other words, selection from beneficial decks increased and selection from disadvantageous decks decreased (Ingram et al., 2021). Previously COVID-19 infected and

COVID-19 uninfected groups were not different in their ability to avoid disadvantageous decks in the last half of the task ("disadvantageous early versus late"). It should be noted that, regardless of biological sex or COVID-19 infection status, on average all participants improved in their ability to avoid disadvantageous decks (M=1.26, SE=0.152). In other words, COVID-19 infection had no effect on one's ability to improve in the Iowa Gambling Task over time, indicating that learning the task, learning from past mistakes, and improving decisions over time was not impaired.

Thus, using evidence from these assessments of executive functioning, these abilities seem to be spared in previously mildly COVID-19 infected individuals. These findings suggest that extensive damage to the neural correlates for these processes (ventrolateral and dorsolateral prefrontal cortex, anterior cingulate cortex, insula, basal ganglia, frontal gyrus, lateral orbitofrontal cortex, and inferior parietal lobe) is unlikely due to the lack of expected deficits observed (Buchsbaum et al., 2005; Nagahama et al., 1996; Lie et al., 2006; Lin et al., 2008; Lawrence et al., 2009).

4.5 SOCIAL ISOLATION

Social isolation scores positively correlated significantly with number of symptoms endorsed for depression, dyslexia, ADHD, and autism spectrum disorder. It is unknown whether social isolation exacerbated the symptoms associated with these disorders or whether having a higher number of symptoms in these disorders cause individuals to be more socially isolated. Previous literature indicates that social isolation is significantly correlated with depression

(Matthews et al., 2016; Courtet et al., 2020), dyslexia (Mugnaini et al., 2009; Baschenis et al., 2021), ADHD (Brod et al., 2012; Sibley et al., 2021), and autism (Kasari and Sterline, 2013). It was initially expected that social isolation would have more prevalence as an influencing factor in the results. However, it is also a possibility that the effects of social isolation due to the pandemic are no longer observable. Data collection for the present study began in the Fall of 2021. By this time, most university services, sporting events, dormitories, and classrooms were back to their pre-pandemic operating procedures; in addition, surrounding restaurants and other social activities were fully open, and many had been since earlier in the year when vaccinations were becoming widely available. There can be no doubting the potential trauma and negative effects that prolonged social isolation had on some individuals, especially those who voluntarily quarantined longer and more strictly than the majority of the population. However, if there was a more widespread effect of social isolation, the current measures used for the present study were not sensitive or relevant enough to pick up on any of those potential differences.

There was a significant correlation observed between backward digit-span ability and social isolation. However, upon accounting for dyslexia (which also correlated with backward digit-span ability), the contribution of social isolation scores to the regression model was determined to be minimal. Assessing backward digit-span ability during the COVID-19 pandemic has shown no significant effect of isolation on task performance (Manca et al., 2022). Because of the low contribution of social isolation scores to an overall regression model

once dyslexia measures were added to the model, it is likely that social isolation does not have a clinically significant effect on backward digit-span task performance. There is evidence to support that social isolation could affect memory in later life (Evans et al., 2018), but other assessments of social isolation have shown no significant effect on this ability (Zubek et al., 1969).

While there were no group differences associated with COVID-19 infection for the Iowa Gambling Task, there was a significant relationship found between social isolation scores and proportion of disadvantageous draws during the last 50 trials. As social isolation scores increased (thus indicating greater levels of isolation), disadvantageous draws in the last half of the task significantly decreased. This is the opposite of the relationship found by Ingram et al. (2021). Upon graphical inspection, it is clear this trend is being influenced by the previously COVID-19 infected group only, as the COVID-19 uninfected group has a slope near zero. In fact, a regression model excluding the COVID-19 uninfected group is still significant (p=0.015) and has a stronger R square value (0.176 as compared to 0.074); a model including only the COVID-19 uninfected group is not significant (p=0.963) (Figure 3.6D). This indicates that in the COVID-19 infected group alone is responsible for the overall trend, such that: % disadvantageous draws in the last half= 0.809 + (-0.007 * social isolation score). This finding is especially unique upon considering that the COVID-19 uninfected and previously COVID-19 infection groups did not differ in mean levels of social isolation. The present data indicates that the higher one's social isolation score was, the lower proportion of disadvantageous draws in the last half of the Iowa

Gambling Task that individual made; this trend was only observed in the previously COVID-19 infected group. For this group only, higher social isolation scores were beneficial for task performance.

This finding prompted an additional look at the dataset to determine whether there were other social isolation differences between groups on any of the cognitive measures. The only other discrepancy observed between these groups in relation to social isolation was on the total number of misses for the Vigilance task. There was a significant relationship found between number of misses and social isolation scores, but only in the COVID-19 uninfected group ($F(1, 30)=6.796$, $R^2=0.185$, $p=0.014$) and not in the previously COVID-19 infected group ($F(1, 43)=0.285$, $p=0.596$) (Figure 4.16). In other words, for the COVID-19 uninfected group, but not the previously COVID-19 infected group, as social isolation scores increased, so did number of misses, such that: number of misses= -9.269 + (0.275 * social isolation score). It is unclear why these two patterns were observed, but it importantly provides further evidence that there are potential group differences between COVID-19 uninfected and previously COVID-19 infected individuals. More specifically, social isolation may have affected these populations differently, potentially becoming either a harmful or a beneficial mechanism that differs depending on infection status and the task at hand.

4.6 SEX DIFFERENCES

For Berg's Card Sorting Task, there was a significant interaction between previous COVID-19 infection status and biological sex, with never infected males

significantly outperforming all other categories. Based on previous literature for the Wisconsin Card Sorting Task, sex differences in this direction were not anticipated. Women have either outperformed men or both men and women have been found to perform equally on CST performance (Boone et al., 1993; van den Bos et al., 2013). However, based on the current data, it is suggested that COVID-19 infection induced deficits in CST performance in males and not females; this finding had a medium effect size. Card Sorting Task performance is thought to be mediated by the ventrolateral and dorsolateral prefrontal cortex, anterior cingulate cortex, and inferior parietal lobe (Buchsbaum et al., 2005; Nagahama et al., 1996; Lie et al., 2006). It is possible that COVID-19 infection and subsequent neuroinflammation causes damage to one of these areas more severely in males than in females. However, other tasks examined that were mediated by these same brain regions did not display the same sex effect as the Card Sorting Task, so it is possible that these sex differences observed are extremely task-specific.

There was also an interaction between COVID-19 infection status and biological sex observed for the Emotional Memory task for distractor word accuracy, wherein COVID-19 uninfected males outperformed all other groups; this finding can be described as having a medium effect size. For the emotional memory task, negative, positive, and neutral words that were both targets and distractor words were presented during the recognition phase. The COVID-19 uninfected biological male group had significantly higher accuracy for determining whether a distractor word was or was not present in the initial list,

regardless of the valence of the word. It is unclear why this finding was significant; this represents the second finding where the COVID-19 uninfected biological male group outperformed all others. It is possible that this group was unintentionally comprised of high performers in a proportion that was not present in the other groups. However, the variance observed in this group among all tasks was consistent with the other 3 groups, and there were no significant outliers identified, so it is unlikely that this group is being influenced by only a few individuals. Of note, the COVID-19 uninfected biological male group was the least vaccinated proportionally than the other groups (76.9% vaccinated compared to 82.9% for female previous COVID-19 infected, 91.7% male previous COVID-19 infected, and 92% female COVID-19 uninfected), however there is no known cognitive advantages, disadvantages, or protective factors associated with COVID-19 vaccination, so this observation is potentially moot. A recent study conducted during the first year of the COVID-19 pandemic showed that aversive emotional memories were recalled and recognized at a lower rate than expected (Leon et al., 2022). While the present sample did not have any differences between COVID-19 uninfected and previously infected COVID-19 groups, there were the expected memory differences between non-emotional and emotional words. It does not seem that COVID-19 infection nor social isolation had any extra effect on emotional memory. However, these null findings should not negate the findings of others who have found that older individuals were better at emotional regulation and were more likely to report positive memories from the pandemic than younger individuals (Carstensen et al., 2020;

Ford et al., 2021). The potential effect long term effects of the pandemic on younger individuals remain to be seen, but it is possible that long-term memory (which was not assessed herein) could be affected in younger individuals more than the delayed memory task chosen.

4.7 OTHER FINDINGS AND LIMITATIONS

Cognitive tasks were chosen for inclusion based on their literature-based relationships to the cognitive constructs of interest. In general, these tasks were minimally modified versions of existing experiments that have been well studied experimentally (e.g., Change Detection) or are commonly used as part of common neuropsychological tests (e.g., Digit Span, Berg Card Sorting Task, Iowa Gambling Task).

The included measures of working memory capacity have generally shown to be reliable, both in terms of internal consistency and stability across testing sessions. Digit span is typically used as part of the Weschler Adult Intelligence Scale and has estimated internal consistency of 0.83 and a test-retest reliability of 0.65, although this varies by age group (Waters et al., 2003). Change detection has become a common task for assessing non-verbal working memory capacity and recent studies have estimated internal consistency (Cronbach's alpha) of around 0.92 and split-half reliability of between 0.76 and 0.91 (Xu et al., 2018; Dai et al., 2019). Continuous performance tasks to assess vigilance or sustained attention generally have moderate to high internal consistency (0.85) and test-retest reliability (ICC ~0.5) (Raz et al., 2014). Flanker tasks also typically have high internal consistency (0.84 to 0.94) and test-retest

reliability (ICC= .73-.82) (e.g., Paap et al., 2016). However, the Flanker task used herein, as previously mentioned, used slightly different stimuli.

Despite their widespread use, however, many of these tasks have only modest internal consistency or test-retest reliability. The Match to Sample task is used as part of multiple neuropsychological batteries and has modest test-retest reliability (0.56; Lowe et al., 1998) and an Emotional Memory task similar to the one used herein has a similar test-retest reliability of around .5 (Thomas et al., 2016). The Berg Card Sorting Task/Wisconsin Card Sorting Task is a widely used neuropsychological assessment that has reasonable internal consistency (Kopp, Lange, & Steinke, 2021) and test-retest reliability (Tate, Perdices, & Maggiotto, 1998), although it has also been shown to produce practice effects with repeated administration (Basso et al., 2001). Similarly, the sequential learning that takes place during the Iowa Gambling Task appears to result in low to moderate internal consistency and test-retest reliability (Buelow & Barnhart, 2018; Schmitz et al., 2020).

Despite the lower reliability of some of the cognitive tasks, these tasks were included due to their widespread use, both clinically and experimentally, and the relationship between their underlying cognitive constructs and other viral infections. However, it is possible that these specific tasks were not ideal for detecting the COVID-19 related cognitive changes of interest. In addition, due to the time constraints of the experiment, many of the tasks used were modified to be shorter in duration than the versions that are commonly used in the literature, which may have reduced the ability to detect differences in the task.

There was a significant, negative correlation between “days since COVID-19 infection” and number of dyslexia and number of depression symptoms. This finding indicates that the longer it has been since being infected with COVID-19, the lower the number of symptoms for dyslexia and depression one reports. This correlation provides further evidence of recovery over time, which has been observed in prior literature (Guo et al., 2022; Williams et al., 2021; Zhao et al., 2022; Mazza et al., 2021; Ferrucci et al., 2021; Kujawa et al., 2020). It is possible that our sample reflected a population that was not only completely resolved of the symptoms of active COVID-19 infection, but also potentially resolved of any PCC as well. The mean “days since COVID-19 infection” for the present sample was around 300 days, which far surpasses the timeframe seen in the majority of current PCC literature. In acute respiratory distress syndrome, cognitive impairment has been found to still have a 20% prevalence rate up to 5 years after hospital discharge (Herridge et al., 2016). While findings related to acute respiratory distress syndrome may be useful for populations that have been seriously infected with COVID-19, it is unclear how long cognitive symptoms may persist in a population that has not experienced extreme respiratory distress.

The consistent occurrence of the dyslexia assessment as an influential variable in the present analyses cannot be ignored. Presence of dyslexia or dyslexia related symptoms can affect one’s performance on certain cognitive tasks, especially those that require reading comprehension to complete the task or to understand the instructions. The regular appearance of number of dyslexia symptoms in many of the cognitive variables as a covariate prompted a closer

look at the symptoms that were most consistently selected by the present sample. The items most frequently endorsed by the sample were (starting with the most frequently endorsed):

- Do you find it difficult to remember the sense of what you have read?
- Do you take longer than you feel you should to read a page of a book?
- Do you dislike reading long books?
- Do you get confused if you speak in public?

While these items have been validated as part of the scale, these items may not traditionally meet the expected definition of dyslexia. These symptoms could simultaneously be measuring a different construct in addition to dyslexia, perhaps attention. It is also worth noting that the present sample consistently endorsed more symptoms of dyslexia than what was expected based upon the parameters of the assessment. While the original assessment predicts 40% of the sample to have more than 4 symptoms, 44% of the sample had more than 4 symptoms. The original assessment also predicts only 10% of the sample to have more than 8 symptoms, while the sample had 18% showing more than 8 symptoms. In brief, the consistent relationship between dyslexia and many of the present measures could be because the dyslexia assessment is also picking up on other domains, such as attention or social anxiety. It could also be that the individuals in the present sample may be displaying more symptoms of dyslexia than were expected due to the effects of the pandemic.

The majority (83%) of the sample for the present study was vaccinated. It should be noted that, of the previously COVID-19 infected individuals, 15 of those that were vaccinated were vaccinated before contracting COVID-19, while 24 of the vaccinated were vaccinated after contracting COVID-19. It is presently

unknown the effect that vaccination has on cognitive abilities, or the effect that it may have on recovering from potential cognitive consequences of COVID-19. Vaccination differences between the different brands available are also presently unknown. For the present sample, vaccination status had no significant effect on any cognitive or mental wellbeing measure, so the present data does not suggest that vaccination is harmful or beneficial to the variables observed.

There exists an obvious disconnect between previously reported deficits and the lack of observed deficits in the present study. Firstly, 47 individuals in the present study identified that they thought the COVID-19 pandemic had a significant effect on their cognitive abilities, with 22 of those individuals reporting that they felt those effects would last “for a long time.” Subsequent analyses showed that these groups did not perform any differently on any of the cognitive measures than those that did not believe the pandemic would have a significant effect on their cognitive abilities. As expected, the “effects will last for a long time” group consistently displayed the greatest number of symptoms for depression, dyslexia, or ADHD. It makes logical sense that the group that believes that negative effects on mental wellbeing will continue to occur for a long period of time will also have a greater of numbers of symptoms for depression and anxiety. Since ADHD is frequently comorbid with anxiety and depression, it is not surprising that this domain displayed a similar pattern (Schatz and Rostain, 2006). The “effect on mental abilities” analyses displayed a similar pattern, with the “effects will last for a long time” group displaying significantly more symptoms

of depression, dyslexia, and ADHD. These expectancies did not translate into observable deficits.

Cognitive deficits are prevalent in prior literature, but evidence for these deficits was not found in the current study. This could be for several reasons. Much of the early literature for cognitive complaints following COVID-19 relied heavily on self-report measures and anecdotal data from patients (Gordon et al., 2021; Grover et al., 2021; Davis et al., 2021; Hampshire et al., 2021). Patient self-advocacy is important and could even be uniquely responsible for helping to legitimize “long-COVID” as an illness (Callard et al., 2021). However, it is possible that patient reporting could be swayed by media misinformation or excessive worry about their infection status, thus causing them to overestimate or overanalyze their perceived deficits (Micallef et al., 2020). While resources were limited during the early pandemic stages, follow-up with validated cognitive assessments should be used in cases where patients complain of cognitive deficits, especially patients who were hospitalized or may be experiencing certain forms of “post-COVID syndrome.”

There is also the possibility that individuals who were previously infected are overestimating their “cognitive deficits” because they are underestimating themselves. The COVID-19 pandemic caused global shutdowns, which led to many individuals working from home, attending classes virtually, changing careers, or even losing their jobs. This environment change led to a shift, and oftentimes an increase, in responsibilities. The change in expectations frequently came in conjunction with decreases in supervision, immediate feedback, and

cues from workplace peers. With many individuals losing their employment or their “spots” in higher education, a sense of “survivor’s guilt” is also possible among individuals who remain in employment or higher education (Hutchins et al., 2017; Bravata et al., 2020). These factors combined create a perfect situation for the development of “Imposter Syndrome,” a phenomenon that occurs when an individual doubts their abilities and accomplishments, feels “like a fraud,” or does not feel as though they “belong” or have “earned their place”. The lack of expected benchmark assessments (i.e., assignments or coursework being restructured due to an online format) or feeling as though the information obtained from previous coursework was not retained can also contribute to feeling “like a fraud” in a degree program. The inability to compare one’s work to another student, or to receive feedback from peers, mentors, or bosses can lead to increased uncertainty in one’s own abilities. Put simply, an individual may be functioning appropriately, but without the cues from others to let them know their standing, that individual may result to holding their abilities to an impossible standard. Rates of Imposter Syndrome are thought to be on the rise due to the COVID-19 pandemic (Pownall et al., 2021; Golding, 2021).

