Personal Experiences and Observations of Cognitive and Emotional Changes in COVID-Encephalopathy patients

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Word count:
Abstract: 246 words
Main body: 9,767 words

Abstract

The COVID-19 virus has claimed many lives and altered others (Koçak et al., 2021; Logue et al., 2021; Nalleballe et al., 2020). A severe neurological complication of the virus is encephalopathy which is characterised by generalised brain dysfunction (Garg et al., 2021). Encephalopathy can lead to significant disabilities and is associated with adverse long-term clinical outcomes (Liotta et al., 2020). Although it is still not clear whether COVID-19 encephalopathy patients report lingering cognitive and emotional deficits, it has been demonstrated that many severely ill COVID-19 patients do (Wilson et al., 2020). This study aimed to document the qualitative experiences of emotional and cognitive changes reported by COVID-encephalopathy patients and to contrast them to critically ill COVID-19 patients who did not manifest with encephalopathy. Participants engaged in semi-structured interviews and three neuropsychological tests were administered for qualitative feedback. Thematic analysis was used to evaluate the data. The results conclude that COVID-19 encephalopathy patients report lasting cognitive and emotional deficits, similarly to those described by participants without an encephalopathy diagnosis but rather with increased severity. Participants' subjective accounts of changes in their thinking and memory appear to correspond most closely to challenges in episodic memory, attention, language, and executive functioning. These difficulties were described as a source of great anxiety and as a major barrier towards returning to independent living. Findings from this study bring attention to the ongoing support required by this cohort of patients and add to our knowledge of the long-term implications of severe COVID-19.

Key Words: Encephalopathy; COVID-19; cognition; emotional trauma; memory; attention; executive functioning; language

Introduction

On the 11th of March 2020, the World Health Organisation (WHO) classified the COVID-19 outbreak as a pandemic (Hao et al., 2020). The virus has since claimed many lives and left lasting impacts on others, physically, neurologically, and psychologically (Koçak et al., 2021; Logue, et al., 2021; Nalleballe et al., 2020). One of the significant and severe neurological manifestations of COVID-19 is encephalopathy. This is a central nervous system condition characterised by generalised brain dysfunction and presents patients with unique challenges, cognitively and emotionally (Garg et al., 2021). Encephalopathy is associated with adverse long-term clinical outcomes and can lead to serious disabilities (Liotta et al., 2020). Some of the long-term effects of encephalopathy include confusion, an altered state of consciousness, behavioural abnormalities, neurological deficits and a loss of quality of life (Grønkjær et al., 2018; Roos, 2014).

Although there have been many studies on the impact of COVID-19 in severely ill COVID patients, studies of COVID-encephalopathy are few. Studies that have been conducted on this topic have been quantitatively focused, creating a gap in literature on the qualitative experiences of COVID-encephalopathy patients (Liotta et al., 2020). As COVID-encephalopathy patients only form a small part of the population, these studies have also only been conducted in high-income areas that have been under-representative of cultural, gender and ethnic diversity (Borno et al., 2020; Nalleballe et al., 2020). This study aims to fill this gap by conducting qualitative research focused on a diverse population on how COVID-encephalopathy patients describe changes in their emotions and cognition during the acute and subacute phases of their illness. It will also examine the emotional experiences and cognitive challenges they face and how this translates into their daily functioning as compared to COVID patients who were absent of encephalopathy. As well as filling a gap in current research, the findings from this study will allow patients to voice their experiences and therefore create awareness on the challenges they face.

I will firstly, discuss what COVID-19 is and what neurological manifestations it causes. I will then examine the neurological manifestations of encephalopathy and its effects on cognition and emotions. Furthermore I will examine the differences between the approaches of past studies and this present study's approach. A comparison will also be made between the challenges faced by COVID-encephalopathy patients and COVID patients absent of encephalopathy. I will present my findings and discuss my interpretation of it as well as the limitations of this study and recommendations for future research.

Symptoms and Sequelae of COVID-19

As of the 6th of January 2022, the WHO has reported over 293 million COVID-19 cases, with South Africa holding the 18th most cases (World Health Organisation, 2022). Clinical manifestations can range from mild to severe (Nalleballe et al., 2020). Common manifestations include fever, dry cough, fatigue, headache, and sore throat, however the virus can also cause complications that can be fatal, for example, acute respiratory distress syndrome (Almeria et al., 2020). Many patients experience psychological distress which can lead to Post Traumatic Stress Disorder (PTSD), depression, and anxiety (Sun et al., 2021). Furthermore, as the research accumulates, more neurological manifestations of the virus are being identified (Almeria et al., 2020; Liotta et al., 2020).

Neurological Manifestations

The COVID-19 virus has been shown to damage multiple organs with many patients' peripheral and central nervous systems being affected (Fouad, 2021; Liotta et al., 2020; Nikhra, 2021; Teixeira et al., 2021). Studies show that the virus can affect the brain and leave lasting cognitive, behavioural, and emotional problems within the patient (Almeria et al., 2020; Nalleballe et al., 2020; Niazkar et al., 2020; Sun et al., 2021; Wilson et al., 2020).

Common neurological manifestations of the COVID-19 virus include headaches, confusion, strokes, giddiness, sleep disorders, seizures, and encephalopathy (Liotta et al., 2020; Nalleballe et al., 2020; Nehme et al., 2021; Niazkar et al., 2020; Viner et al., 2021; Wilson et al., 2020). Several studies have shown that patients' cognition and emotions may also be severely affected due to the aforementioned damage (Almeria et al., 2020; Koçak et al., 2021; Logue et al., 2021; Wilson et al., 2020; Yang et al., 2020). However, there has been huge variation across studies, and it is likely that demographics, pre-morbidities, and the heterogeneity of pathological pathways play a role in influencing long-term clinical outcomes in patients (Nalleballe et al., 2020).

In this regard, several theories exist to explain how the virus causes neurological symptoms but there are still many unknowns (Chen et al., 2021; Hao et al., 2020). These theories look at direct central nervous system (CNS) infiltration, post infectious autoimmune responses, cytokine network dysregulation and peripheral immune cells transmission to describe neurological manifestations (Hao et al., 2020; Liotta et al., 2020; Nalleballe et al., 2020; Nikhra, 2021; Teixeira et al., 2021). The virus can also travel to the brain via the olfactory system, which can cause the brainstem to be affected and, as a result, cardiac and respiratory functions become inflamed and dysregulated (Garg et al., 2021).

Encephalopathy

One severe neurological complication of the virus is encephalopathy. Encephalopathy is characterized by generalised brain dysfunction and can result from multiple aetiologies, including toxic, metabolic, sepsis, inflammatory and anoxic-ischemic aetiologies (CCCHC Clinic, 2017). Encephalopathy arises due to inflammation or infection of the brain and presents itself symptomatically through fevers, headaches, a modified mental state, seizures, neurological deficits, and reduced consciousness (Roos, 2014). It is an inflammation of the brain parenchyma that is often caused by the body's immune response to an infection or by the infection itself (Ellul et al., 2020). Patients are often confused and present with behaviour abnormalities, such as agitation and delirium, and flu like symptoms including nausea, myalgias, diarrhea, vomiting and respiratory illness (Roos, 2014). Encephalopathy can lead to disability and sepsis and is associated with higher rates of mortality in COVID-19 patients (Liotta et al., 2020).

Reports from the COVID-19 pandemic reveal that COVID-19-related encephalopathy (COVID-encephalopathy) can result from multiple pathological disturbances, including severe systemic inflammatory responses to the virus that cause hypoxic or metabolic changes in the body, as well as direct inflammation of the brain (Frontera et al., 2021; Garg et al., 2021). These changes are thought to be responsible for the presentation of encephalopathy in COVID-19.

Experiences of Effects on Cognition and Emotions

Although it is still not clear whether COVID-19 patients experiencing encephalopathy, specifically, report lingering cognitive deficits, it has been established that many severely ill COVID-19 patients do (Koçak et al., 2021; Logue et al., 2021; Wilson et al., 2020). These deficits include problems with memory, attention, executive functioning, and processing of information (Wilson et al., 2020). These problems have major repercussions for patients and their functioning but also for those who look after them (Almeria et al., 2020). Not being able to work has a big effect on the finances of patients and their socioeconomic statuses (Grønkjær et al., 2018). Not only is cognition affected, but patients are also impacted psychologically (Sun et al., 2021). Thus, although there are currently no reports of cognitive deficits in COVID survivors who presented with encephalopathy specifically, there is reason to believe that these patients will also experience numerous setbacks, social isolation, and a dependency on others (Grønkjær et al., 2018). For example, prior studies show that emotional reactivity and regulation are impaired post-encephalitis (Salas et al., 2014). Post-encephlitis patients have also reported problems with memory, concentration, executive function, processing speed, visuo-spatial deficits and communication (Grønkjær et al., 2018; Hopkins et al., 2004; Iwashyna et al., 2010).

Despite this literature, there are few qualitative studies that document the subjective accounts of mental changes in encephalopathy patients, and the neuro-cognitive outcomes in COVID-19 patients which additionally addresses the challenges when designing effective rehabilitation programmes (Fabrellas et al., 2020; Grønkjær et al., 2018). Literature in the ‘neuro-COVID’ field has rapidly emerged with impressive sample sizes, but it consists of the use of quantitative instruments (Hao et al., 2020; Sun et al., 2021). These studies are able to illustrate what domains of cognition are affected, however they are lacking in that they cannot show how these deficits translate into difficulties in everyday living (Grønkjær et al., 2018).

According to Sacks (1998), “The patient’s essential being is very relevant in the higher reaches of neurology, and in psychology, for here the patient’s personhood is essentially involved, and the study of disease and identity cannot be disjoined” (p. 6). Therefore, some authors argue that purely quantitative measures cannot capture the scope of experience and the extent of suffering endured by brain injury patients (Salas et al., 2017). Instead, rehabilitation efforts that are guided by a neuropsychoanalytic approach may be particularly appropriate for the emerging cohort of neuro-COVID patients (Coetzer et al., 2018). The main features of this approach would emphasise personality and emotions, a person’s self-awareness, the self, relationship and systemic aspects, and therapeutic methods that use non-confrontational approaches (Coetzer et al., 2018).