It is also possible that the perceived deficits that individuals are self-reporting are more of an academic nature rather than a reflection of their basic cognitive skills. The inability to pay attention for long periods of time such as during reading or studying was observed in the present sample via the dyslexia assessment, and the most frequently endorsed symptom of adult ADHD was “At home, work, or school, I find my mind wandering from tasks that are

uninteresting or difficult." Potentially, the "cognitive" deficits that participants felt they had were deficits related to their academic performance (such as issues reading, taking notes, paying attention for a lengthy lecture) rather than their everyday, basic cognitive functioning (remembering a shopping list, paying attention while driving). Young adults (like the present sample) were put in a difficult position regarding their education during the COVID-19 pandemic. Many individuals completed high school virtually and were forced to choose between attending college virtually (or "hybrid") or take time off from their studies until higher education largely returned to a face-to-face format. Satisfaction with online education has been mixed even among individuals who had a choice between virtual or in-person education (Blackmon et al., 2012). Additionally, satisfaction with the learning experience has been identified as a correlate with cognitive and learning outcomes for online courses (Heckel et al., 2019). Some individuals chose to take a "gap year" before attending, or returning to, college, and others lost out on valuable learning time due to school closures in Spring of 2020 because of the COVID-19 pandemic. Long breaks from the classroom can lead to learning loss of not just course materials, but also the loss of learning strategies that could be used to acquire new information (van de Sande et al., 2018; Turner et al., 2020).

In addition, it is possible that because being a college student is an inherently cognitively demanding task, individuals who had PCC with noticeable cognitive decline as a symptom may have chosen not to enroll or reenroll in higher education, and thus were not part of the population we sampled from.

While not possible for the current study, a larger community sample of young adults may have been better able to identify changes in basic cognition after COVID-19 infection. Lastly, as discussed similarly with social isolation, it is possible that at one point the individuals in our current sample experienced cognitive symptoms that could have been associated with PCC, but at the time of testing they had recovered from those symptoms. Data collection did not begin until Fall of 2021, and by this point it is possible that participants had made a full recovery from any deficits they may have previously had outside of our testing window.

There were several factors that set the present sample apart from others that have assessed cognitive functioning post COVID-19 infection. Firstly, no participant reported hospitalization from COVID-19. Much of the research conducted thus far on the potential cognitive consequences of COVID-19 infection exclusively included previously hospitalized patients of COVID-19. In addition, no participant in the present study reported severe symptoms associated with COVID-19 infection, reported being diagnosed with PCC or Long-COVID, nor did any participant require oxygen treatment. The present sample represents mildly infected individuals who were able to recover outside of a hospital, which is relevant as severity of infection has been heavily implicated in severity of deficits seen at a later time point. The present research provides more data to support that mildly infected individuals do not tend to display severe deficits, especially when they've been given time to recover. No participant indicated suffering from PCC. This could be for several reasons. PCC is not

consistently diagnosed, and PCC does not have a current, agreed upon definition. Therefore, even if participants went to a clinician with symptoms that could be consistent with PCC, those symptoms may be ignored or misdiagnosed. It is worth noting that, in the present sample, fatigue (as assessed by question 17 from the Beck Depression Inventory) was endorsed at similar rates between previously COVID-19 infected and COVID-19 uninfected, with 33% and 30% endorsing option 1, 48% and 46% endorsing option 2, 17% and 18% for option 3, and 0% and 4% for option 4. However, despite our sample not claiming a diagnosis of Long-COVID or PCC, nor endorsing fatigue at an increased rate, the possibility that our sample was comprised of individuals with PCC cannot be ruled out. In the future, studies should include a questionnaire for participants to complete that assesses them for PCC, as a division of a previously COVID-19 group based upon the presence of lingering symptoms post infection would create more valuable results.

A second strength of the current project is that the present sample consists of young adults, which taps into a segment of the population that has not been as extensively tested regarding COVID-19 infection. The lack of extensive significant findings in the present research may also reflect the plasticity of the developing brain to overcome damage that may be causing PCC.

There are several important limitations to consider when it comes to the present study. Firstly, the sample size was likely not sufficient to detect group differences, particularly when stratified by sex. As mentioned above, due to difficulty recruiting enough participants, it is possible that we were unable to

detect effects in our data. Moreover, the sample itself could have been more diverse regarding biological sex, race, and ethnicity. Statistical analyses stratified by race and ethnicity could not be reliably conducted due to the low amount of individuals in certain groups. The effect sizes that were found in the limited significant findings were of a medium size with few statistically significant findings; it is possible that with more subjects new statistically significant results could have emerged. The present study did not target certain participants to recruit (i.e., participants of a certain COVID-19 infection status or participants of a certain biological sex). This was done to increase the sample size as much as possible, but a more targeted approach to recruitment could have better balanced the planned groups. The present study was also unable to obtain pre- and post-infection measures, nor were we able to obtain pre- and post-pandemic measures.

Certain factors were not assessed in the present study, as they were outside of the scope of the research. However, they are important factors nonetheless, and they may contribute in an important way to potential changes between groups. Socioeconomic status, employment status (or employment loss due to the pandemic), education achievements or delays, and deaths of loved ones are all relevant factors to consider if one hopes to truly encompass the effects the pandemic, global shutdowns and lockdowns, and social isolation may have had on an individual, their family, and their community. Future research should include items to assess these important factors that can affect the individual.

The cognitive testing of the study itself lasted approximately one hour. The tasks changed frequently and required a variety of inputs, which assisted in keeping participants interested and engaged with the task. However, all participants may not have been diligent and attentive to the tasks at hand. This is seen most prominently in the Iowa Gambling task, where many individuals were automatically removed from the task for not engaging with it properly. Participants were permitted to take breaks or leave the testing room between tasks if they so desired, but very few of the participants chose to take any breaks and most instead preferred to continue with the experiment without breaks. Data on fatigue of the participant, both before and after cognitive testing, was not collected. Future research should carefully consider the downsides of long-form testing, especially in a population that may be inordinately suffering from fatigue. Other individual differences, such as the amount of sleep obtained recently, caffeine consumption, or medication adherence (or non-adherence) are also known to influence performance on cognitive tasks. Future research should perhaps aim to exclude or otherwise statistically account for participants who do not meet certain “alertness” criteria. The cognitive assessments used, while spanning many difference facets and domains of cognition, did not cover all areas; prospective memory, social cognition, and long-term memory are examples of cognitive domains that are equally important to quality of life and could be assessed in future research.

An additional limitation is the unpredictable nature of the COVID-19 pandemic. During the planning and execution phase of the present project,

restrictions have changed drastically, and new information is learned about COVID-19 daily. In the past year alone, many individuals have gone from a place of instability and worry to one of assurance and normalcy. For some, families have been restructured, jobs have been lost, and important lives have been taken by COVID-19. These changes will have a long-lasting impact on the mental wellbeing of many individuals. However, hope for many has come from the relative “re-opening” of society, the return to face-to-face lectures and meetings, or the ability to travel and visit with friends and family without restriction. In general, the “return to normal” for many individuals may have alleviated any potential deficits that could have manifested because of longer restrictions and periods of social isolation.

Concerning COVID-19 itself, many new variants have been discovered since its initial identification. There is currently no quick and easy method to test which variant an individual has been infected with, so the variant that an individual has been infected with is up for speculation unless additional lab testing is performed. If an easier and quicker way to identify COVID-19 strain is developed, then strain differences should be examined to determine whether the strain someone was infected with may influence their long-term health outcome. However, for the present study, COVID-19 strain differences were not known. It is also unknown what the long-term effects of the COVID-19 virus may have on the body and brain. There is potential for the COVID-19 virus to lay dormant and later “reactive,” similar to Herpes Zoster, although no evidence has yet supported

this possibility. Even so, at present the COVID-19 virus is still incredibly new, and long-term effects cannot be known.

It is unknown whether American society will again see the same levels of quarantine, social isolation, and fear that was observed during the initial years of the COVID-19 pandemic. It is possible that the surfacing of a new strain of COVID-19 could again force individuals into social isolation. While the present study showed that the social isolation experienced by many during the COVID-19 pandemic did not have as extensive of an influence as was previously thought, it is entirely unknown what effects could manifest with a similar “shut down” so soon after the previous one. It is worth noting that many participants in the present study indicated that they believed the pandemic will affect them both mentally and cognitively “for a long time,” despite all of the data collection occurring when their university and surrounding city of Columbia, SC, was relatively “open.”

4.8 CONCLUSIONS

The prominence of the many null findings in the present research provides hope for those that were, or may be in the future, mildly infected with COVID-19. While many individuals self-report deficits in their cognitive abilities, these deficits were largely not measurable in the present sample. Ongoing cognitive deficits seem to be most prevalent in individuals who were hospitalized or older, which were two populations that were not represented in the present sample. Unique attention by researchers and health professionals should be allotted to individuals who perceive cognitive deficits but show no evidence of them; these

individuals may instead be suffering from poor mental health. As the COVID-19 pandemic has continued, the view of the COVID-19 virus has been constantly adapting, and new discoveries (such as vaccination) have changed the landscape of the disease. While cognitive deficits and other symptoms of PCC are of particular concern in specific populations and during certain stages of COVID-19 infection, the current findings provide limited evidence for such deficits in mildly infected young adults that have had a sufficient time to recover from viral infection.

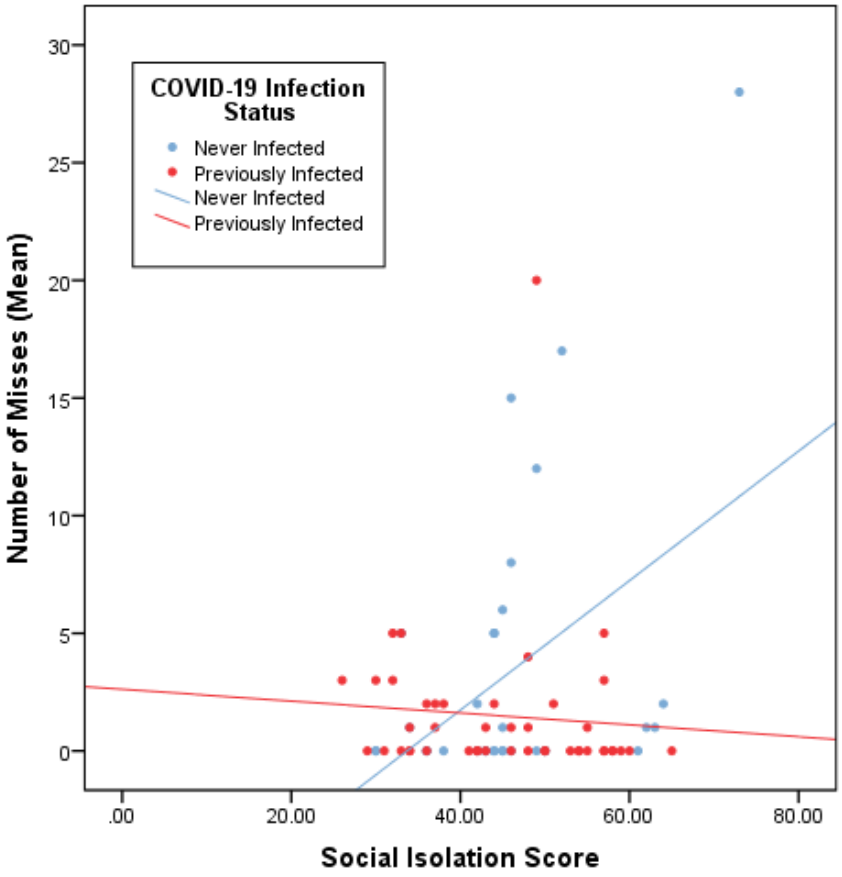

Figure 4.1. Scatterplot of social isolation scores and number of misses during the Iowa Gambling Task.

REFERENCES

Aleman, A., & van't Wout, M. (2008). Repetitive transcranial magnetic stimulation over the right dorsolateral prefrontal cortex disrupts digit span task performance. *Neuropsychobiology*, *57*(1-2), 44-48.

Alemanno, F., Houdayer, E., Parma, A., Spina, A., Del Forno, A., Scatolini, A., ... & Iannaccone, S. (2021). COVID-19 cognitive deficits after respiratory assistance in the subacute phase: A COVID-rehabilitation unit experience. *Plos one*, *16*(2), e0246590.

Alkodaymi, M. S., Omrani, O. A., Fawzy, N. A., Abou Shaar, B., Almamlouk, R., Riaz, M., ... & Tleyjeh, I. M. (2022). Prevalence of post-acute COVID-19 syndrome symptoms at different follow-up periods: A systematic review and meta-analysis. *Clinical Microbiology and Infection*.

Almeria, M., Cejudo, J. C., Sotoca, J., Deus, J., & Krupinski, J. (2020). Cognitive profile following COVID-19 infection: Clinical predictors leading to neuropsychological impairment. *Brain, behavior, & immunity-health*, *9*, 100163.

Almutairi, M. A. (2016). Awareness about middle east respiratory syndrome-corona virus (mers-cov) among dental students in Riyadh, Saudi Arabia. *Pakistan Oral & Dental Journal*, *36*(3).

Andrews, M. G., Mukhtar, T., Eze, U. C., Simoneau, C. R., Ross, J., Parikshak, N., ... & Kriegstein, A. R. (2022). Tropism of SARS-CoV-2 for human

cortical astrocytes. *Proceedings of the National Academy of Sciences*, *119*(30), e2122236119.

Antinori, A., Arendt, G., Becker, J. T., Brew, B. J., Byrd, D. A., Cherner, M., ... & Wojna, V. E. (2007). Updated research nosology for HIV-associated neurocognitive disorders. *Neurology*, *69*(18), 1789-1799.

Arbour, N., Day, R., Newcombe, J., & Talbot, P. J. (2000). Neuroinvasion by human respiratory coronaviruses. *Journal of virology*, *74*(19), 8913-8921.

Atwood, W. J., Berger, J. R., Kaderman, R., Tornatore, C. S., & Major, E. O. (1993). Human immunodeficiency virus type 1 infection of the brain. *Clinical Microbiology Reviews*, *6*(4), 339-366.

Awh, E., Vogel, E. K., & Oh, S. H. (2006). Interactions between attention and working memory. *Neuroscience*, *139*(1), 201-208.

Baliyan, S., Cimadevilla, J. M., de Vidania, S., Pulopulos, M. M., Sandi, C., & Venero, C. (2021). Differential susceptibility to the Impact of the COVID-19 pandemic on working memory, empathy, and perceived stress: The Role of cortisol and resilience. *Brain sciences*, *11*(3), 348.

Baron-Cohen, S., Wheelwright, S., Skinner, R., Martin, J., & Clubley, E. (2001). The autism-spectrum quotient (AQ): Evidence from asperger syndrome/high-functioning autism, malesand females, scientists and mathematicians. *Journal of autism and developmental disorders*, *31*(1), 5-17.

Bartlett, M. S. (1954). A further note on the multiplying factors for various chi-square approximations in factor analysis. Journal of the Royal Statistical Society, Series B, 16, 296-298.

Baschenis, I. M. C., Farinotti, L., Zavani, E., Grumi, S., Bernasconi, P., Rosso, E., ... & Chiappedi, M. (2021). Reading skills of children with dyslexia improved less than expected during the COVID-19 lockdown in Italy. *Children*, *8*(7), 560.

Basso, M. R., Lowery, N., Ghormley, C., & Bornstein, R. A. (2001) Practice Effects on the Wisconsin Card Sorting Test–64 Card Version Across 12 Months, The Clinical Neuropsychologist, 15:4, 471-478.

Bauer, L., Lendemeijer, B., Leijten, L., Embregts, C. W., Rockx, B., Kushner, S. A., ... & van Riel, D. (2021). Replication kinetics, cell tropism, and associated immune responses in SARS-CoV-2-and H5N1 virus-infected human induced pluripotent stem cell-derived neural models. *Msphere*, *6*(3), e00270-21.

Beck, A. T., Epstein, N., Brown, G., & Steer, R. A. (1988). An inventory for measuring clinical anxiety: psychometric properties. *Journal of consulting and clinical psychology*, *56*(6), 893.

Beck, D. M., Rees, G., Frith, C. D., & Lavie, N. (2001). Neural correlates of change detection and change blindness. *Nature neuroscience*, *4*(6), 645-650.

Becker, J. H., Lin, J. J., Doernberg, M., Stone, K., Navis, A., Festa, J. R., & Wisnivesky, J. P. (2021). Assessment of cognitive function in patients after COVID-19 infection. *JAMA network open*, *4*(10), e2130645-e2130645.

Blackmon, S. J., & Major, C. (2012). STUDENT EXPERIENCES IN ONLINE COURSES A Qualitative Research Synthesis. *Quarterly Review of Distance Education*, *13*(2).

Bland, A. R., Roiser, J. P., Mehta, M. A., Sahakian, B. J., Robbins, T. W., & Elliott, R. (2022). The impact of COVID-19 social isolation on aspects of emotional and social cognition. *Cognition and Emotion*, *36*(1), 49-58.

Blomberg, B., Mohn, K. G. I., Brokstad, K. A., Zhou, F., Linchausen, D. W., Hansen, B. A., ... & Langeland, N. (2021). Long COVID in a prospective cohort of home-isolated patients. *Nature medicine*, *27*(9), 1607-1613.

Boldrini, M., Canoll, P. D., & Klein, R. S. (2021). How COVID-19 affects the brain. *JAMA psychiatry*, *78*(6), 682-683.

Boone, K. B., Ghaffarian, S., Lesser, I. M., Hill-Gutierrez, E., & G. Berman, N. (1993). Wisconsin Card Sorting Test performance in healthy, older adults: Relationship to age, sex, education, and IQ. *Journal of Clinical Psychology*, *49*(1), 54-60.

Bougakov, D., Podell, K., & Goldberg, E. (2021). Multiple neuroinvasive pathways in COVID-19. *Molecular neurobiology*, *58*(2), 564-575.

Bowen, H. J., Kark, S. M., & Kensinger, E. A. (2018). NEVER forget: negative emotional valence enhances recapitulation. *Psychonomic bulletin & review*, *25*(3), 870-891.