Open-ended interview-based studies are well suited to achieving these ends as they provide rich descriptions of subjective understandings of how functionality in these patients has been impacted and how psychologically and cognitively, they have been affected in their unique social-cultural contexts (Hao et al., 2020). In studying brain damage, and encephalopathy, the consideration of ethnocultural factors is increasingly recognised. Different cultural factors play a role in how patients respond to illness (Mahoney et al., 2005). For example, in Chinese culture, there is an emphasis on fulfilling family responsibilities and if you are unable to do so, you are looked down on and face increased stigma in addition to your illness (Sun et al., 2021). Currently there are not many studies on encephalopathy in COVID-19 patients, however those that exist have taken place in high income countries (Borno et al., 2020). It is therefore important that literature includes findings from vulnerable groups (Sun et al., 2021).

In conclusion, there is a clear gap in research of the understanding of encephalopathy in COVID-19 patients and its effect on the individual, their functioning and those who look after them. A qualitative study, as well as a study in a vulnerable population will fill a gap that no research project currently fills. An attempt to humanise the experiences of these individuals and produce data that is immediately relatable must be made while also considering patients’ social and economic backgrounds. This research has the potential to create awareness and produce tailored rehabilitation programmes that significantly impact patients’ recovery (Liotta et al., 2020).

Aims and objectives

Aims:

The overall objective of this study was to document the subjective accounts and qualitative experiences of emotional and cognitive changes that took place in COVID-encephalopathy patients during the acute and subacute phases of the virus. This study aimed to gain an understanding of the experiences of COVID-encephalopathy patients in their everyday life. A comparison between COVID-encephalopathy patients and those absent of encephalopathy was additionally made. A comparison was chosen to highlight any unique challenges that COVID-encephalopathy patients face and to see where any differences or similarities lie when comparing the two groups. The study aimed to create awareness, especially for the health care workers and patients' family members, of the difficulties that these patients face on a daily basis.

Main research questions:

- How do COVID-encephalopathy patients describe changes in their emotions and cognition during the acute and subacute phase of their illness?
- What are the emotional experiences of these patients?
- What are the lingering cognitive deficits that patients experience?
- What are the daily life challenges that COVID-encephalopathy patients describe?

Method

Theoretical framework

The brain relates to our mental lives in a way that no other organ does (Solms & Turnbull, 2018). The theoretical framework for this study was therefore drawn from general principles that modern clinical neuropsychology is based on. The recognition of clinical neuropsychology as its own scope of knowledge has led to the establishment of neuropsychological strategies of a qualitative and quantitative nature for clinical use; experimental research in cognitive, comparative, and physiological psychology; and an analysis of the behavioural effects of lesions on the central nervous system (Meier, 1992). Basically, the field of clinical neuropsychology is built upon relationships that exist between the brain and the mind, the latter of which includes cognition and thoughts, feelings, and emotions, and behavioural control. This interaction of the brain and behaviour affects subjective experiences and information processing, that is, cognition (Martin, 2016).

When brain injuries result in the breakdown of the brain's ability to effectively process information, certain general categories of deficit arise in the way a person interacts with the world. Cognitive deficits are well described in the literature and are generally assessed objectively using standardised tests (Tranel, 2007). However, Alexander Luria, who revolutionised modern clinical neuropsychology assessment, founded the idea that a qualitative analysis is needed of the signs and symptoms in patients to evaluate their conditions and where the areas of dysfunction are in their brains (Morgan & Ricker, 2017). This study drew from this theory when interpreting patterns of problems that patients described on the basis that they could be indicative of cognitive deficits as a result of their illness. It was used to infer, based on the clinico-anatomical method that is informed by this framework, what deficits in the brain these patients may have.

Research design

This study took on a qualitative approach and interviews took place at the Neuroscience Institute in Cape Town at the participants convenience (Appendix C). Psychometric data collected from neuropsychological tests was used for subjective feedback and descriptive purposes to complement the voiced experiences of the participants in their qualitative interviews. Qualitative research enables the understanding of perspectives and experiences to make sense of the world (Blanche et al., 2012). It allows for in depth research to take place on selected issues and for an understanding to take place on the themes that emerge from these issues. As I was interested in the experiences of individuals, this method was appropriate. Additionally, qualitative research develops knowledge that deals with the ‘how’ and ‘why’ questions which contributes greatly to medical service research (Kingstone et al., 2020).

Semi-structured interviews were employed as well as psychometric tools for descriptive purposes. Experiences are seen as realities and the study engaged with these experiences to better understand what these participants are going through and how this can inform rehabilitation (Blanche et al., 2012). Participants were selected from all income areas.