Bravata, D. M., Watts, S. A., Keefer, A. L., Madhusudhan, D. K., Taylor, K. T., Clark, D. M., ... & Hagg, H. K. (2020). Prevalence, predictors, and treatment of impostor syndrome: a systematic review. *Journal of General Internal Medicine*, *35*(4), 1252-1275.

Brod, M., Schmitt, E., Goodwin, M., Hodgkins, P., & Niebler, G. (2012). ADHD burden of illness in older adults: a life course perspective. *Quality of Life Research*, *21*(5), 795-799.

Buchsbaum, B. R., Greer, S., Chang, W. L., & Berman, K. F. (2005). Meta-analysis of neuroimaging studies of the Wisconsin Card-Sorting task and component processes. *Human brain mapping*, *25*(1), 35-45.

Buelow, M.T. & Barnhart, W.R. (2018). Test–Retest Reliability of Common Behavioral Decision Making Tasks, *Archives of Clinical Neuropsychology*, 33(1), 125-129.

Bulfamante, G., Bocci, T., Falleni, M., Campiglio, L., Coppola, S., Tosi, D., ... & Priori, A. (2021). Brainstem neuropathology in two cases of COVID-19: SARS-CoV-2 trafficking between brain and lung. *Journal of Neurology*, *268*(12), 4486-4491.

Bullen, C. K., Hogberg, H. T., Bahadirli-Talbott, A., Bishai, W. R., Hartung, T., Keuthan, C., ... & Smirnova, L. (2020). Infectability of human BrainSphere neurons suggests neurotropism of SARS-CoV-2. *ALTEX-Alternatives to animal experimentation*, *37*(4), 665-671.

Bunders, M. J., & Altfeld, M. (2020). Implications of sex differences in immunity for SARS-CoV-2 pathogenesis and design of therapeutic interventions. *Immunity*, *53*(3), 487-495.

Cagnazzo, F., Arquizan, C., Derraz, I., Dargazanli, C., Lefevre, P. H., Riquelme, C., ... & Costalat, V. (2021). Neurological manifestations of patients infected with the SARS-CoV-2: a systematic review of the literature. *Journal of neurology*, *268*(8), 2656-2665.

Cai, X., Hu, X., Ekumi, I. O., Wang, J., An, Y., Li, Z., & Yuan, B. (2020). Psychological distress and its correlates among COVID-19 survivors during early convalescence across age groups. *The American journal of geriatric psychiatry*, *28*(10), 1030-1039.

Callard, F., & Perego, E. (2021). How and why patients made Long Covid. *Social science & medicine*, *268*, 113426.

Carroll, A., & Brew, B. (2017). HIV-associated neurocognitive disorders: recent advances in pathogenesis, biomarkers, and treatment. *F1000Research*, *6*.

Carstensen, L. L., Shavit, Y. Z., & Barnes, J. T. (2020). Age advantages in emotional experience persist even under threat from the COVID-19 pandemic. *Psychological Science*, *31*(11), 1374-1385.

Carvalho, T., Krammer, F., & Iwasaki, A. (2021). The first 12 months of COVID-19: a timeline of immunological insights. *Nature Reviews Immunology*, *21*(4), 245-256.

Ceban, F., Ling, S., Lui, L. M., Lee, Y., Gill, H., Teopiz, K. M., ... & 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.

Centers for Disease Control and Prevention. Anxiety and Depression Household Pulse Survey. Atlanta, GA: US Department of Health and Human Services, CDC; 2022, June 27th. https://www.cdc.gov/nchs/covid19/pulse/mental-health.htm

Centers for Disease Control and Prevention. COVID Data Tracker. Atlanta, GA: US Department of Health and Human Services, CDC; 2022, June 27. https://covid.cdc.gov/covid-data-tracker

Centers for Disease Control and Prevention. What You Need to Know About Variants. Atlanta, GA:US Department of Health and Human Services, CDC; 2022, June 27. https://www.cdc.gov/coronavirus/2019-ncov/variants/about-variants.html

Centers for Disease Control and Prevention: Long COVID or Post-COVID Conditions. Atlanta, GA:US Department of Health and Human Services, CDC; 2022, July 19th. https://www.cdc.gov/coronavirus/2019-ncov/long-term-effects/index.html

Chang, L., Jiang, C., Cunningham, E., Buchthal, S., Douet, V., Andres, M., & Ernst, T. (2014). Effects of APOE ε4, age, and HIV on glial metabolites and cognitive deficits. *Neurology*, *82*(24), 2213-2222.

Chang, L., Løhaugen, G. C., Douet, V., Miller, E. N., Skranes, J., & Ernst, T. (2016). Neural correlates of working memory training in HIV patients: study protocol for a randomized controlled trial. *Trials*, *17*(1), 1-15.

Chen, C., Haupert, S. R., Zimmermann, L., Shi, X., Fritsche, L. G., & Mukherjee, B. (2022). Global Prevalence of Post COVID-19 Condition or Long COVID: A Meta-Analysis and Systematic Review. *The Journal of Infectious Diseases*.

Choi, E. P. H., Hui, B. P. H., & Wan, E. Y. F. (2020). Depression and anxiety in Hong Kong during COVID-19. *International journal of environmental research and public health*, *17*(10), 3740.

Cinini, S. M., Barnabe, G. F., Galvão-Coelho, N., de Medeiros, M. A., Perez-Mendes, P., Sousa, M. B., ... & Mello, L. E. (2014). Social isolation disrupts hippocampal neurogenesis in young non-human primates. *Frontiers in neuroscience*, *8*, 45.

Cirillo, R. A., Horel, J. A., & George, P. J. (1989). Lesions of the anterior temporal stem and the performance of delayed match-to-sample and visual discriminations in monkeys. *Behavioural Brain Research*, *34*(1-2), 55-69.

Courtet, P., Olié, E., Debien, C., & Vaiva, G. (2020). Keep socially (but not physically) connected and carry on: preventing suicide in the age of COVID-19. *The Journal of clinical psychiatry*, *81*(3), 15527.

COVID-19 rapid guideline: managing the long-term effects of COVID-19. (2020). National Institute for Health and Care Excellence (NICE).

Cowan, N. (2010). The magical mystery four: How is working memory capacity limited, and why?. *Current directions in psychological science*, *19*(1), 51-57.

Crivelli, L., Palmer, K., Calandri, I., Guekht, A., Beghi, E., Carroll, W., ... & Kivipelto, M. (2022). Changes in cognitive functioning after COVID-19: A systematic review and meta-analysis. *Alzheimer's & Dementia*.

Czeisler MÉ , Lane RI, Petrosky E, et al. Mental Health, Substance Use, and Suicidal Ideation During the COVID-19 Pandemic — United States, June 24–30, 2020. MMWR Morb Mortal Wkly Rep 2020;69:1049–1057. DOI: http://dx.doi.org/10.15585/mmwr.mm6932a1

Dai, M., Li, Y., Gan, S., & Du, F. (2019). The reliability of estimating visual working memory capacity. *Scientific reports*, *9*(1), 1-8.

Daniel, T. A., Katz, J. S., & Robinson, J. L. (2016). Delayed match-to-sample in working memory: A BrainMap meta-analysis. *Biological Psychology*, *120*, 10-20.

Davis, C. W., Nguyen, H. Y., Hanna, S. L., Sánchez, M. D., Doms, R. W., & Pierson, T. C. (2006). West Nile virus discriminates between DC-SIGN and DC-SIGNR for cellular attachment and infection. *Journal of virology*, *80*(3), 1290-1301.

Davis, H. E., Assaf, G. S., McCorkell, L., Wei, H., Low, R. J., Re'em, Y., ... & Akrami, A. (2021). Characterizing long COVID in an international cohort: 7 months of symptoms and their impact. *EClinicalMedicine*, *38*, 101019.

De Chiara, G., Piacentini, R., Fabiani, M., Mastrodonato, A., Marcocci, M. E., Limongi, D., ... & Palamara, A. T. (2019). Recurrent herpes simplex virus-1 infection induces hallmarks of neurodegeneration and cognitive deficits in mice. *PLoS pathogens*, *15*(3), e1007617.

de Melo, G. D., Lazarini, F., Levallois, S., Hautefort, C., Michel, V., Larrous, F., ... & Lledo, P. M. (2021). COVID-19–related anosmia is associated with viral persistence and inflammation in human olfactory epithelium and brain infection in hamsters. *Science translational medicine*, *13*(596), eabf8396.

Del Corral, T., Menor-Rodríguez, N., Fernández-Vega, S., Díaz-Ramos, C., Aguilar-Zafra, S., & López-de-Uralde-Villanueva, I. (2022). Longitudinal study of changes observed in quality of life, psychological state cognition and pulmonary and functional capacity after COVID-19 infection: A six-to seven-month prospective cohort. *Journal of Clinical Nursing*.

Ding, H., Yin, S., Cheng, Y., Cai, Y., Huang, W., & Deng, W. (2020). Neurologic manifestations of nonhospitalized patients with COVID-19 in Wuhan, China. *MedComm*, *1*(2), 253.

do Carmo Filho, A., van Duinkerken, E., Tolentino, J. C., & Schmidt, S. L. (2022). Attention profile of physically recovered COVID-19 inpatients on the day of discharge. *Journal of Psychiatric Research*, *150*, 189-196.

Dondaine, T., Ruthmann, F., Vuotto, F., Carton, L., Gelé, P., Faure, K., ... & Bordet, R. (2022). Long-term cognitive impairments following COVID-19: a possible impact of hypoxia. *Journal of Neurology*, 1-8.

Elbay, R. Y., Kurtulmuş, A., Arpacıoğlu, S., & Karadere, E. (2020). Depression, anxiety, stress levels of physicians and associated factors in Covid-19 pandemics. *Psychiatry research*, *290*, 113130.

Engle, R. W. (2002). Working memory capacity as executive attention. *Current directions in psychological science*, *11*(1), 19-23.

Erickson, M. A., Dohi, K., & Banks, W. A. (2012). Neuroinflammation: a common pathway in CNS diseases as mediated at the blood-brain barrier. *Neuroimmunomodulation*, *19*(2), 121-130.

Evans, I. E., Llewellyn, D. J., Matthews, F. E., Woods, R. T., Brayne, C., Clare, L., & CFAS-Wales Research Team. (2018). Social isolation, cognitive reserve, and cognition in healthy older people. *PloS one*, *13*(8), e0201008.

Fernández-de-Las-Peñas, C., Martín-Guerrero, J. D., Pellicer-Valero, Ó. J., Navarro-Pardo, E., Gómez-Mayordomo, V., Cuadrado, M. L., ... & Arendt-Nielsen, L. (2022). Female sex is a risk factor associated with long-term post-COVID related-symptoms but not with COVID-19 symptoms: The LONG-COVID-EXP-CM multicenter study. *Journal of clinical medicine*, *11*(2), 413.

Ferrucci, R., Dini, M., Groppo, E., Rosci, C., Reitano, M. R., Bai, F., ... & Priori, A. (2021). Long-lasting cognitive abnormalities after COVID-19. *Brain Sciences*, *11*(2), 235.

Ferrucci, R., Dini, M., Rosci, C., Capozza, A., Groppo, E., Reitano, M. R., ... & Priori, A. (2022). One-year cognitive follow-up of COVID-19 hospitalized patients. *European Journal of Neurology*.

Fone, K. C., & Porkess, M. V. (2008). Behavioural and neurochemical effects of post-weaning social isolation in rodents—relevance to developmental neuropsychiatric disorders. *Neuroscience & Biobehavioral Reviews*, *32*(6), 1087-1102.

Ford, J. H., Garcia, S. M., Fields, E. C., Cunningham, T. J., & Kensinger, E. A. (2021). Older adults remember more positive aspects of the COVID-19 pandemic. *Psychology and Aging*, *36*(6), 694.

Fromm, N. M., Salisbury, D. B., Driver, S. J., Dahdah, M. N., & Monden, K. R. (2015). Functional recovery from neuroinvasive West Nile Virus: A tale of two courses. *Rehabilitation Psychology*, *60*(4), 383.

Frontera, J. (2021, July 14-15). Neurovascular events in COVID-19. NIH Neurologic and Psychiatric Effects of SARS-CoV-2 Meeting, virtual. https://www.nimh.nih.gov/news/media/2021/neurologic-and-psychiatric-effects-of-sars-cov-2-meeting-day-1

Fukuda, K., & Vogel, E. K. (2019). Visual short-term memory capacity predicts the “bandwidth” of visual long-term memory encoding. *Memory & cognition*, *47*(8), 1481-1497.

Galea, S., Merchant, R. M., & Lurie, N. (2020). The mental health consequences of COVID-19 and physical distancing: the need for prevention and early intervention. *JAMA internal medicine*, *180*(6), 817-818.

Gandhi, S., Srivastava, A. K., Ray, U., & Tripathi, P. P. (2020). Is the collapse of the respiratory center in the brain responsible for respiratory breakdown in COVID-19 patients?. *ACS chemical neuroscience*, *11*(10), 1379-1381.

Garg, M., Maralakunte, M., Garg, S., Dhooria, S., Sehgal, I., Bhalla, A. S., ... & Sandhu, M. S. (2021a). The conundrum of ‘long-COVID-19: a narrative review. *International journal of general medicine*, *14*, 2491.

Garg, R. K., Paliwal, V. K., & Gupta, A. (2021b). Encephalopathy in patients with COVID-19: a review. *Journal of Medical Virology, 93*(1), 206-222.

Geva, S., Truneh, T., Seghier, M. L., Hope, T. M., Leff, A. P., Crinion, J. T., ... & Price, C. J. (2021). Lesions that do or do not impair digit span: a study of 816 stroke survivors. *Brain communications*, *3*(2), fcab031.

Gnann, J. W., & Whitley, R. J. (2017). Herpes simplex encephalitis: an update. *Current infectious disease reports*, *19*(3), 1-12.

Golding, J. (2021). Flexible learner or imposter? Learning A Level mathematics in England through the COVID-19 pandemic. *Teaching Mathematics and its Applications: An International Journal of the IMA*, *40*(4), 263-276.

Gomes, I., Karmirian, K., Oliveira, J. T., da SG Pedrosa, C., Mendes, M. A., Rosman, F. C., ... & Rehen, S. (2021). SARS-CoV-2 infection of the central nervous system in a 14-month-old child: a case report of a complete autopsy. *The Lancet Regional Health-Americas*, *2*, 100046.

Gordon, M. N., Heneka, M. T., Le Page, L. M., Limberger, C., Morgan, D., Tenner, A. J., ... & Willette, S. A. (2022). Impact of COVID-19 on the Onset and Progression of Alzheimer's Disease and Related Dementias: A Roadmap for Future Research. *Alzheimer's & Dementia*, *18*(5), 1038-1046.

Graham, E. L., Clark, J. R., Orban, Z. S., Lim, P. H., Szymanski, A. L., Taylor, C., ... & Koralnik, I. J. (2021). Persistent neurologic symptoms and cognitive dysfunction in non-hospitalized Covid-19 “long haulers”. *Annals of clinical and translational neurology*, *8*(5), 1073-1085.

Grover, S., Sahoo, S., Mishra, E., Gill, K. S., Mehra, A., Nehra, R., ... & Puri, G. D. (2021). Fatigue, perceived stigma, self-reported cognitive deficits and psychological morbidity in patients recovered from COVID-19 infection. *Asian journal of psychiatry*, *64*, 102815.

Gu, J., Gong, E., Zhang, B., Zheng, J., Gao, Z., Zhong, Y., ... & Leong, A. S. Y. (2005). Multiple organ infection and the pathogenesis of SARS. *The Journal of experimental medicine*, *202*(3), 415-424.

Gu, J., Gong, E., Zhang, B., Zheng, J., Gao, Z., Zhong, Y., ... & Leong, A. S. Y. (2005). Multiple organ infection and the pathogenesis of SARS. *The Journal of experimental medicine*, *202*(3), 415-424.

Guadarrama-Ortiz, P., Choreño-Parra, J. A., Sánchez-Martínez, C. M., Pacheco-Sanchez, F. J., Rodriguez-Nava, A. I., & Garcia-Quintero, G. (2020). Neurological aspects of SARS-CoV-2 infection: mechanisms and manifestations. *Frontiers in Neurology*, *11*, 1039.

Guo, P., Benito Ballesteros, A., Yeung, S. P., Liu, R., Saha, A., Curtis, L., ... & Cheke, L. G. (2022). COVCOG 2: Cognitive and Memory Deficits in Long COVID: A Second Publication From the COVID and Cognition Study. *Frontiers in aging neuroscience*, *14*.

Guo, Q., Zheng, Y., Shi, J., Wang, J., Li, G., Li, C., ... & Yang, Z. (2020). Immediate psychological distress in quarantined patients with COVID-19 and its association with peripheral inflammation: a mixed-method study. *Brain, behavior, and immunity*, *88*, 17-27.

Habeck, C., Rakitin, B. C., Moeller, J., Scarmeas, N., Zarahn, E., Brown, T., & Stern, Y. (2004). An event-related fMRI study of the neurobehavioral impact of sleep deprivation on performance of a delayed-match-to-sample task. *Cognitive brain research*, *18*(3), 306-321.

Hampshire, A., Trender, W., Chamberlain, S. R., Jolly, A. E., Grant, J. E., Patrick, F., ... & Mehta, M. A. (2021). Cognitive deficits in people who have recovered from COVID-19. *EClinicalMedicine*, *39*, 101044.

Han, Y., Yang, L., Kim, T. W., Nair, M. S., Harschnitz, O., Wang, P., ... & Chen, S. (2021). SARS-CoV-2 infection causes dopaminergic neuron senescence. *Research Square*.

Hang, W., Chen, C., Zhang, X. A., & Wang, D. W. (2021). Endothelial dysfunction in COVID-19 calls for immediate attention: the emerging roles of the endothelium in inflammation caused by SARS-CoV-2. *Frontiers of Medicine*, *15*(4), 638-643.

Hao, F., Tan, W., Jiang, L. I., Zhang, L., Zhao, X., Zou, Y., ... & Tam, W. (2020). Do psychiatric patients experience more psychiatric symptoms during COVID-19 pandemic and lockdown? A case-control study with service and research implications for immunopsychiatry. *Brain, behavior, and immunity*, *87*, 100-106.

Hao, F., Tan, W., Jiang, L. I., Zhang, L., Zhao, X., Zou, Y., ... & Tam, W. (2020). Do psychiatric patients experience more psychiatric symptoms during COVID-19 pandemic and lockdown? A case-control study with service and

research implications for immunopsychiatry. *Brain, behavior, and immunity*, *87*, 100-106.

Hart, J., Tillman, G., Kraut, M. A., Chiang, H. S., Strain, J. F., Li, Y., ... & Whitley, R. J. (2014). West Nile virus neuroinvasive disease: neurological manifestations and prospective longitudinal outcomes. *BMC infectious diseases*, *14*(1), 1-10.

Hawkes, M. A., Hocker, S. E., & Leis, A. A. (2018). West Nile virus induces a post-infectious pro-inflammatory state that explains transformation of stable ocular myasthenia gravis to myasthenic crises. *Journal of the neurological sciences*, *395*, 1-3.

He, H., Sharer, L. R., Chao, W., Gu, C. J., Borjabad, A., Hadas, E., ... & Volsky, D. J. (2014). Enhanced human immunodeficiency virus Type 1 expression and neuropathogenesis in knockout mice lacking Type I interferon responses. *Journal of Neuropathology & Experimental Neurology*, *73*(1), 59-71.

Heckel, C., & Ringeisen, T. (2019). Pride and anxiety in online learning environments: Achievement emotions as mediators between learners' characteristics and learning outcomes. *Journal of Computer Assisted Learning*, *35*(5), 667-677.

Helms, J., Kremer, S., Merdji, H., Clere-Jehl, R., Schenck, M., Kummerlen, C., ... & Meziani, F. (2020). Neurologic features in severe SARS-CoV-2 infection. *New England Journal of Medicine*, *382*(23), 2268-2270.

Herridge, M. S., Moss, M., Hough, C. L., Hopkins, R. O., Rice, T. W., Bienvenu, O. J., & Azoulay, E. (2016). Recovery and outcomes after the acute respiratory distress syndrome (ARDS) in patients and their family caregivers. *Intensive care medicine*, *42*(5), 725-738.

Hinkin, C. H., Stefaniak, M. B., Castellon, S. A., Lam, M. N., Hardy, D., Zolnikov, B., & Durvasula, R. S. (2000). Executive dysfunction in HIV-1 infection. *Archives of Clinical Neuropsychology*, *8*(15), 717.

Hoshi, Y., Oda, I., Wada, Y., Ito, Y., Yamashita, Y., Oda, M., ... & Tamura, M. (2000). Visuospatial imagery is a fruitful strategy for the digit span backward task: a study with near-infrared optical tomography. *Cognitive brain research*, *9*(3), 339-342.

Hoste, L., Van Paemel, R., & Haerynck, F. (2021). Multisystem inflammatory syndrome in children related to COVID-19: a systematic review*. European journal of pediatrics, 180*(7), 2019-2034.

Huang, C., Wang, Y., Li, X., Ren, L., Zhao, J., Hu, Y., ... & Cao, B. (2020). Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The lancet*, *395*(10223), 497-506.

Hueston, C. M., Cryan, J. F., & Nolan, Y. M. (2017). Adolescent social isolation stress unmasks the combined effects of adolescent exercise and adult inflammation on hippocampal neurogenesis and behavior. *Neuroscience*, *365*, 226-236.

Hughes, J. M., Wilson, M. E., & Sejvar, J. J. (2007). The long-term outcomes of human West Nile virus infection. *Clinical infectious diseases*, *44*(12), 1617-1624.

Hugon, J. (2022). Long-COVID: Cognitive deficits (brain fog) and brain lesions in non–hospitalized patients. *Presse Medicale* (*Paris, France: 1983)*, *51*(2), 104090.

Hutchins, H. M., & Rainbolt, H. (2017). What triggers imposter phenomenon among academic faculty? A critical incident study exploring antecedents, coping, and development opportunities. *Human Resource Development International*, *20*(3), 194-214.

Hyland, P., Shevlin, M., McBride, O., Murphy, J., Karatzias, T., Bentall, R. P., ... & Vallières, F. (2020). Anxiety and depression in the Republic of Ireland during the COVID-19 pandemic. *Acta Psychiatrica Scandinavica*, *142*(3), 249-256.

Ibi, D., Takuma, K., Koike, H., Mizoguchi, H., Tsuritani, K., Kuwahara, Y., ... & Yamada, K. (2008). Social isolation rearing-induced impairment of the hippocampal neurogenesis is associated with deficits in spatial memory and emotion-related behaviors in juvenile mice. *Journal of neurochemistry*, *105*(3), 921-932.

Ingram, J., Hand, C. J., & Maciejewski, G. (2021). Social isolation during COVID-19 lockdown impairs cognitive function. *Applied Cognitive Psychology*, *35*(4), 935-947.

Ismail, I. I., Kamel, W. A., & Al-Hashel, J. Y. (2021). Association of COVID-19 pandemic and rate of cognitive decline in patients with dementia and mild cognitive impairment: a cross-sectional study. *Gerontology and Geriatric Medicine*, *7*, 23337214211005223.

Jackson-Koku, G. (2016). Beck depression inventory. *Occupational Medicine*, *66*(2), 174-175.

Jacobs, J. L., Bain, W., Naqvi, A., Staines, B., Castanha, P. M., Yang, H., ... & Mellors, J. W. (2022). Severe acute respiratory syndrome coronavirus 2 viremia is associated with coronavirus disease 2019 severity and predicts clinical outcomes. *Clinical Infectious Diseases*, *74*(9), 1525-1533.

Jamieson, G. A., Maitland, N. J., Wilcock, G. K., Yates, C. M., & Itzhaki, R. F. (1992). Herpes simplex virus type 1 DNA is present in specific regions of brain from aged people with and without senile dementia of the Alzheimer type. *The Journal of pathology*, *167*(4), 365-368.

JASP Team (2022). JASP (Version 0.16.3). https://jasp-stats.org/ [Computer software].

Jasper, L., & Goldberg, I (1993). Adult ADD Screening Examination – Version 5.0. NY: Psychopharmacologic Institute.

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.

Jotz, G. P., Voegels, R. L., & Bento, R. F. (2020). Otorhinolaryngologists and coronavirus disease 2019 (COVID-19). *International Archives of Otorhinolaryngology*, *24*, 125-128.

Kaiser, H. F. (1974). An index of factorial simplicity. Psychometrika, 39, 31-36.

Kandemirli, S. G., Dogan, L., Sarikaya, Z. T., Kara, S., Akinci, C., Kaya, D., ... & Kocer, N. (2020). Brain MRI findings in patients in the intensive care unit with COVID-19 infection. *Radiology*, *297*(1), E232.

Kandemirli, S. G., Dogan, L., Sarikaya, Z. T., Kara, S., Akinci, C., Kaya, D., ... & Kocer, N. (2020). Brain MRI findings in patients in the intensive care unit with COVID-19 infection. *Radiology*, *297*(1), E232.

Kao, A. (2021). *Determining the long-term impact of contracting COVID-19 on cognitive ability* (No. THESIS). University of Chicago.

Kasari, C., & Sterling, L. (2013). Loneliness and social isolation in children with autism spectrum disorders. *The handbook of solitude: Psychological perspectives on social isolation, social withdrawal, and being alone*, 409-426.

Kopp, B., Lange, F., & Steinke, A. (2021). The Reliability of the Wisconsin Card Sorting Test in Clinical Practice. *Assessment*, *28*(1), 248–263.

Krasemann, S., Haferkamp, U., Pfefferle, S., Woo, M. S., Heinrich, F., Schweizer, M., ... & Pless, O. (2022). The blood-brain barrier is dysregulated in COVID-19 and serves as a CNS entry route for SARS-CoV-2. *Stem cell reports*, *17*(2), 307-320.

Kuchinke, L., Jacobs, A. M., Grubich, C., Vo, M. L. H., Conrad, M., & Herrmann, M. (2005). Incidental effects of emotional valence in single word processing: an fMRI study. *NeuroImage*, *28*(4), 1022-1032.

Kujawa, A., Green, H., Compas, B. E., Dickey, L., & Pegg, S. (2020). Exposure to COVID-19 pandemic stress: Associations with depression and anxiety in emerging adults in the United States. *Depression and anxiety*, *37*(12), 1280-1288.

Lambert, S. L., Aviles, D., Vehaskari, V. M., & Ashoor, I. F. (2016). Severe West Nile virus meningoencephalitis in a pediatric renal transplant recipient: successful recovery and long-term neuropsychological outcome. *Pediatric Transplantation*, *20*(6), 836-839.

Lange, F., Kröger, B., Steinke, A., Seer, C., Dengler, R., & Kopp, B. (2016). Decomposing card-sorting performance: Effects of working memory load and age-related changes. Neuropsychology, 30(5), 579–590.

Lawrence, N. S., Jollant, F., O'Daly, O., Zelaya, F., & Phillips, M. L. (2009). Distinct roles of prefrontal cortical subregions in the Iowa Gambling Task. *Cerebral cortex*, *19*(5), 1134-1143.

Laws, K. R., Irvine, K., & Gale, T. M. (2018). Sex differences in Alzheimer's disease. *Current opinion in psychiatry*, *31*(2), 133-139.

Lebel, C., MacKinnon, A., Bagshawe, M., Tomfohr-Madsen, L., & Giesbrecht, G. (2020). Elevated depression and anxiety symptoms among pregnant individuals during the COVID-19 pandemic. *Journal of affective disorders*, *277*, 5-13.

Lee, M. H., Perl, D. P., Nair, G., Li, W., Maric, D., Murray, H., ... & Nath, A. (2021). Microvascular injury in the brains of patients with Covid-19. *New England Journal of Medicine*, *384*(5), 481-483.

Lehto, J. (1996). Are executive function tests dependent on working memory capacity?. The Quarterly Journal of Experimental Psychology Section A, 49(1), 29-50.

Lentz, M. R., Kim, W. K., Lee, V., Bazner, S., Halpern, E. F., Venna, N., ... & Gonzalez, R. G. (2009). Changes in MRS neuronal markers and T cell phenotypes observed during early HIV infection. *Neurology*, *72*(17), 1465-1472.

Leon, C. S., Bonilla, M., Benítez, F. A. U., Brusco, L. I., Wang, J., & Forcato, C. (2022). Impairment of aversive episodic memories during Covid-19 pandemic: The impact of emotional context on memory processes. *Neurobiology of learning and memory*, *187*, 107575.

Levine, A. J., Hardy, D. J., Miller, E., Castellon, S. A., Longshore, D., & Hinkin, C. H. (2006). The effect of recent stimulant use on sustained attention in HIV-infected adults. *Journal of Clinical and Experimental Neuropsychology*, *28*(1), 29-42.

Lew, B. J., McDermott, T. J., Wiesman, A. I., O'Neill, J., Mills, M. S., Robertson, K. R., Fox, H.S., Swindells, S., & Wilson, T. W. (2018). Neural dynamics of selective attention deficits in HIV-associated neurocognitive disorder. *Neurology*, *91*(20), e1860-e1869.

Lewin, J. S., Friedman, L., Wu, D., Miller, D. A., Thompson, L. A., Klein, S. K., ... & Duerk, J. L. (1996). Cortical localization of human sustained attention: detection with functional MR using a visual vigilance paradigm. *Journal of computer assisted tomography*, *20*(5), 695-701.

Lewis, P. A., & Critchley, H. D. (2003). Mood-dependent memory. *Trends in cognitive sciences*, *7*(10), 431-433.

Li, G., He, X., Zhang, L., Ran, Q., Wang, J., Xiong, A., ... & Chang, C. (2020). Assessing ACE2 expression patterns in lung tissues in the pathogenesis of COVID-19. *Journal of autoimmunity*, *112*, 102463.

Lie, C. H., Specht, K., Marshall, J. C., & Fink, G. R. (2006). Using fMRI to decompose the neural processes underlying the Wisconsin Card Sorting Test. *Neuroimage*, *30*(3), 1038-1049.

Lin, C. H., Chiu, Y. C., Cheng, C. M., & Hsieh, J. C. (2008). Brain maps of Iowa gambling task. *BMC neuroscience*, *9*(1), 1-15.

Liu, J., Ji, H., Zheng, W., Wu, X., Zhu, J. J., Arnold, A. P., & Sandberg, K. (2010). Sex differences in renal angiotensin converting enzyme 2 (ACE2) activity are 17β-oestradiol-dependent and sex chromosome-independent. *Biology of sex differences*, *1*(1), 1-11.

Liu, N., Wang, Y., An, A. Y., Banker, C., Qian, Y. H., & O'Donnell, J. M. (2020). Single housing-induced effects on cognitive impairment and depression-like behavior in male and female mice involve neuroplasticity-related signaling. *European Journal of Neuroscience*, *52*(1), 2694-2704.

Liu, Y. H., Chen, Y., Wang, Q. H., Wang, L. R., Jiang, L., Yang, Y., ... & Wang, Y. J. (2022). One-year trajectory of cognitive changes in older survivors of COVID-19 in Wuhan, China: a longitudinal cohort study. *JAMA neurology*, *79*(5), 509-517.

Lowe, C., & Rabbitt, P. (1998). Test\re-test reliability of the CANTAB and ISPOCD neuropsychological batteries: theoretical and practical issues. Neuropsychologia, 36(9), 915-923.

Luks, T. L., Oliveira, M., Possin, K. L., Bird, A., Miller, B. L., Weiner, M. W., & Kramer, J. H. (2010). Atrophy in two attention networks is associated with performance on a Flanker task in neurodegenerative disease. *Neuropsychologia*, *48*(1), 165-170.

Luo, M., Guo, L., Yu, M., Jiang, W., & Wang, H. (2020). The psychological and mental impact of coronavirus disease 2019 (COVID-19) on medical staff and general public–A systematic review and meta-analysis. *Psychiatry research*, *291*, 113190.

Luporini, R. L., Joice, M. D. A., Kubota, L. T., Martin, A. C. B. M., Cominetti, M. R., de Freitas Anibal, F., & Pott-Junior, H. (2021). IL-6 and IL-10 are associated with disease severity and higher comorbidity in adults with COVID-19. *Cytokine*, *143*, 155507.

Majolo, F., Silva, G. L. D., Vieira, L., Anli, C., Timmers, L. F. S. M., Laufer, S., & Goettert, M. I. (2021). Neuropsychiatric Disorders and COVID-19: What We Know So Far. *Pharmaceuticals*, *14*(9), 933.

Maley, J. H., Sandsmark, D. K., Trainor, A., Bass, G. D., Dabrowski, C. L., Magdamo, B. A., ... & Lane-Fall, M. B. (2022). Six-Month Impairment in Cognition, Mental Health, and Physical Function Following COVID-19–Associated Respiratory Failure. *Critical care explorations*, *4*(4).

Manca, R., De Marco, M., Colston, A., Raymont, V., Amin, J., Davies, R., ... & Venneri, A. (2022). The impact of social isolation due to the COVID-19 pandemic on patients with dementia and caregivers. *Acta Neuropsychiatrica*, 1-6.

Mao, L., Jin, H., Wang, M., Hu, Y., Chen, S., He, Q., ... & Hu, B. (2020). Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. *JAMA neurology*, *77*(6), 683-690.

Marcotte, T. D., Lazzaretto, D., Cobb Scott, J., Roberts, E., Woods, S. P., Letendre, S., & HNRC Group. (2006). Visual attention deficits are associated with driving accidents in cognitively-impaired HIV-infected individuals. *Journal of Clinical and Experimental Neuropsychology*, *28*(1), 13-28.

Matschke, J., Lütgehetmann, M., Hagel, C., Sperhake, J. P., Schröder, A. S., Edler, C., ... & Glatzel, M. (2020). Neuropathology of patients with COVID-19 in Germany: a post-mortem case series. *The Lancet Neurology*, *19*(11), 919-929.

Matthews, T., Danese, A., Wertz, J., Odgers, C. L., Ambler, A., Moffitt, T. E., & Arseneault, L. (2016). Social isolation, loneliness and depression in young

adulthood: a behavioural genetic analysis. *Social psychiatry and psychiatric epidemiology*, *51*(3), 339-348.

Mattioli, F., Stampatori, C., Righetti, F., Sala, E., Tomasi, C., & De Palma, G. (2021). Neurological and cognitive sequelae of Covid-19: a four month follow-up. *Journal of neurology*, *268*(12), 4422-4428.

Mazza, M. G., De Lorenzo, R., Conte, C., Poletti, S., Vai, B., Bollettini, I., ... & COVID-19 BioB Outpatient Clinic Study Group. (2020). Anxiety and depression in COVID-19 survivors: Role of inflammatory and clinical predictors. *Brain, behavior, and immunity*, *89*, 594-600.

McArthur, J. C., Brew, B. J., & Nath, A. (2005). Neurological complications of HIV infection. *The Lancet Neurology*, *4*(9), 543-555.