Participants

In order for participants to partake in the study, participants had to be hospitalised for COVID-19. Allocation to one of the two subgroups was made on the basis of a positive diagnosis of encephalopathy by a medical professional as a result of COVID-19 during the hospital stay. Participants needed to be aged between 18 to 70 years. This upper band cut-off was imposed because cognitive decline has shown to increase after the age of 70 (Salthouse, 2009). Therefore, this excluded the confounding factor of cognitive decline relating to age instead of COVID-encephalopathy. Participants must have had no transient impairment post discharge, meaning that participants must have had no short-term significant disturbances to their functioning. They also needed to be able to communicate in English, Afrikaans, Xhosa or Zulu. They needed to be deemed medically stable by a physician to participate.

Participants were excluded if they had a history of pre-morbid neurological illness or a major neurological injury. They were also excluded if they had advanced Human Immunodeficiency Virus (HIV) and alcohol or metabolic abnormalities. This criterion was filtered through the referring doctor during the recruitment process. There was no exclusion or inclusion criteria when it came to race, culture, and gender. Information was collected on participants' gender, race or ethnicity, , level of education, and age as displayed in Table 1. This information was collected to show that it affected all people, regardless of gender, race or ethnicity, level of education, and age. All information collected from participants was and will remain strictly confidential as stipulated by the Protection of Personal Information (POPI) Act (Theys et al., 2021).

Table 1

Participant Characteristics

Participants	**Sex**	**Race**	**Level Of Education**	**Age**
1	Female	Coloured	Grade 8 (Primary school completion)	69
2	Female	Coloured	Honours	60
3	Male	Black	NSC Certificate	56
4	Female	White	Diploma	36
5	Female	Coloured	Bachelors	45
6	Male	White	Bachelors	42

Note. Appropriate descriptions in the South African context.

This study employed non-probability, purposive sampling techniques which is a convenient recruitment method. Since this study was time-constrained, a convenient recruitment method was the most appropriate. Participants were primarily recruited from the Neurology and COVID ICU departments at Groote Schuur Hospital in Cape Town. Doctors from the hospital were contacted to identify possible participants and they were asked to explain the study thereafter requesting permission from the participants to pass on their contact details. Once candidate participants' contact details had been attained, contact with them was made first via Short Message Service (SMS), followed by a phone call and a reminder SMS the day before the interviews. A total of 6 participants were recruited into the current study. 3 participants were COVID-encephalopathy patients and 3 participants had been hospitalized for COVID, without being diagnosed with encephalopathy.

Data collection methods

Ethical approval was granted by the Psychology department (PSY2021-037) and Health Sciences faculty (526/2021) at the University of Cape Town before data collection began (Appendix E & F) . Data was collected primarily through face-to-face semi-structured interviews. Additionally, a questionnaire on subjective cognitive decline was utilized (Subjective Changes in Cognition questionnaire; Appendix D). Semi-structured interviews differ in that specific questions are asked to evoke conversation that allows the participant to express a response that they feel is most relevant and important (McIntosh & Morse, 2015). The interview schedule slowly guided participants through the course of their illness as well as asked questions in a systematic manner about any changes they have been experiencing with regards to their memory, attention, language, and functioning (Appendix C). The schedule of questions was structured qualitatively and avoided close-ended questions that only provide for one-word answers (Qu & Dumay, 2011). Instead, open-ended questions were used to maintain the flow of the participants' experiences. Loaded questions and double negatives were also avoided (Qu & Dumay, 2011).

The Subjective Changes in Cognition questionnaire let participants self-report on the changes they had experienced in their cognition. It examined various cognitive domains such as language, memory, attention, and executive functioning. This was executed in a manner that was easily understandable and practical. Participants also engaged in three psychometric tests to complement their voiced experiences.

Cognitive Tests

The psychometric component of data collection for this study was comprised of 3 cognitive tools. This component of data collection was purely for descriptive purposes and provided participants with the opportunity to give subjective feedback on what their experiences of each assessment was. The first tool, the Digit Span Test, forwards and backwards is a subtest of the Wechsler Adult Intelligence Scale (WAIS, Wechsler, 1955) and the Wechsler Memory Scales (WMS, Wechsler, 1945). The researcher read out a series of random numbers. Remembering the sequence in the forward order is a test of attention capacity and efficacy, while in reverse it is a test of executive functioning, in particular working memory (Hale et al., 2002).

For the second tool, the initial part of The Rey Auditory Verbal Learning Test was used. Participants were asked to recall five unrelated objects that the researcher had listed. The words kept being repeated until the patient had learnt all five words and after a period of 5 minutes the subject was asked to recall the words again and was scored from 0-5 (Paula et al., 2012). .

In the last tool, the Rey–Osterrieth Complex Figure, participants were given a complex line drawing that they needed to first copy freehand and then draw from memory. The test was scored according to the guidelines that were created by Spreen and Strauss (1998). This test assessed executive functioning, such as memory, attention, working memory and planning (Shin et al., 2006).

Procedure

Participants were invited by their doctor to take part in the study. If they agreed for their contact details to be passed on, an SMS was sent to them outlining what the study is about and asking them if they were comfortable to telephonically discuss their participation. During this call the purpose and the aims of the research was explained, they were told what kinds of questions they can expect to be asked and why the research was important. This was followed up with a reminder SMS the day before the interviews were meant to take place. The session strictly adhered to COVID-19 health regulations (protocol is outlined under Ethical Considerations).

Upon the participant’s arrival, the researcher outlined the general format of the session. Each session lasted between 60 and 90 minutes with the first 30-60 minutes being for the interview and the remaining 30 minutes for the brief cognitive assessment. Participants were interviewed alone, without the presence of a family member. The researcher explained the consent form to the best of their understanding (Appendix A & B), ensured that the participants read through the form and obtained signed consent before the family member left. The researcher verified the participant’s understanding of the consent form and told participants that they could ask any questions at any time (McGrath et al., 2019). Other key issues, for example, confidentiality, the right to withdraw from the study and protection of data were covered. The participant was informed verbally and in writing that the session would remain confidential, as well as ensured the participant that the interview and results would not affect their medical treatment and be presented in their medical records and shared with anyone else. Protection of data is in line with the POPI Act (Theys et al., 2021).

The semi-structured interview was guided by a template (Appendix C). If participants veered from the topic, they were given the space to explore their topic and then gently reminded to return to their experiences with COVID-19. The researcher also asked questions about specific mental changes that the patient may be experiencing. These questions focused on the following functions: attention, memory, language, appetite, mood, motivation, sleep and executive functioning (Appendix D). During the interview, the researcher audio-recorded the session with permission from the participant. After the interview, participants took a short break, if needed, followed by taking part in the cognitive tools as outlined above chronologically. Thereafter, participants were asked if they had any further questions, were thanked for their participation and handed a support resources flyer (Appendix G).

Data analysis

All collected data was transferred to the researcher’s personal password-protected laptop which only the researcher has access to. Audio recordings were transcribed word-for-word except for information that could reveal the participants’ identities. These transcripts were imported and organised using NVivo Qualitative Analysis Software. Data were analysed using a thematic approach which is a method that involves examining data to identify any recurring patterns or themes (Braun & Clarke, 2006). Analysis allowed for themes to emerge naturally but were also coded according to themes that occur in clinical neuropsychology in the cognitive domains. The themes were further developed into sub-themes to underline the ways in which their cognitive functioning was affected.

The guidelines to thematic analysis as outlined by Braun and Clarke (2006) were followed. Initially, the collected data was read twice to identify any preliminary themes before the software organised the data for coding. The organised data was then reread numerous times to further categorise the experiences of the participants. This forms part of an inductive approach and themes were assigned and reformulated until all data were categorised appropriately. All codes that exist within one theme were collated into their own documents and themes were modified or dropped if they were not adequately covered by the excerpts. In the end, a thematic map was created with major themes and their sub themes and within each, main theme excerpts were identified to later refer to. The researcher remained aware of response bias and used non-leading questions.

Data gathered from the cognitive assessment tools were transferred to Excel and formulated into tables for descriptive purposes. Any pictures from the tools were uploaded to the aforementioned laptop. The researcher scored the performance of participants, and scores were classified according to standardised cut-off scores such as “severely impaired”, “mildly impaired” or “normal”. A second round of evaluations took place while considering various factors, such levels of education.

Triangulation was employed in this study to strengthen the validity of the data collected. Triangulation involves using multiple data sources or methods to gain a thorough understanding of what is being studied in qualitative research (Carter et al., 2014). This study achieved triangulation by making use of qualitative semi-structured interviews, psychometric cognitive tests and observations made during the interviews.

Ethical Considerations

This study was conducted in compliance with UCT's protocol on the use of human subjects and with the Declaration of Helsinki (2013). Ethical approval was gained through the Psychology and Health Sciences departments (Appendix E & F).

Informed Consent

Prospective participants, during the recruitment stage, were made fully aware of what their commitment entailed. There was transparency on the purpose and aims of the study and the nature of the questions. The researcher went through the informed consent forms with the participants (Appendix A & B). These forms clearly defin the goals of the study, how it will be executed, possible risks and inconveniences, how confidentiality is guaranteed, how the findings will be used and who will have access to the findings. The forms also provided information regarding participants' right to withdraw from the study without any consequences. Participants who did not understand the information in the consent form were considered ineligible. Consent was obtained from the participants before data collection began.

Confidentiality

All data collected during the course of the study was kept confidential and stored on a password protected laptop. This laptop was only accessible by the research team and participants' identities were anonymised with each participant being referred to via a number and not by their names.

Foreseeable harms

Participants faced minimal risk by taking part in the study as there was very little harm involved with participation. If participants needed to be accompanied by a family member, it was assumed that they would make their own arrangements for this, however it was enquired about in the telephonic conversation. During this conversation, participants were also asked if they needed help with getting to the venue. Between R50-R100 was given to all participantsto compensate for their travel arrangements. With the COVID-19 pandemic, there was the risk that participants and their family members could get re-infected; therefore, all COVID-19 safety precautions were followed, and every precaution was taken to minimise this risk. Rooms were sanitised, only one session took place a day, the room was well ventilated, everyone was required to wear a mask and they sat 1.8 metres apart with a screen between them. Before entering the venue, screening questionnaires were completed, and hands were sanitised.