Meinhardt, J., Radke, J., Dittmayer, C., Franz, J., Thomas, C., Mothes, R., ... & Heppner, F. L. (2021). Olfactory transmucosal SARS-CoV-2 invasion as a port of central nervous system entry in individuals with COVID-19. *Nature neuroscience*, *24*(2), 168-175.

Meinhardt, J., Radke, J., Dittmayer, C., Franz, J., Thomas, C., Mothes, R., ... & Heppner, F. L. (2021). Olfactory transmucosal SARS-CoV-2 invasion as a port of central nervous system entry in individuals with COVID-19. *Nature neuroscience*, *24*(2), 168-175.

Méndez, R., Balanzá-Martínez, V., Luperdi, S. C., Estrada, I., Latorre, A., González-Jiménez, P., ... & Menéndez, R. (2021). Short-term neuropsychiatric outcomes and quality of life in COVID-19 survivors. *Journal of internal medicine*, *290*(3), 621-631.

Méndez, R., Balanzá-Martínez, V., Luperdi, S. C., Estrada, I., Latorre, A., González-Jiménez, P., ... & Menéndez, R. (2022). Long-term neuropsychiatric outcomes in COVID-19 survivors: A 1-year longitudinal study. *Journal of Internal Medicine*, *291*(2), 247-251.

Micallef, J., Soeiro, T., Jonville-Béra, A. P., & of Pharmacology, F. S. (2020). Non-steroidal anti-inflammatory drugs, pharmacology, and COVID-19 infection. *Therapies*, *75*(4), 355-362.

Misra, S., Kolappa, K., Prasad, M., Radhakrishnan, D., Thakur, K. T., Solomon, T., ... & Prasad, K. (2021). Frequency of neurologic manifestations in COVID-19: a systematic review and meta-analysis. *Neurology*, *97*(23), e2269-e2281.

Molina-Gil, J., González-Fernández, L., & García-Cabo, C. (2021). Trigeminal neuralgia as the sole neurological manifestation of COVID-19: a case report. *Headache: The Journal of Head and Face Pain*, *61*(3), 560-562.

Molteni, E., Sudre, C. H., Canas, L. S., Bhopal, S. S., Hughes, R. C., Antonelli, M., ... & Duncan, E. L. (2021). Illness duration and symptom profile in symptomatic UK school-aged children tested for SARS-CoV-2. *The Lancet Child & Adolescent Health*, *5*(10), 708-718.

Morales, D., Acevedo, S. F., Skolasky, R. L., Hechavarria, R., Santiago, S., De La Torre, T., Maldonado, E., & Wojna, V. (2012). Translational spatial task and its relationship to HIV-associated neurocognitive disorders and apolipoprotein E in HIV-seropositive women. *Journal of neurovirology*, *18*(6), 488–502. https://doi.org/10.1007/s13365-012-0128-8

Moriguchi, T., Harii, N., Goto, J., Harada, D., Sugawara, H., Takamino, J., ... & Shimada, S. (2020). A first case of meningitis/encephalitis associated with SARS-Coronavirus-2. *International journal of infectious diseases*, *94*, 55-58.

Mugnaini, D., Lassi, S., La Malfa, G., & Albertini, G. (2009). Internalizing correlates of dyslexia. *World Journal of Pediatrics*, *5*(4), 255-264.

Nagahama, Y., Fukuyama, H., Yamauchi, H., Matsuzaki, S., Konishi, J., Shibasaki, H., & Kimura, J. (1996). Cerebral activation during performance of a card sorting test. *Brain*, *119*(5), 1667-1675.

Nakao, A., Yamanouchi, J., Takenaka, K., & Takada, K. (2020). The Iowa Gambling Task on HIV-infected subjects. *Journal of Infection and Chemotherapy*, *26*(3), 240-244.

Nannoni, S., de Groot, R., Bell, S., & Markus, H. S. (2021). Stroke in COVID-19: a systematic review and meta-analysis. *International Journal of Stroke, 16*(2), 137-149.

National Health Service UK: Long-term effects of coronavirus (long COVID). United Kingdom; 2022, July 19. https://www.nhs.uk/conditions/coronavirus-covid-19/long-term-effects-of-coronavirus-long-covid/

Navarro-Soria, I., Real-Fernández, M., Juarez-Ruiz de Mier, R., Costa-López, B., Sánchez, M., & Lavigne, R. (2021). Consequences of Confinement due to COVID-19 in Spain on Anxiety, sleep and executive functioning of children and adolescents with ADHD. *Sustainability*, *13*(5), 2487.

Nersesjan, V., Fonsmark, L., Christensen, R. H., Amiri, M., Merie, C., Lebech, A. M., ... & Benros, M. E. (2022). Neuropsychiatric and Cognitive Outcomes in Patients 6 Months After COVID-19 Requiring Hospitalization Compared With Matched Control Patients Hospitalized for Non–COVID-19 Illness. *JAMA psychiatry*, *79*(5), 486-497.

Oken, B. S., Salinsky, M. C., & Elsas, S. (2006). Vigilance, alertness, or sustained attention: physiological basis and measurement. *Clinical neurophysiology*, *117*(9), 1885-1901.

Orsini, A., Corsi, M., Santangelo, A., Riva, A., Peroni, D., Foiadelli, T., ... & Striano, P. (2020). Challenges and management of neurological and psychiatric manifestations in SARS-CoV-2 (COVID-19) patients. *Neurological Sciences*, *41*(9), 2353-2366.

Özdin, S., & Bayrak Özdin, Ş. (2020). Levels and predictors of anxiety, depression and health anxiety during COVID-19 pandemic in Turkish society: The importance of gender. *International Journal of Social Psychiatry*, *66*(5), 504-511.

Paap, K. R., & Sawi, O. (2016). The role of test-retest reliability in measuring individual and group differences in executive functioning. *Journal of Neuroscience Methods*, *274*, 81-93.

Pappa, S., Ntella, V., Giannakas, T., Giannakoulis, V. G., Papoutsi, E., & Katsaounou, P. (2020). Prevalence of depression, anxiety, and insomnia among healthcare workers during the COVID-19 pandemic: A systematic review and meta-analysis. *Brain, behavior, and immunity*, *88*, 901-907.

Park, M., Thwaites, R. S., & Openshaw, P. J. (2020). COVID-19: lessons from SARS and MERS. *European Journal of Immunology*, *50*(3), 308.

Pellegrini, L., Albecka, A., Mallery, D. L., Kellner, M. J., Paul, D., Carter, A. P., ... & Lancaster, M. A. (2020). SARS-CoV-2 infects the brain choroid plexus and disrupts the blood-CSF barrier in human brain organoids. *Cell stem cell*, *27*(6), 951-961.

Pennington, B. F., & Ozonoff, S. (1996). Executive functions and developmental psychopathology. *Journal of child psychology and psychiatry*, *37*(1), 51-87.

Penninx, B. W. (2021). Psychiatric symptoms and cognitive impairment in “Long COVID”: the relevance of immunopsychiatry. *World Psychiatry*, *20*(3), 357.

Pérez-González, A., Araújo-Ameijeiras, A., Fernández-Villar, A., Crespo, M., & Poveda, E. (2022). Long COVID in hospitalized and non-hospitalized patients in a large cohort in Northwest Spain, a prospective cohort study. *Scientific reports*, *12*(1), 1-8.

Pezzini, A., & Padovani, A. (2020). Lifting the mask on neurological manifestations of COVID-19. *Nature Reviews Neurology*, *16*(11), 636-644.

Pfefferbaum, B., & North, C. S. (2020). Mental health and the Covid-19 pandemic. *New England Journal of Medicine*, *383*(6), 510-512.

Poletti, P., Tirani, M., Cereda, D., Trentini, F., Guzzetta, G., Sabatino, G., ... & Force, T. (2021). Association of age with likelihood of developing symptoms and critical disease among close contacts exposed to patients

with confirmed SARS-CoV-2 infection in Italy. *JAMA network open*, *4*(3), e211085-e211085.

Pownall, M., Harris, R., & Blundell-Birtill, P. (2022). Supporting students during the transition to university in COVID-19: Five key considerations and recommendations for educators. *Psychology Learning & Teaching*, *21*(1), 3-18.

Poyiadji, N., Shahin, G., Noujaim, D., Stone, M., Patel, S. C., & Griffith, B. (2020). COVID-19-associated acute hemorrhagic necrotizing encephalopathy: imaging features. *Radiology*, *296*(2), 119.

Qiao, X., Lin, H., Chen, X., Ning, C., Wang, K., Shen, W., ... & Ding, Y. (2019). Sex differences in neurocognitive screening among adults living with HIV in China. *Journal of NeuroVirology*, *25*(3), 363-371.

Rao, V. R., Ruiz, A. P., & Prasad, V. R. (2014). Viral and cellular factors underlying neuropathogenesis in HIV associated neurocognitive disorders (HAND). *AIDS research and therapy*, *11*(1), 1-15.

Raveendran, A. V., Jayadevan, R., & Sashidharan, S. (2021). Long COVID: an overview. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*, *15*(3), 869-875.

Raz, S., Bar-Haim, Y., Sadeh, A., & Dan, O. (2014). Reliability and Validity of the Online Continuous Performance Test Among Young Adults. *Assessment*, *21*(1), 108–118.

Roebuck, H., Freigang, C., & Barry, J. G. (2016). Continuous performance tasks: Not just about sustaining attention. *Journal of speech, language, and hearing research*, *59*(3), 501-510.

Rogers, J. P., Watson, C. J., Badenoch, J., Cross, B., Butler, M., Song, J., ... & Rooney, A. G. (2021). Neurology and neuropsychiatry of COVID-19: a systematic review and meta-analysis of the early literature reveals frequent CNS manifestations and key emerging narratives. *Journal of Neurology, Neurosurgery & Psychiatry*, *92*(9), 932-941.

Romero-Sánchez, C. M., Díaz-Maroto, I., Fernández-Díaz, E., Sánchez-Larsen, Á., Layos-Romero, A., García-García, J., ... & Segura, T. (2020). Neurologic manifestations in hospitalized patients with COVID-19: the ALBACOVID registry. *Neurology*, *95*(8), e1060-e1070.

Rubin, L. H., Neigh, G. N., Sundermann, E. E., Xu, Y., Scully, E. P., & Maki, P. M. (2019). Sex differences in neurocognitive function in adults with HIV: patterns, predictors, and mechanisms. *Current psychiatry reports*, *21*(10), 1-12.

Rusnáková, Š., Daniel, P., Chládek, J., Jurak, P., & Rektor, I. (2011). The executive functions in frontal and temporal lobes: a flanker task intracerebral recording study. *Journal of clinical neurophysiology*, *28*(1), 30-35.

Russell, D. W. (1996). UCLA Loneliness Scale (Version 3): Reliability, validity, and factor structure. *Journal of personality assessment*, *66*(1), 20-40.

Sadek, J. R., Pergam, S. A., Harrington, J. A., Echevarria, L. A., Davis, L. E., Goade, D., ... & Haaland, K. Y. (2010). Persistent neuropsychological impairment associated with West Nile virus infection. *Journal of clinical and experimental neuropsychology*, *32*(1), 81-87.

Salo, E., Salmela, V., Salmi, J., Numminen, J., & Alho, K. (2017). Brain activity associated with selective attention, divided attention and distraction. *Brain research*, *1664*, 25-36.

Sanmarti, M., Ibáñez, L., Huertas, S., Badenes, D., Dalmau, D., Slevin, M., ... & Jaen, A. (2014). HIV-associated neurocognitive disorders. *Journal of molecular psychiatry*, *2*(1), 1-10.

Santos, R. E. A., da Silva, M. G., do Monte Silva, M. C. B., Barbosa, D. A. M., do Vale Gomes, A. L., Galindo, L. C. M., ... & Ferraz-Pereira, K. N. (2021). Onset and duration of symptoms of loss of smell/taste in patients with COVID-19: A systematic review. *American Journal of Otolaryngology*, *42*(2), 102889.

Sarter, M., Givens, B., & Bruno, J. P. (2001). The cognitive neuroscience of sustained attention: where top-down meets bottom-up. *Brain research reviews*, *35*(2), 146-160.

Savarraj, J., Park, E. S., Colpo, G. D., Hinds, S. N., Morales, D., Ahnstedt, H., ... & Choi, H. A. (2021). Brain injury, endothelial injury and inflammatory markers are elevated and express sex-specific alterations after COVID-19. *Journal of neuroinflammation*, *18*(1), 1-12.

Saylor, D., Dickens, A. M., Sacktor, N., Haughey, N., Slusher, B., Pletnikov, M., Mankowski, J. L., Brown, A., Volsky, D. J., & McArthur, J. C. (2016). HIV-associated neurocognitive disorder--pathogenesis and prospects for treatment. *Nature reviews. Neurology*, *12*(4), 234–248. https://doi.org/10.1038/nrneurol.2016.27

Schain, M., & Kreisl, W. C. (2017). Neuroinflammation in neurodegenerative disorders—a review. *Current neurology and neuroscience reports*, *17*(3), 1-11.

Schaller, T., Hirschbühl, K., Burkhardt, K., Braun, G., Trepel, M., Märkl, B., & Claus, R. (2020). Postmortem examination of patients with COVID-19. *Jama*, *323*(24), 2518-2520.

Schatz, D. B., & Rostain, A. L. (2006). ADHD with comorbid anxiety: a review of the current literature. *Journal of Attention disorders*, *10*(2), 141-149.

Schmitz, F., Kunina-Habenicht, O., Hildebrandt, A., Oberauer, K., & Wilhelm, O. (2020). Psychometrics of the Iowa and Berlin Gambling Tasks: Unresolved Issues With Reliability and Validity for Risk Taking. *Assessment*, *27*(2), 232–245.

Schouten, J., Cinque, P., Gisslen, M., Reiss, P., & Portegies, P. (2011). HIV-1 infection and cognitive impairment in the cART era: a review. *Aids*, *25*(5), 561-575.

Schurink, B., Roos, E., Radonic, T., Barbe, E., Bouman, C. S., de Boer, H. H., ... & Bugiani, M. (2020). Viral presence and immunopathology in patients

with lethal COVID-19: a prospective autopsy cohort study. *The Lancet Microbe*, *1*(7), e290-e299.

Scully, E. P. (2018). Sex differences in HIV infection. *Current HIV/AIDS Reports*, *15*(2), 136-146.

Serrano, G. E., Walker, J. E., Tremblay, C., Piras, I. S., Huentelman, M. J., Belden, C. M., ... & Beach, T. G. (2022). SARS-CoV-2 Brain Regional Detection, Histopathology, Gene Expression, and Immunomodulatory Changes in Decedents with COVID-19. *Journal of Neuropathology & Experimental Neurology*.

Shang, J., Wan, Y., Luo, C., Ye, G., Geng, Q., Auerbach, A., & Li, F. (2020). Cell entry mechanisms of SARS-CoV-2. *Proceedings of the National Academy of Sciences*, *117*(21), 11727-11734.

Shankar, A., Hamer, M., McMunn, A., & Steptoe, A. (2013). Social isolation and loneliness: relationships with cognitive function during 4 years of follow-up in the English Longitudinal Study of Ageing. *Psychosomatic medicine*, *75*(2), 161-170.

Sibley, M. H., Ortiz, M., Gaias, L. M., Reyes, R., Joshi, M., Alexander, D., & Graziano, P. (2021). Top problems of adolescents and young adults with ADHD during the COVID-19 pandemic. *Journal of psychiatric research*, *136*, 190-197.

Sodagar, A., Javed, R., Tahir, H., Razak, S. I. A., Shakir, M., Naeem, M., ... & Al-Harrasi, A. (2022). Pathological Features and Neuroinflammatory

Mechanisms of SARS-CoV-2 in the Brain and Potential Therapeutic Approaches. *Biomolecules*, *12*(7), 971.

Solomon, I. H., Normandin, E., Bhattacharyya, S., Mukerji, S. S., Keller, K., Ali, A. S., ... & Sabeti, P. (2020). Neuropathological features of Covid-19. *New England Journal of Medicine*, *383*(10), 989-992.

Somma, F., Bartolomeo, P., Vallone, F., Argiuolo, A., Cerrato, A., Miglino, O., ... & Gigliotta, O. (2021). Further to the left: Stress-induced increase of spatial pseudoneglect during the COVID-19 lockdown. *Frontiers in Psychology*, *12*, 573846.

Sønderskov, K. M., Dinesen, P. T., Santini, Z. I., & Østergaard, S. D. (2020). The depressive state of Denmark during the COVID-19 pandemic. *Acta neuropsychiatrica*, *32*(4), 226-228.

Song, E., Zhang, C., Israelow, B., Lu-Culligan, A., Prado, A. V., Skriabine, S., ... & Iwasaki, A. (2021). Neuroinvasion of SARS-CoV-2 in human and mouse brain. *Journal of Experimental Medicine*, *218*(3).

Stefanou, M. I., Palaiodimou, L., Bakola, E., Smyrnis, N., Papadopoulou, M., Paraskevas, G. P., ... & Tsivgoulis, G. (2022). Neurological manifestations of long-COVID syndrome: A narrative review. *Therapeutic advances in chronic disease*, *13*, 20406223221076890.

Stephenson, T., Allin, B., Nugawela, M. D., Rojas, N., Dalrymple, E., Pereira, S. P., ... & CLoCk Consortium. (2022). Long COVID (post-COVID-19 condition) in children: a modified Delphi process. *Archives of Disease in Childhood*.

Stewart, C. C., Yu, L., Glover, C. M., Mottola, G., Bennett, D. A., Wilson, R. S., & Boyle, P. A. (2020). Loneliness interacts with cognition in relation to healthcare and financial decision making among community-dwelling older adults. *The Gerontologist*, *60*(8), 1476-1484.