A week after the interviews, participants were contacted to see if they needed any extra support if discussions may have negatively affected them and caused psychological distress. As participants were asked to discuss their personal subjective experiences of the difficulties they faced, they may have felt the need for counselling after the session. If this was the case, participants were referred to the Psychiatry unit at Groote Schuur Hospital.

Benefits

There were no direct benefits to participants in taking part in this study. Although, the participants may have benefitted in having an opportunity to express their experiences to the interviewer without any feelings of judgment. The benefit of the study as a whole is to create awareness in healthcare workers and patient’s family members on the difficulties those with COVID-encephalopathy face on a daily basis. It will also allow for rehabilitation programmes to be better informed. In conclusion, participants might experience satisfaction from contributing to this type of knowledge production and may find comfort in knowing that there are possibly other patients who are going through similar experiences.

Reflexivity

“Reflexivity involves awareness that the researcher and the object of study affect each other mutually and continually in the research process” (Haynes, 2012, p. 80). As the sole researcher of this study, I was fully responsible for collecting the data and interpreting the direct expressions and indirect body language of the participants. This meant I had to continuously be aware of any preconceptions I may have had and how my worldview might influence my interviews and my interpretations of the data. I also needed to be aware of how the aim of my study might have influenced my behaviour. Any individual experiences that I have had with patients that have been neurologically ill, as well as any preconceptions on emotional control and brain injuries were noted. As my mom was diagnosed with a neuromuscular disease when I was growing up, I needed to put aside any fears that I may have developed towards working with individuals with neurological problems. I was also nervous about dealing with critically ill COVID survivors as I didn’t know what to expect, so I went into my first interview with trepidation. I took note of any personal biases I may have had towards participants' individual traits. For example, as a female researcher I also find it more difficult to work with men than with women. However, once facing all the participants I knew all my worries were unfounded and I was able to comfortably interview them. My main goal was to be objective, neutral and unbiased.

I was also aware of racial and gender power dynamics that can be at play during interviews due to me being a white female. As most of my participants were of another race I was aware that they may feel uncomfortable opening up and may say what they think I want to hear instead of what they have experienced. As I was also conducting the three psychometric tests I also picked up that the participants felt embarrassed that they had not done as well as they would have liked to. However, during the interviews I made sure to pose participants as the experts on what they were discussing. I constantly reminded myself of the impact subjectivity can have in creating biased research, although I struggled to find the balance between empathy and subjectivity. The reflexivity tools I used were to take notes before and after each interview, reflecting on my personal worldviews and perceptions that could have influenced my interpretations and behaviour.

Results

The aim of this study was to gain an understanding of the emotional and cognitive changes that have taken place in COVID-encephalopathy patients. Two main themes emerged after conducting a thematic analysis, being cognitive deficits and emotional trauma. Both of these umbrella themes had numerous subthemes. Subthemes under cognitive deficits included concentration, memory, communication and executive functioning. While subthemes under emotional trauma included guilt, hospital negligence, motivation, social support and resilience. All the participants had common experiences when it came to both of these themes.

Cognitive deficits: “My mind is slipping away”

This theme depicts how participants still experience problems when trying to think and process information in the environment. They reported difficulties that were indicative of problems with concentration, language, memory, and processing speed after being sick. This was expressed by participants verbally and on the Subjective Changes in Cognition questionnaire as seen in Table 2. The table describes how many participants struggled with specific cognitive difficulties. As seen below, most participants, 5 out of 6, struggled with receptive and expressive language, as well as difficulties in paying attention for long periods of time. 4 out of 6 participants described their difficulties in remembering events or had difficulties in recalling information. 3 out of 6 participants experienced difficulties with executive functioning and planning. In relation to this, 2 out of the 3 COVID-encephalopathy participants struggled with this. The additional cognitive difficulties will be further discussed below.

Table 2

Cognitive Domains Wherein Participants Experience Difficulties As Collected In The Subjective Changes In Cognition Questionnaire

Areas of cognitive difficulties	Number of participants (maximum of 6)
Language	5
Memory	4
Attention	5
Executive functioning	3
Visuo-spatial functioning	0
Additional cognitive difficulties	3

Concentration

During the interviews, almost all of the participants expressed during their interviews how they could not stay focused on one thing for an extended period of time.

> *Driving at the moment, my biggest fear is driving. Not because I don't know how to drive. It's just the concentration around driving. I won't go drive somewhere that I know I'm going to drive for hours on end or more than 30 minutes. I avoid that now because the longer I drive, the more my concentration… I can feel it's not there.*

In the quote seen above, Participant 4 expresses how something they once found very easy to do, has become a challenging ordeal due to the amount of concentration it takes. Other participants expressed similar experiences when it came to reading, watching TV and having conversations with others.

Language

Not only do participants struggle to concentrate on conversations with others, but they also are experiencing difficulties in expressing themselves.

> *But going into the working environment, there's some words that I know exactly what I want to say, and I can't get it out. I can't get that word. And it will bug me. You know, it'll bug me until the next day, and I'll wake up the next day like, "Oh! Sanitiser. That's the word I was looking for."*

Participant 6 explains how when communicating with others, they struggle to find the words to express themselves. This had never plagued this participant before and has only been occurring since they fell sick. Participants 1, 2 and 3 also experience difficulties in communicating and conveying what they want to say to others. The interviewer observed the manner in which the participants would explain or express themselves with repetition. This is indicative of cognitive difficulties affecting the way they communicate. These difficulties associated with communicating, directly link to problems with memory as the participants cannot remember the words they want to use.

Memory

All the participants conveyed experiencing forgetfulness, starting from the days they spent in hospital to the small things in everyday life.

> *I keep forgetting some, some thing, some thing. Maybe but it's happening every day for me. That there will be something I forgot to do or forgot to, but I will forget*

> *something. I will forget something and every day. It might be the phone, might be my wallet, might be something.*

Participant 3 expressed how they often forget to do things they needed to do that their wife has asked them to do or things they needed to carry with them. They express how there is often not a pattern to what they forget and that it can be anything.

> *I can't remember anything. I can't remember anything. I must use this notebook. That's the best thing I can do. I don't know how else.*

Participant 2 has had to change their behaviour in order to counteract their forgetfulness. They now carry around a notebook in which they write down whatever they need to remember or do. They have expressed that they have tried many other ways in which to remember things, but nothing has worked to lessen their forgetfulness. This also illustrates how these participants are struggling with the area of working memory which forms part of executive functioning.

Executive functioning

Participants, especially the participants who had COVID-encephalopathy, mention that in terms of executive functioning they are lacking in many areas, such as impulse control, flexible thinking, organisation, self-monitoring and task initiation.

> *It takes me more time to do things. I used to be able to problem solve on the fly, and to some extent, I can still do that, but other things, I have to think for a bit and then, okay, maybe this way, or I have to plan it out a little or rationalise it for a little, but before I can get there, so, yeah.*
>
> *Whatever you say, if you say it's okay, it's okay. I can't judge you now. Okay, or trying to investigate what is going on now, to you. Uh-uh. I don't have that intelligence, that intelligence now.*

> *I must process things when I'm alone. Because the answers don't come, and I do stupid things…*

All these participants as well as the other three expressed how their thinking has slowed down, how it takes them longer to do things and that they need time and space to process what is happening around them. Participant 3 expresses how they have lost the ability to make judgements or discernments and how after their illness they can longer tell if their daughter is trying to deceive them. Four out of six participants expressed that they feel their brain has been severely affected and that this has changed their abilities and intelligence.

Quantitative data collected. The psychometric data collected coheres with findings from the interview regarding cognitive deficits as it showed that all three of the COVID-encephalopathy participants could be classified as severely impaired due to their test scores and one of the COVID participants absent of encephalopathy as mildly impaired. Scores for these four participants on the Rey–Osterrieth Complex Figure were very low, with the three participants who had COVID-encephalopathy scoring in the 10th percentile (Spreen & Strauss, 1998). This further maintains that their attention, concentration, memory and executive functioning has been impaired (Zhang et al., 2021). The same three participants also displayed below average scores in both the forwards and backwards Digit Span Test which indicates that their attention capacity and efficacy and their executive functioning, in particular working memory has been impaired which supports their accounts (Hale et al., 2002). Participants 1 and 3 also displayed below average scores on The Rey Auditory Verbal Learning Test exhibiting also that their learning capacity and memory has resulted in cognitive deficits (McMinn et al., 1988).

Emotional trauma: “I was the survivor that shouldn’t have survived.”

This theme focuses on what participants went through in hospital, the lasting emotional impact it has had on them and how they are struggling to adjust to normal life.

Sub-themes were found including guilt, hospital negligence, motivation, resilience and social support.

Guilt

Many of the participants express guilt over being alive while many of the patients in their wards passed away.

> *And being there, amongst other people who were really sick, other people who were really sick and battling and going to sleep at night and waking up the next morning and the bed across from you is empty. That's yeah, that was really… I don't know, life changing.*
>
> *Six people died, just in front of me, in front of me and that, that was the thing. The other thing because I saw these guys coming in, they were better than me, but they're dying. Then I said, "Hey, I mean the day is coming for me also." So, that thing is traumatizing because you, you just waiting for your time to come. I was just waiting for my time to come because the guys would just pass away while, while we are talking, just talking, talking. You'll just see a guy is dropping.*

Even though the two excerpts quoted above were made by participants 3 and 6, all six of the participants witnessed people dying right in front of them. Many people who they had been together with for weeks and who they had made friends with. This is something that is distinctly remembered, they still think of it often and it caused them to wonder why they had survived.

Hospital negligence

All the participants were scared they were going to die in hospital and, for four of the participants, this was aggravated by the fact that they felt they were not getting adequate medical treatment.

> *That is not my prayer for anyone to go to hospital.*

> *Even the doctors say, "Hey, we don't know really what exactly is happening to you."*

Participants 1 and 2 expressed that they would never want anyone to be treated the way they were treated in hospital. One of the participants, being a nurse themselves, expressed shock and disappointment at the level of care they received. Participants 3 and 6 also felt uneasy as they perceived that even the doctors didn't fully know how to treat them and lacked an understanding of what damage the virus could cause. All the participants also expressed that they felt the nurses were scared of them and in many cases were negligent because of this.