Stranahan, A. M., Khalil, D., & Gould, E. (2006). Social isolation delays the positive effects of running on adult neurogenesis. *Nature neuroscience*, *9*(4), 526-533.

Streit, W. J. (2004). Microglia and Alzheimer's disease pathogenesis. *Journal of neuroscience research*, *77*(1), 1-8.

Swanstrom, R., & Coffin, J. (2012). HIV-1 pathogenesis: the virus. *Cold Spring Harbor perspectives in medicine*, *2*(12), a007443.

Takahashi, T., Ellingson, M. K., Wong, P., Israelow, B., Lucas, C., Klein, J., ... & Iwasaki, A. (2020). Sex differences in immune responses that underlie COVID-19 disease outcomes. *Nature*, *588*(7837), 315-320.

Tandon, M., Kataria, S., Patel, J., Mehta, T. R., Daimee, M., Patel, V., ... & Sriwastava, S. (2021). A Comprehensive Systematic Review of CSF analysis that defines Neurological Manifestations of COVID-19. International Journal of Infectious Diseases, 104, 390-397.

Tate, R. L., Perdices, M. and Maggiotto, S. (1998). Stability of the Wisconsin Card Sorting Test and the Determination of Reliability of Change in Scores. The Clinical Neuropsychologist, 12:3, 348 – 357

Thomas, J. M., Higgs, S., & Dourish, C. T. (2016). Test–retest reliability and effects of repeated testing and satiety on performance of an Emotional

Test Battery. *Journal of clinical and experimental neuropsychology*, *38*(4), 416-433.

Townsend, L., Dowds, J., O'Brien, K., Sheill, G., Dyer, A. H., O'Kelly, B., ... & Bannan, C. (2021). Persistent poor health after COVID-19 is not associated with respiratory complications or initial disease severity. *Annals of the American Thoracic Society*, *18*(6), 997-1003.

Turner, K. L., Hughes, M., & Presland, K. (2020). Learning loss, a potential challenge for transition to undergraduate study following COVID19 school disruption. *Journal of Chemical Education*, *97*(9), 3346-3352.

Van de Sande, C., & Reiser, M. (2018). The Effect of Summer Break on Engineering Student Success in Calculus. *International Journal of Research in Education and Science*, *4*(2), 349-357.

van den Bos, R., Homberg, J., & de Visser, L. (2013). A critical review of sex differences in decision-making tasks: focus on the Iowa Gambling Task. *Behavioural brain research*, *238*, 95-108.

van Riel, D., Embregts, C. W., Sips, G. J., van den Akker, J. P., Endeman, H., van Nood, E., ... & GeurtsvanKessel, C. H. (2021). Temporal kinetics of RNAemia and associated systemic cytokines in hospitalized COVID-19 patients. *Msphere*, *6*(3), e00311-21.

Vannorsdall, T. D., Brigham, E., Fawzy, A., Raju, S., Gorgone, A., Pletnikova, A., ... & Oh, E. S. (2022). Cognitive dysfunction, psychiatric distress, and functional decline after COVID-19. *Journal of the Academy of Consultation-liaison Psychiatry*, *63*(2), 133-143.

Varga, Z., Flammer, A. J., Steiger, P., Haberecker, M., Andermatt, R., Zinkernagel, A. S., ... & Moch, H. (2020). Endothelial cell infection and endotheliitis in COVID-19. *The Lancet*, *395*(10234), 1417-1418.

vel Grajewska, B. Ż., Sim, E. J., Hoenig, K., Herrnberger, B., & Kiefer, M. (2011). Mechanisms underlying flexible adaptation of cognitive control: Behavioral and neuroimaging evidence in a flanker task. *Brain research*, *1421*, 52-65.

Vinegard, M. (1994). A revised adult dyslexia check list. *EDUCARE-LONDON-NATIONAL BUREAU FOR HANDICAPPED STUDENTS-*, 21-21.

Walker, A. J., MacKenna, B., Inglesby, P., Tomlinson, L., Rentsch, C. T., Curtis, H. J., ... & Evans, S. J. (2021). Clinical coding of long COVID in English primary care: a federated analysis of 58 million patient records in situ using OpenSAFELY. *British Journal of General Practice*, *71*(712), e806-e814.

Walker, K. A., & Brown, G. G. (2018). HIV-associated executive dysfunction in the era of modern antiretroviral therapy: A systematic review and meta-analysis. *Journal of clinical and experimental neuropsychology*, *40*(4), 357-376.

Waters, G. S., & Caplan, D. (2003). The reliability and stability of verbal working memory measures. *Behavior Research Methods, Instruments, & Computers*, *35*(4), 550-564.

Weissbourd, R., Batanova, M., Lovison, V., & Torres, E. (2021). How the Pandemic Has Deepened an Epidemic of Loneliness and What We Can Do About It (pp. 1–13). *Harvard University*.

Whittaker, E., Bamford, A., Kenny, J., Kaforou, M., Jones, C. E., Shah, P., ... & Levin, M. (2020). Clinical characteristics of 58 children with a pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2. *Jama*, *324*(3), 259-269.

WHO COVID-19 Dashboard. Geneva: World Health Organization, 2020. Available online: https://covid19.who.int/ (last cited: June 27, 2022).

Williams, A., Branscome, H., Khatkar, P., Mensah, G. A., Al Sharif, S., Pinto, D. O., ... & Kashanchi, F. (2021). A comprehensive review of COVID-19 biology, diagnostics, therapeutics, and disease impacting the central nervous system. *Journal of NeuroVirology*, *27*(5), 667-690.

Wilson, T. W., Proskovec, A. L., Heinrichs-Graham, E., O'Neill, J., Robertson, K. R., Fox, H. S., & Swindells, S. (2017). Aberrant neuronal dynamics during working memory operations in the aging HIV-infected brain. *Scientific reports*, *7*, 41568.

Wittmann, B. C., Schiltz, K., Boehler, C. N., & Düzel, E. (2008). Mesolimbic interaction of emotional valence and reward improves memory formation. *Neuropsychologia*, *46*(4), 1000-1008.

Woods, S. P., Moore, D. J., Weber, E., & Grant, I. (2009). Cognitive neuropsychology of HIV-associated neurocognitive disorders. *Neuropsychology review*, *19*(2), 152-168.

Xie, W., Campbell, S., & Zhang, W. (2020). Working memory capacity predicts individual differences in social-distancing compliance during the COVID-

19 pandemic in the United States. *Proceedings of the National Academy of Sciences*, *117*(30), 17667-17674.

Xu, Z., Adam, K. C. S., Fang, X., & Vogel, E. K. (2018). The reliability and stability of visual working memory capacity. *Behavior Research Methods*, *50*(2), 576-588.

Yoo, H. (2022). Verbal Working Memory Decline After COVID-19 in 20s. *Archives of Physical Medicine and Rehabilitation*, *103*(3), e14.

Zavaleta, D., Samuel, K., & Mills, C. T. (2017). Measures of social isolation. *Social Indicators Research*, *131*(1), 367-391.

Zhang, B. Z., Chu, H., Han, S., Shuai, H., Deng, J., Hu, Y. F., ... & Huang, J. D. (2020). SARS-CoV-2 infects human neural progenitor cells and brain organoids. *Cell research*, *30*(10), 928-931.

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), fcab295.

Ziauddeen, N., Gurdasani, D., O'Hara, M. E., Hastie, C., Roderick, P., Yao, G., & Alwan, N. A. (2022). Characteristics and impact of Long Covid: Findings from an online survey. *PloS one*, *17*(3), e0264331.

Ziauddeen, N., Gurdasani, D., O'Hara, M. E., Hastie, C., Roderick, P., Yao, G., & Alwan, N. A. (2022). Characteristics and impact of Long Covid: Findings from an online survey. *PloS one*, *17*(3), e0264331.

Zimmermann, P., Pittet, L. F., & Curtis, N. (2022). The challenge of studying long COVID: an updated review. *The Pediatric infectious disease journal*, *41*(5), 424.

Zovetti, N., Rossetti, M. G., Perlini, C., Brambilla, P., & Bellani, M. (2021). Neuroimaging studies exploring the neural basis of social isolation. *Epidemiology and Psychiatric Sciences*, *30*.

Zubek, J. P., Bayer, L., & Shephard, J. M. (1969). Relative effects of prolonged social isolation and confinement: Behavioral and EEG changes. *Journal of Abnormal Psychology*, *74*(5), 625.

Zurlo, M. C., Cattaneo Della Volta, M. F., & Vallone, F. (2020). COVID-19 student stress questionnaire: development and validation of a questionnaire to evaluate students' stressors related to the coronavirus pandemic lockdown. *Frontiers in psychology*, *11*, 576758.

APPENDIX A

GOOGLE FORM

Consent:

[ ] I consent to participate in this experiment and comply with all COVID-19 health procedures.

[ ] I do not wish to participate at this time and would like to cancel my appointment.

COVID-19 Screening

Please read through each of the following questions from the UofSC daily COVID-19 screening form:

In the past 14 days:
- have you been diagnosed with the Novel Coronavirus/COVID-19?
- have you had a temperature reading of 100.0°F or higher or felt feverish?
- have you lived with or been within 6 feet of someone for 10 consecutive minutes who has been diagnosed with COVID-19?
- have you lived with or been within 6 feet of someone for 10 consecutive minutes who is quarantined or isolated due to suspicion of COVID-19?

In the past 7 days have you experienced any of the following symptoms:
- Cough
- Headache
- Shortness of breath
- Chills / shaking
- Sore throat
- Muscle aches
- Loss of taste or smell

Did you answer "yes" to any of the above questions?

[ ] Yes

[ ] No

COVID-19 Questions:

Have you been vaccinated for COVID-19?

[ ] Yes, fully (two shots or one depending on vaccination)

[ ] I am "partially" vaccinated (one shot of a two shot vaccination series)

[ ] No, not vaccinated

[ ] Would prefer not to say

If vaccinated, which vaccine have you been vaccinated with?

[ ] I have not been vaccinated/would prefer not to say

[ ] Moderna

[ ] Pfizer/BioNTech

[ ] Johnson & Johnson/Janssen

Approximately when did you receive your first vaccination dose? If you have not been vaccinated, or would prefer not to say, select January 1, 2019 (01/01/2019)

Have you ever been officially diagnosed by a medical professional (via nasal swab, saliva, or antibody test) with COVID-19?

[ ] Yes

[ ] No

Yes, diagnosed with COVID-19 Questions:

When did you have COVID-19?

Which of the following best describes your experience with COVID-19?

[ ] Individuals who test positive for SARS-CoV-2 using a virologic test (i.e., a nucleic acid amplification test or an antigen test) but who have no symptoms that are consistent with COVID-19.

[ ] Individuals who have any of the various signs and symptoms of COVID-19 (e.g., fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell) but who do not have shortness of breath, dyspnea, or abnormal chest imaging.

[ ] Individuals who show evidence of lower respiratory disease during clinical assessment or imaging and who have saturation of oxygen (SpO2) ≥94% on room air at sea level.

[ ] Individuals who have SpO2 <94% on room air at sea level, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO2/FiO2) <300 mm Hg, respiratory frequency>30 breaths/min, or lung infiltrates >50%.

[ ] Individuals who have respiratory failure, septic shock, and/or multiple organ Dysfunction

Did you lose your sense of taste and smell?

Taste: [ ] Did not lose [ ] Lost, but has now returned [ ] Lost, but has not fully returned back to "normal"

Smell: [ ] Did not lose [ ] Lost, but has now returned [ ] Lost, but has not fully returned back to "normal"

If you have ever been diagnosed a second time with COVID-19. please provide additional details below (such as when you were diagnosed a second time, if that time was more severe than the first time, or if you lost taste/smell again)

Not diagnosed with COVID-19 Questions:

At any point, did you think that you had COVID-19 but were not officially diagnosed?

[ ] Yes {reroutes back to “Yes, diagnosed with COVID-19 Questions”}

[ ] No

Quarantine Questions:

Think back to the height of COVID-19 quarantining ("lockdown"). Please select the activities that you regularly did IN PERSON during the specified period of time. [March 15, 2020-August 15, 2020; August 15, 2020-January 15, 2021; January 15, 2021-May 15, 2021; May 15, 2021-present]

See some family (excluding elderly relatives such as grandparents)

See all family (including elderly relatives such as grandparents)

See existing friends

Meet new people (such as at a bar, restaurant, or through a friend-of-a-friend)

Attend social gatherings (such as concerts, parties, weddings) consisting of 30+ people

If you experienced social isolation during COVID-19, do you personally think that it has had lasting effects on your mental wellbeing (i.e., has it heightened any depression, anxiety, etc.)?

[ ] Yes, and I think these effects will last for a long time

[ ] Yes, but I think these effects will not last for very long

[ ] No, my mental wellbeing has remained the same

[ ] No, and my mental wellbeing is better than it was before quarantine

[ ] I did not experience social isolation during COVID-19

If you experienced social isolation during COVID-19, do you personally think that it has had lasting effects on your mental abilities (attention span, memory, cognition)?

[ ] Yes, and I think these effects will last for a long time

[ ] Yes, but I think these effects will not last for very long

[ ] No, my mental wellbeing has remained the same

[ ] No, and my mental wellbeing is better than it was before quarantine

[ ] I did not experience social isolation during COVID-19

For the following items, please indicate how often each of the statements below is descriptive of you [Never, Rarely, Sometimes, Often].

1. How often do you feel that you are "in tune" with the people around you?

2. How often do you feel that you lack companionship?

3. How often do you feel that there is no one you can turn to?

4. How often do you feel alone?

5. How often do you feel part of a group of friends?

6. How often do you feel that you have a lot in common with the people around you?

7. How often do you feel that you are no longer close to anyone?

8. How often do you feel that your interests and ideas are not shared by those around you?

9. How often do you feel outgoing and friendly?

10. How often do you feel close to people?

11. How often do you feel left out?

12. How often do you feel that your relationships with others are not meaningful?

13. How often do you feel that no one really knows you well?

14. How often do you feel isolated from others?

15. How often do you feel you can find companionship when you want it?

16. How often do you feel that there are people who really understand you?

17. How often do you feel shy?

18. How often do you feel that people are around you but not with you?

19. How often do you feel that there are people you can talk to?

20. How often do you feel that there are people you can turn to?

Do you think that you answers to the previous statements would have been different if there had been no COVID-19?

[ ] Almost 100% of answers would have been different; I do not feel that the answers I gave reflect how I "usually" feel

[ ] About 75% of answers would have been different

[ ] About 50% of answers would have been different

[ ] About 25% of answers would have been different

[ ] Almost 0% of answers would have been different; I feel that the answers I gave reflect how I "usually" feel, pandemic or not

Questionnaires:

You are about to start a series of questionnaires that will allow us to examine individual differences in cognition. All responses are voluntary and you can decline to answer any question that you are not comfortable with. Your identity will never be associated with your responses, only your assigned subject number.

At the end of each questionnaire you will be prompted to press a button to continue on to the next page. Once all questionnaires are completed you will be prompted to press a button to submit your responses.

Beck Anxiety Inventory: Below is a list of common symptoms of anxiety. Please carefully read each item in the list. Indicate how much you have been bothered by that symptom during the past month, including today, by selecting the corresponding button in the column next to each symptom. [Not at all; Mildly, but it didn't bother me much; Moderately - it wasn't pleasant at times; Severely - bothered me a lot]

1. Numbness or tingling

2. Feeling hot

3. Wobbliness in legs

4. Unable to relax

5. Fear of worst happening

6. Dizzy or lightheaded

7. Heart pounding/racing

8. Unsteady

9. Terrified or afraid

10. Nervous

11. Feeling of choking

12. Hands trembling

13. Shaky / unsteady

14. Fear of losing control

15. Difficulty in breathing

16. Fear of Dying

17. Scared

18. Indigestion

19. Faint / lightheaded

20. Face flushed

21. Hot/cold sweats

Beck Depression Inventory

1.

0 I do not feel sad.

1 I feel sad

2 I am sad all the time and I can't snap out of it.

3 I am so sad and unhappy that I can't stand it.

2.

0 I am not particularly discouraged about the future.

1 I feel discouraged about the future.

2 I feel I have nothing to look forward to.

3 I feel the future is hopeless and that things cannot improve.

3.

0 I do not feel like a failure.

1 I feel I have failed more than the average person.

2 As I look back on my life, all I can see is a lot of failures.

3 I feel I am a complete failure as a person.

4.

0 I get as much satisfaction out of things as I used to.

1 I don't enjoy things the way I used to.

2 I don't get real satisfaction out of anything anymore.

3 I am dissatisfied or bored with everything.

5.

0 I don't feel particularly guilty

1 I feel guilty a good part of the time.

2 I feel quite guilty most of the time.

3 I feel guilty all of the time.

6.

0 I don't feel I am being punished.

1 I feel I may be punished.

2 I expect to be punished.

3 I feel I am being punished.

7.

0 I don't feel disappointed in myself.

1 I am disappointed in myself.

2 I am disgusted with myself.

3 I hate myself.

8.

0 I don't feel I am any worse than anybody else.

1 I am critical of myself for my weaknesses or mistakes.

2 I blame myself all the time for my faults.

3 I blame myself for everything bad that happens.

9.

0 I don't have any thoughts of killing myself.

1 I have thoughts of killing myself, but I would not carry them out.

2 I would like to kill myself.

3 I would kill myself if I had the chance.

10.

0 I don't cry any more than usual.

1 I cry more now than I used to.

2 I cry all the time now.

3 I used to be able to cry, but now I can't cry even though I want to.

11.

0 I am no more irritated by things than I ever was.

1 I am slightly more irritated now than usual.

2 I am quite annoyed or irritated a good deal of the time.

3 I feel irritated all the time.

12.

0 I have not lost interest in other people.

1 I am less interested in other people than I used to be.

2 I have lost most of my interest in other people.

3 I have lost all of my interest in other people.

13.

0 I make decisions about as well as I ever could.

1 I put off making decisions more than I used to.

2 I have greater difficulty in making decisions more than I used to.

3 I can't make decisions at all anymore.

14.

0 I don't feel that I look any worse than I used to.

1 I am worried that I am looking old or unattractive.

2 I feel there are permanent changes in my appearance that make me look unattractive

3 I believe that I look ugly.

15.

0 I can work about as well as before.

1 It takes an extra effort to get started at doing something.

2 I have to push myself very hard to do anything.

3 I can't do any work at all.

16.

0 I can sleep as well as usual.

1 I don't sleep as well as I used to.

2 I wake up 1-2 hours earlier than usual and find it hard to get back to sleep.

3 I wake up several hours earlier than I used to and cannot get back to sleep.

17.

0 I don't get more tired than usual.

1 I get tired more easily than I used to.

2 I get tired from doing almost anything.

3 I am too tired to do anything.

18.

0 My appetite is no worse than usual.

1 My appetite is not as good as it used to be.

2 My appetite is much worse now.

3 I have no appetite at all anymore.

19.

0 I haven't lost much weight, if any, lately.

1 I have lost more than five pounds.

2 I have lost more than ten pounds.

3 I have lost more than fifteen pounds.

20.

0 I am no more worried about my health than usual.

1 I am worried about physical problems like aches, pains, upset stomach, or constipation.

2 I am very worried about physical problems and it's hard to think of much else.

3 I am so worried about my physical problems that I cannot think of anything else.

21.

0 I have not noticed any recent change in my interest in sex.

1 I am less interested in sex than I used to be.

2 I have almost no interest in sex.

3 I have lost interest in sex completely.

Revised Dyslexia Checklist

1. Do you find it difficult telling left from right? Yes / No

2. Do you find map reading or finding your way to a strange place confusing? Yes / No

3. Do you dislike reading aloud? Yes / No

4. Do you take longer than you feel you should to read a page of a book? Yes / No

5. Do you find it difficult to remember the sense of what you have read? Yes / No

6. Do you dislike reading long books? Yes / No

7. Is your spelling poor? Yes / No

8. Is your writing difficult to read? Yes / No

9. Do you get confused if you speak in public? Yes / No

10. Do you find it difficult to take messages on the telephone and pass them on correctly? Yes / No

11. When you have to say a long word, do you sometimes find it difficult to get all the sounds in the right order? Yes / No

12. Do you find it difficult to do sums in your head without using your fingers or paper? Yes / No

13. When using the telephone, do you tend to get the numbers mixed up when you dial? Yes / No

14. Do you find it difficult to say the months of the year forwards in a fluent manner? Yes / No

15. Do you find it difficult to say the months of year backwards? Yes / No

16. Do you mix up dates and times and miss appointments? Yes / No

17. When writing cheques, do you frequently find yourself making mistakes? Yes / No

18. Do you find forms difficult and confusing? Yes / No

19. Do you mix up bus numbers like 19 and 91? Yes / No

20. Did you find it hard to learn your multiplication tables at school? Yes / No

Adult ADHD Self-Test: Please read each statement and indicate how much it applies to you [Not at all; Just a little; Somewhat; Moderately; Quite a lot; Very much]

1. At home, work, or school, I find my mind wandering from tasks that are uninteresting or difficult.

2. I find it difficult to read written material unless it is very interesting or very easy.

3. Especially in groups, I find it hard to stay focused on what is being said in conversations.

4. I have a quick temper, a short fuse.

5. I am irritable and get upset by minor annoyances.

6. I say things without thinking, and later regret having said them.

7. I make quick decisions without thinking enough about consequences.

8. My relationships with people are made difficult by my tendency to talk first and think later.

9. My moods have highs and lows.

10. I have trouble planning in what order to do a series of tasks or activities.

11. I easily become upset.

12. I seem to be thin skinned and many things upset me.

13. I almost always am on the go.

14. I am more comfortable when moving than when sitting still.

15. In conversations, I start to answer questions before the questions have been fully asked.

16. I usually work on more than one project at a time, and fail to finish many of them.

17. There is a lot of "static" or "chatter" in my head.

18. Even when sitting quietly, I am usually moving my hands or feet.

19. In group activities it is hard for me to wait my turn.

20. My mind gets so cluttered that it is hard for it to function.

21. My thoughts bounce around as if my mind were a pinball machine.

22. My brain feels as if it were a television set with all the channels going at once.

23. I am unable to stop daydreaming.

24. I am distressed by the disorganized way my brain works.

Autism Quotient: Please read each statement and select the appropriate response

1. I prefer to do things with others rather than on my own.

2. I prefer to do things the same way over and over again.

3. If I try to imagine something, I find it very easy to create a picture in my mind.

4. I frequently get so strongly absorbed in one thing that I lose sight of other things.

5. I often notice small sounds when others do not.

6. I usually notice car number plates or similar strings of information.

7. Other people frequently tell me that what I've said is impolite, even though I think it is polite.

8. When I'm reading a story, I can easily imagine what the characters might look like.

9. I am fascinated by dates.

10. In a social group, I can easily keep track of several different people's conversations.

11. I find social situations easy.

12. I tend to notice details that others do not.

13. I would rather go to a library than a party.

14. I find making up stories easy.

15. I find myself drawn more strongly to people than to things.

16. I tend to have very strong interests which I get upset about if I can't pursue.

17. I enjoy social chit-chat.

18. When I talk, it isn't always easy for others to get a word in edgeways.

19. I am fascinated by numbers.

20. When I'm reading a story, I find it difficult to work out the characters' intentions.

21. I don't particularly enjoy reading fiction.

22. I find it hard to make new friends.

23. I notice patterns in things all the time.

24. I would rather go to the theatre than a museum.

25. It does not upset me if my daily routine is disturbed.

26. I frequently find that I don't know how to keep a conversation going.

27. I find it easy to "read between the lines" when someone is talking to me.

28. I usually concentrate more on the whole picture, rather than the small details.

29. I am not very good at remembering phone numbers.

30. I don't usually notice small changes in a situation, or a person's appearance.

31. I know how to tell if someone listening to me is getting bored.

32. I find it easy to do more than one thing at once.

33. When I talk on the phone, I'm not sure when it's my turn to speak.

34. I enjoy doing things spontaneously.

35. I am often the last to understand the point of a joke.

36. I find it easy to work out what someone is thinking or feeling just by looking at their face.

37. If there is an interruption, I can switch back to what I was doing very quickly.

38. I am good at social chit-chat.

39. People often tell me that I keep going on and on about the same thing.

40. When I was young, I used to enjoy playing games involving pretending with other children.

41. I like to collect information about categories of things (e.g. types of car, types of bird, types of train, types of plant, etc.).

42. I find it difficult to imagine what it would be like to be someone else.

43. I like to plan any activities I participate in carefully.

44. I enjoy social occasions.

45. I find it difficult to work out people's intentions.

46. New situations make me anxious.

47. I enjoy meeting new people.

48. I am a good diplomat.

49. I am not very good at remembering people's date of birth.

50. I find it very easy to play games with children that involve pretending.

Demographic Information:

Date of birth

Handedness: (Left/Right)

Biological Sex:

[ ] Male

[ ] Female

[ ] Other

Ethnicity:

[ ] Hispanic or Latino/a

[ ] Not Hispanic or Latino/a

Race: {could select multiple}

[ ] American Indian/Alaskan Native

[ ] Asian

[ ] Black/African American

[ ] Native Hawaiian/Other Pacific Islander

[ ] White/Caucasian

[ ] Unknown/Do not wish to say

Details of any known problems with vision or hearing (e.g., colour blindness):

Have you ever been diagnosed with:

Any learning disability(e.g., dyslexia, auditory processing disorder, dyscalculia)? (Yes/No)

Attention deficit disorder? (Yes/No)

Any autism spectrum disorder (e.g., Asperger's)? (Yes/No)

If you answered 'yes' to any of the above, please provide information about your specific diagnosis here:

APPENDIX B

EXAMPLE STIMULI FOR THE COGNITIVE ASSESSMENTS

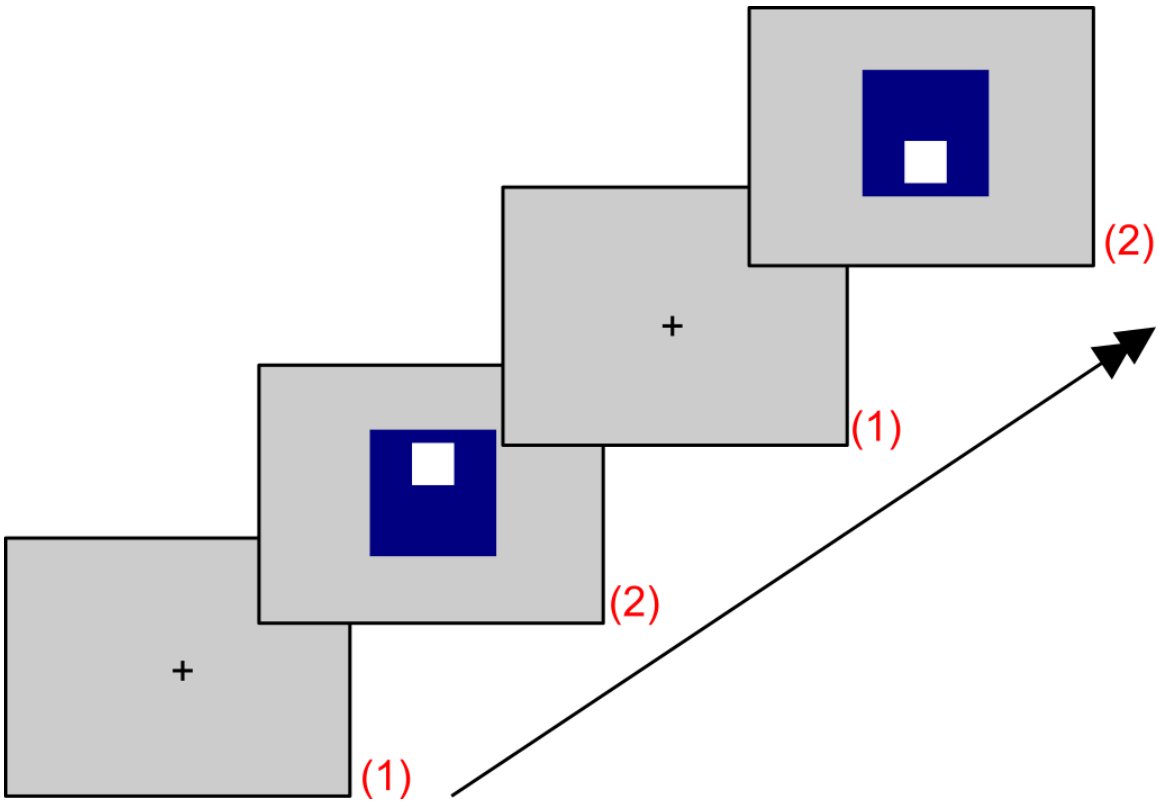

Figure B1. Example stimuli for the Vigilance task (as provided by Neurobehavioral Systems).

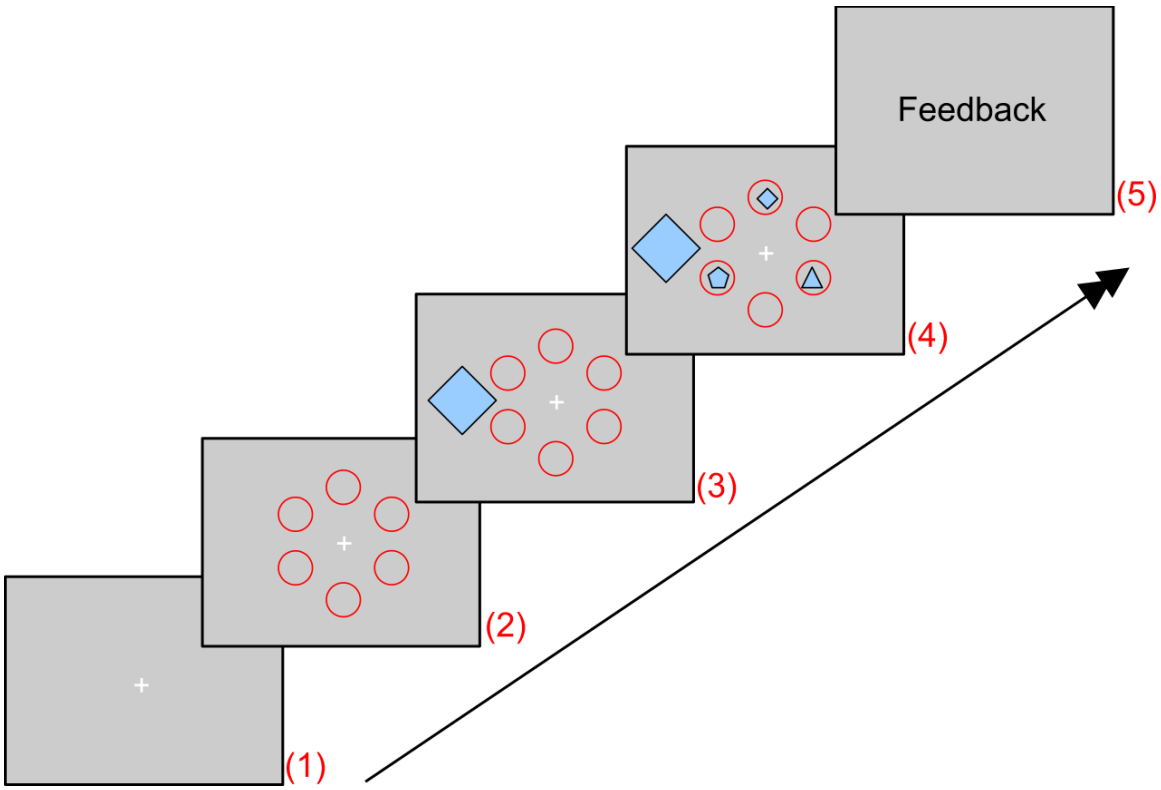

Figure B2. Example stimuli for the Flanker Task (as provided by Neurobehavioral Systems)

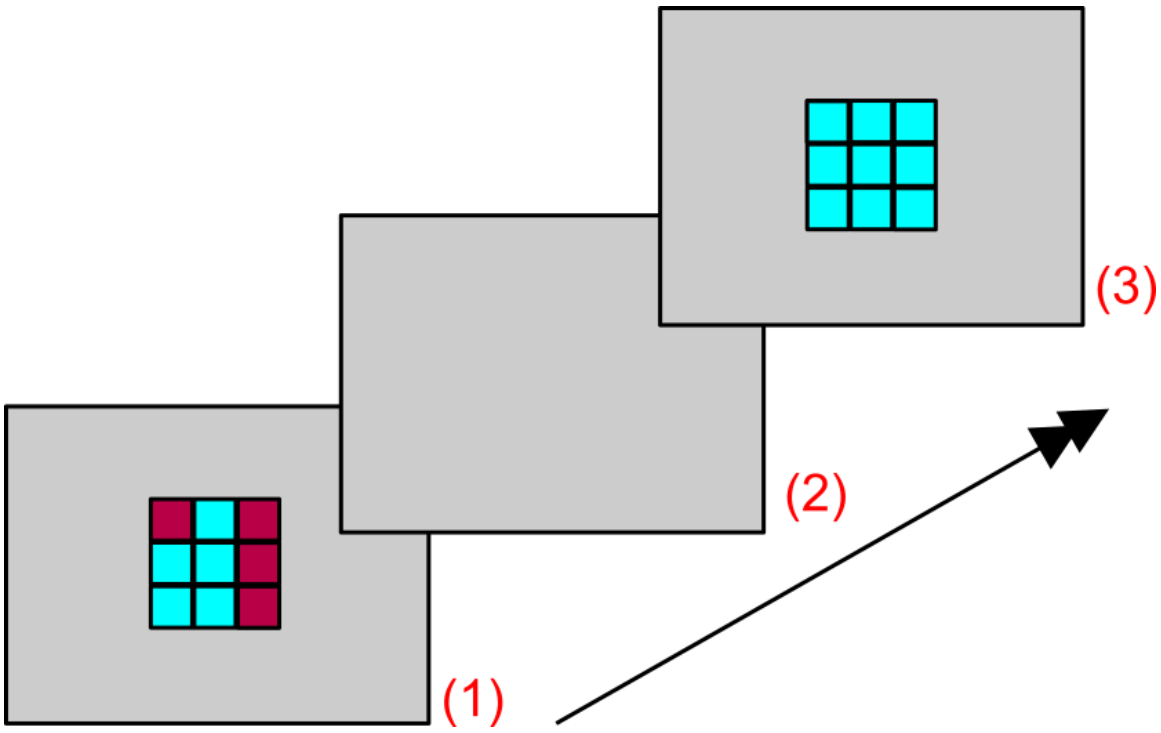

Figure B3. Example stimuli for the Match to Sample Task (as provided by Neurobehavioral Systems)

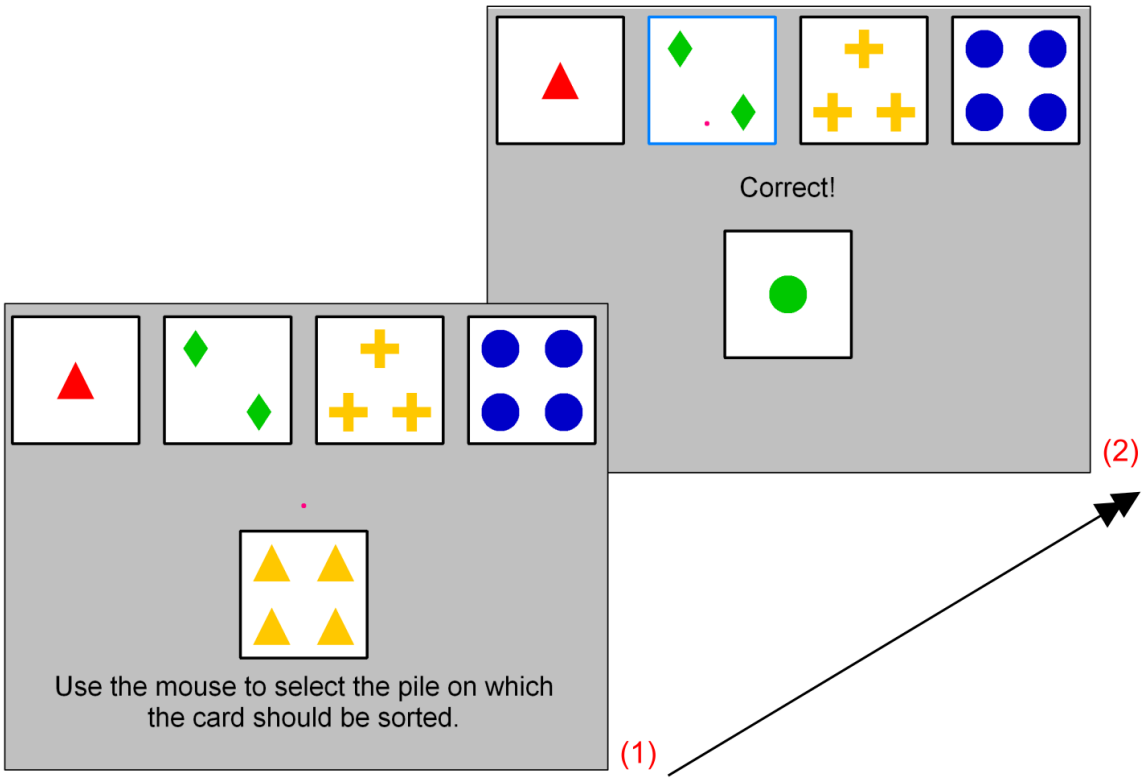

Figure B4. Example stimuli for Berg's Card Sorting Task (as provided by Neurobehavioral Systems).

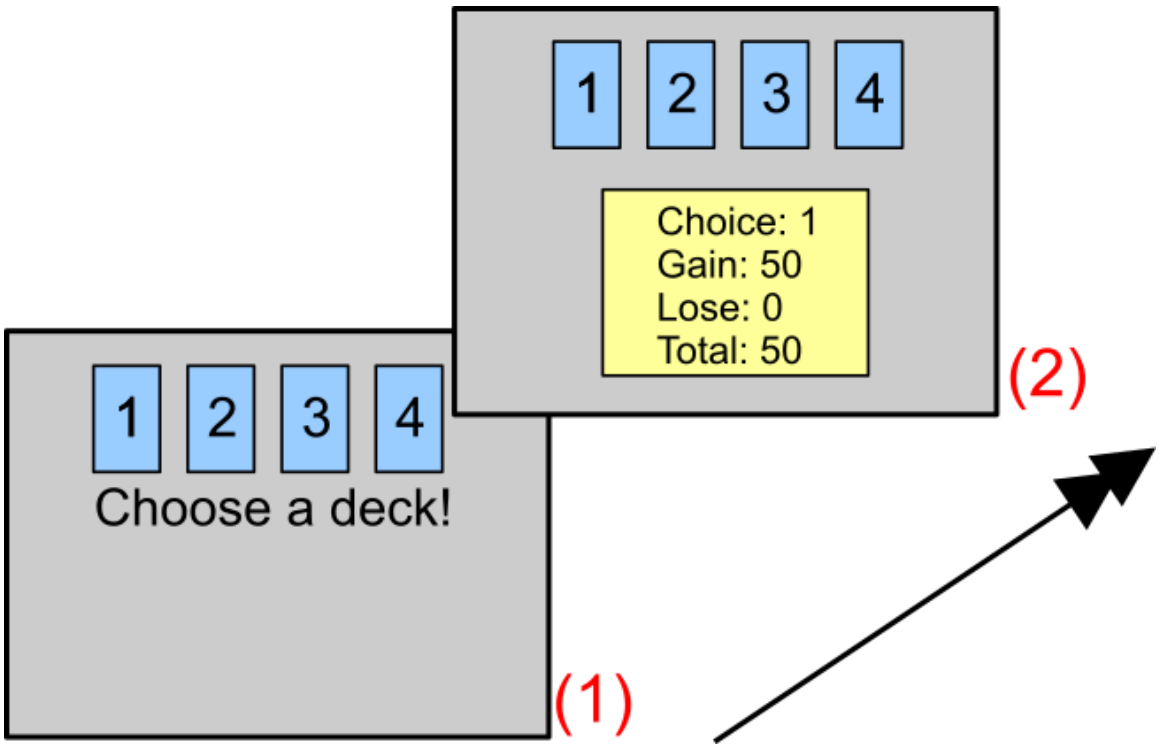

Figure B5. Example stimuli for the Iowa Gambling Task (as provided by Neurobehavioral Systems).

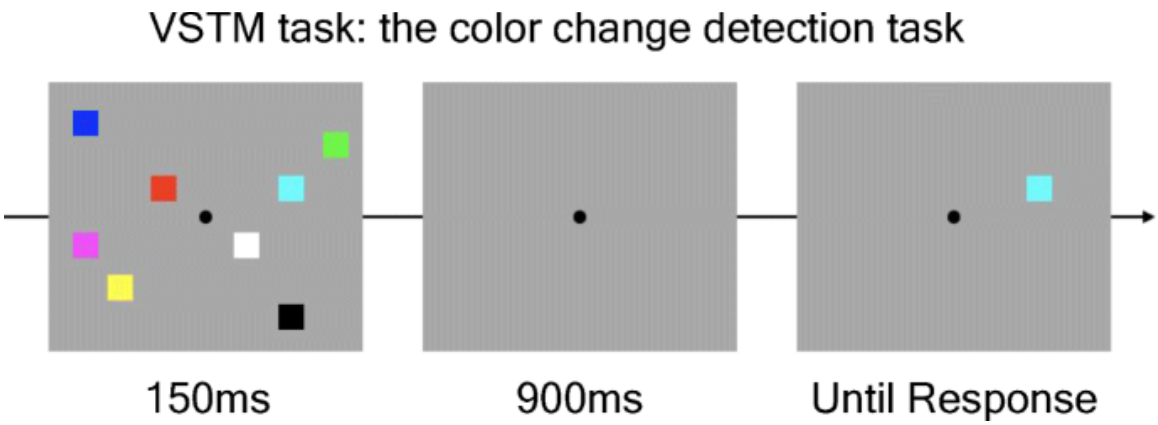

Figure B6. Example stimuli for the Change Detection Task (as seen in Fukuda and Vogel et al., 2019)

APPENDIX C: CORRELATION MATRIX

	Beck's Anxiety Inventory	UCLA Isolation	Beck's Depression Inventory	Dyslexia Checklist	Adult ADHD	Autism Quotient	Vigilance Accuracy	Vigilance Comparison	Vigilance False Alarm	Vigilance Misses	BCST Sorts	Digit Span Forward	Digit Span Backward	Match to Sample 5s acc	Match to Sample 5s RT	Match to Sample 1s acc	Match to Sample 1s RT	Emotional Memory Negative	Emotional Memory Positive	Emotional Memory Neutral	Emotional Memory Distractor	Emotional Memory Emotional Words	Emotional Memory Non-Emotional Words	IGT HRHR	IGT Disadvantageous last half	IGT Disadvantageous Comparison	IGT FRHR	Memory Capacity Estimate	Flanker Comparison Acc	Flanker Comparison RT	Days Since Having COVID-19
Beck's Anxiety Inventory	1	.279*	.624**	.222*	.587**	.208*	.003	.176	.113	.061	.090	-.065	.139	-.028	-.001	-.025	-.015	.111	.021	.081	.108	.072	.121	-.084	-.129	.101	-.071	.161	-.320**	-.094	-.164
UCLA Isolation	.279*	1	.504**	.331**	.415**	.567**	-.201	-.059	.062	.209	.191	-.083	-.230*	-.202	-.030	-.164	.092	.102	-.127	.155	.052	-.018	.137	-.170	-.273*	.222	-.166	.002	.017	-.115	-.276
Beck's Depression Inventory	.624**	.504**	1	.218	.693**	.383**	-.092	.061	.189	.128	.048	-.093	.042	-.034	-.051	-.086	.066	.199	-.061	.081	.119	.072	.128	.024	-.108	.124	-.242	.097	-.196	-.028	-.227
Dyslexia Checklist	.222*	.331**	.218	1	.429**	.298**	-.189	.039	.217*	.230*	.319**	-.153	-.300**	-.365**	.031	-.520**	-.003	-.133	-.168	-.077	-.250*	-.169	-.207	.076	.033	-.073	-.087	-.227*	-.291**	.053	-.341*
Adult ADHD	.587**	.415**	.693**	.429**	1	.318**	-.007	.048	.123	.026	.193	-.059	.023	-.160	.013	-.224*	-.002	.042	-.082	.011	-.050	-.025	-.023	-.051	-.102	.193	-.086	.048	-.141	.080	-.162
Autism Quotient	.208*	.567**	.383**	.298**	.318**	1	-.136	-.008	.231*	.152	.227*	-.033	-.166	-.180	.039	-.230*	.139	.010	-.156	.054	-.010	-.085	.030	-.153	-.242	.135	-.143	-.166	-.086	-.076	-.089
Vigilance Accuracy	.003	-.201	-.092	-.189	-.007	-.136	1	.531**	-.411**	-.951**	-.016	.048	.121	.263*	-.200	.016	-.058	-.051	.081	-.037	-.014	.021	-.035	-.244	-.204	.097	.100	.147	.011	.181	.003
Vigilance Comparison	.176	-.059	.061	.039	.048	-.008	.531**	1	.115	-.245*	.141	-.132	-.029	.172	-.083	-.285*	.070	.161	.179	.087	-.007	.194	.059	-.142	-.085	.012	.121	.005	-.120	.065	-.128
Vigilance False Alarm	.113	.062	.189	.217	.123	.231*	-.411**	.115	1	.513**	.095	-.101	-.181	-.111	.188	-.296**	.099	.023	-.054	-.042	-.077	-.019	-.077	.170	.214	-.155	.061	-.234*	-.011	-.180	-.196
Vigilance Misses	.061	.209	.128	.230*	.026	.152	-.951**	-.245*	.513**	1	.070	-.103	-.149	-.251*	.208	-.124	.095	.117	-.028	.074	.014	.047	.062	.232	.205	-.106	-.075	-.167	-.056	-.184	-.057
BCST Sorts	.090	.191	.048	.319**	.193	.227*	-.016	.141	.095	.070	1	-.193	-.412**	-.437**	.002	-.248*	-.008	-.161	-.213	-.156	-.191	-.210	-.224*	-.013	.058	-.114	.130	-.395**	.022	-.271*	.225
Digit Span Forward	-.065	-.083	-.093	-.153	-.059	-.033	.048	-.132	-.101	-.103	-.193	1	.364**	.183	-.109	.198	-.163	.263*	-.007	.141	.027	.139	.112	-.125	-.278*	.355**	-.263*	.372**	.057	-.032	.000
Digit Span Backward	.139	-.230*	.042	-.300**	.023	-.166	.121	-.029	-.181	-.149	-.412**	.364**	1	.485**	.009	.397**	-.021	.254*	.223*	.145	.271*	.267*	.265*	.117	.124	.114	-.005	.478**	-.151	.074	.066
Match to Sample 5s acc	-.028	-.202	-.034	-.365**	-.160	-.180	.263*	.172	-.111	-.251*	-.437**	.183	.485**	1	.004	.483**	-.004	.289**	.367**	.196	.316**	.369**	.328**	-.092	-.005	.049	.170	.528**	.018	.013	.054
Match to Sample 5s RT	-.001	-.030	-.051	.031	.013	.039	-.200	-.083	.188	.208	.002	-.109	.009	.004	1	.023	.810**	-.214	-.235*	-.062	-.079	-.252*	-.091	.210	.187	-.123	-.065	-.107	-.008	.050	.158
Match to Sample 1s acc	-.025	-.164	-.086	-.520**	-.224*	-.230*	.016	-.285*	-.296**	-.124	-.248*	.198	.397**	.483**	.023	1	-.068	.222*	.242*	.179	.366**	.261*	.347**	-.044	.007	.072	.099	.487**	.100	-.022	-.086
Match to Sample 1s RT	-.015	.092	.066	-.003	-.002	.139	-.058	.070	.099	.095	-.008	-.163	-.021	-.004	.810**	-.068	1	-.221	-.197	-.004	-.050	-.234*	-.034	.092	.017	-.008	-.148	-.185	-.138	.027	.154
Emotional Memory Negative	.111	.102	.199	-.133	.042	.010	-.051	.161	.023	.117	-.161	.263*	.254*	.289**	-.214	.222*	-.221	1	.593**	.533**	.283*	.885**	.535**	-.034	-.169	.187	-.241	.329**	-.050	-.036	-.272
Emotional Memory Positive	.021	-.127	-.061	-.168	-.082	-.156	.081	.179	-.054	-.028	-.213	-.007	.223*	.367**	-.235*	.242*	-.197	.593**	1	.542**	.219	.900**	.502**	.088	.046	.065	-.087	.251*	-.061	.056	-.208
Emotional Memory Neutral	.081	.155	.081	-.077	.011	.054	-.037	.087	-.042	.074	-.156	.141	.145	.196	-.062	.179	-.004	.533**	.542**	1	.193	.602**	.796**	.014	-.152	.149	-.304*	.288*	.128	-.036	-.166
Emotional Memory Distractor	.108	.052	.119	-.250*	-.050	-.010	-.014	-.007	-.077	.014	-.191	.027	.271*	.316**	-.079	.366**	-.050	.283*	.219	.193	1	.280*	.747**	-.275*	-.204	.055	.163	.222*	-.057	.043	-.288
Emotional Memory Emotional Words	.072	-.018	.072	-.169	-.025	-.085	.021	.194	-.019	.047	-.210	.139	.267*	.369**	-.252*	.261*	-.234*	.885**	.900**	.602**	.280*	1	.580**	.032	-.064	.137	-.179	.325**	-.063	.014	-.261
Emotional Memory Non-Emotional Words	.121	.137	.128	-.207	-.023	.030	-.035	.059	-.077	.062	-.224*	.112	.265*	.328**	-.091	.347**	-.034	.535**	.502**	.796**	.747**	.580**	1	-.155	-.224	.133	-.107	.332**	.058	.000	-.289
IGT HRHR	-.084	-.170	.024	.076	-.051	-.153	-.244	-.142	.170	.232	-.013	-.125	.117	-.092	.210	-.044	.092	-.034	.088	.014	-.275*	.032	-.155	1	.860**	-.522**	-.375**	-.085	-.008	.076	.240
IGT Disadvantageous last half	-.129	-.273*	-.108	.033	-.102	-.242	-.204	-.085	.214	.205	.058	-.278*	.124	-.005	.187	.007	.017	-.169	.046	-.152	-.204	-.064	-.224	.860**	1	-.702**	.151	-.141	-.033	.033	.300
IGT Disadvantageous Comparison	.101	.222	.124	-.073	.193	.135	.097	.012	-.155	-.106	-.114	.355**	.114	.049	-.123	.072	-.008	.187	.065	.149	.055	.137	.133	-.522**	-.702**	1	-.263*	.116	-.034	.006	-.214
IGT FRHR	-.071	-.166	-.242	-.087	-.086	-.143	.100	.121	.061	-.075	.130	-.263*	-.005	.170	-.065	.099	-.148	-.241	-.087	-.304*	.163	-.179	-.107	-.375**	.151	-.263*	1	-.086	-.043	-.086	.099
Memory Capacity Estimate	.161	.002	.097	-.227*	.048	-.166	.147	.005	-.234*	-.167	-.395**	.372**	.478**	.528**	-.107	.487**	-.185	.329**	.251*	.288*	.222*	.325**	.332**	-.085	-.141	.116	-.086	1	-.115	.199	-.222
Flanker Comparison Acc	-.320**	.017	-.196	-.291**	-.141	-.086	.011	-.120	-.011	-.056	.022	.057	-.151	.018	-.008	.100	-.138	-.050	-.061	.128	-.057	-.063	.058	-.008	-.033	-.034	-.043	-.115	1	-.279*	.263
Flanker Comparison RT	-.094	-.115	-.028	.053	.080	-.076	.181	.065	-.180	-.184	-.271*	-.032	.074	.013	.050	-.022	.027	-.036	.056	-.036	.043	.014	.000	.076	.033	.006	-.086	.199	-.279*	1	-.225
Days Since Having COVID-19	-.164	-.276	-.227	-.341*	-.162	-.089	.003	-.128	-.196	-.057	.225	.000	.066	.054	.158	-.086	.154	-.272	-.208	-.166	-.288	-.261	-.289	.240	.300	-.214	.099	-.222	.263	-.225	1