> *They didn't die because of the COVID was over. They died because of the oxygen, the pipe was not tight, you know. So, you were supposed to, to, to safeguard the pipe, that you mustn't come out. There was... It was supposed to, to, to, to have a nurse all the time around us, but the nurses there, they were also scared. They would just put us, check us and go out. Maybe they will leave us more than three hours. No one. Then the pipe, if the pipe come out of your nose, you can't breathe. Then the other... When she come, someone is dead because of that pipe. One might think that, oh, if the pipe was in, in the, in the nose, this person couldn't die, but he died because of this thing.*

Participant 4 expressed that they still have trouble sleeping at night due to what they experienced in hospital and due to the fact that they felt a loss of control when they were ill.

> *You don't, it's almost like you're afraid to go to sleep because if you go to sleep, you either forget things, or you wake up disorientated, and it takes a second to realize. Oh, I'm actually at home, not at the hospital.*

Motivation

The participants also face a loss of motivation to get back to who they were and to do the activities that used to interest them. It affected them emotionally, as many of them were no longer functioning at work in the same manner they used to. Participant 2 was unsure if they would be able to return to work at all. Participants communicated that they experience frustration at not getting better as quickly as they would like to and due to this have feelings of depression as expressed by participants 4 and 6 below.

> *You get more and more depressed. It's also very, very angry because there are some days where you just feel like this is never going to end.*
>
> *Yeah, and, as I said, I try to stay positive as much as I can, and try keep the wife happy, and she tries to help a bit. But it looks like we're fighting a losing battle. You want to go forward but you're not going anywhere.*

Resilience

Even though the participants' experienced survivor's guilt, loss of motivation, frustration and depression, all of them expressed thankfulness to still be alive. It seems as if they have built up resilience to the difficulties they have faced.

> *It is not exactly where it must be but from where I'm coming, I know that I'm getting there. Yes, I know. I know. I know I'm getting there. Yes. I also thought people die with this COVID and stuff. And I was thinking, "But I survived." I thank God.*
>
> *I am dealing with what was happening in my life as best as I possibly can and reassuring myself that I can do this. I can do this. I am going to be OK, although I don't know if I'm going to be OK but I'm going to be OK.*

Participants 1 and 6's subjective accounts illustrate how they hope they eventually will not be experiencing the same difficulties that they currently face and how there has been some progress from how they were in hospital. The participants communicated that the next steps they would take would be to try and continuously improve themselves and figure out who they are at present after their illness. Participant 2 indicated this throughout their interview.

> *I think my motivation is because I want to, I want to improve myself- I shouldn't say improve myself. I want to find out what is the new me. We can never ever be what we were but we can choose to be a better person.*

Social Support

All of the participants expressed that they would not be where they are now without the support of their families and communities. Participants 1, 2 and 3 distinctly conveyed their gratitude for their support structures.

> *My wife supported me, supported me very much. Because the time I came from, from hospital, it was hard for me to, to wash myself even. My wife washed me, supported when, when... And my kids also supported. My family supporting me*
>
> *I had a lot of support and I realized how much my children love me and that also the grandchildren.*
>
> *My biggest source of strength was knowing that there was a praying church behind me. I really knew.*

As seen above, the findings strongly support that both the COVID-encephalopathy participants and the COVID participants who were absent of encephalopathy experienced long-lasting difficulties cognitively and emotionally. However, the COVID-encephalopathy participants reported more cognitive deficits which was supported by their test scores.

Discussion

This study aimed to document the subjective accounts of emotional and cognitive changes that took place in COVID-encephalopathy patients at the time of hospitalisation and in the months thereafter. It aimed to ascertain what challenges these patients still experience cognitively and emotionally. By comparing COVID encephalopathy patients and COVID patients absent of encephalopathy, the data collected shows similar experiences and where there were differences. Current COVID-19 studies have taken on only quantitative approaches and have been situated in high income areas that have been under-representative of cultural, gender and ethnic diversity (Borno et al., 2020). Individuals from minority backgrounds are twice as likely to die from COVID-19 and research data is not uniformly collected when it comes to race with black patients' disease burden being underrepresented (Borno et al., 2020; Wilson et al., 2020). Yet the COVID-19 virus is not discriminatory and affects individuals of all cultures, races, and genders and it is therefore imperative that research in this study was carried out in diverse population groups (Sun et al., 2021). By studies only adopting quantitative approaches, the "insider" perspective or the patient-experienced perspective is missed (Grønkjær et al., 2018). To aid the rehabilitation of these patients, qualitative research was needed to create an understanding of the difficulties these patients face in everyday living

The theoretical framework drawn from in this study was based on the general principles that current clinical neuropsychology is founded upon. The medical nomenclature of this field was used to scaffold interpretations of clinical data, which has been empirically formulated according to relationships between the brain and behaviour, which in turn can explain patterns in cognition and mood (Solms & Turnbull, 2018). This framework was used to infer from subjective experiences, what cognitive deficits these patients may have. In conjunction, stories of mental changes were anlysed using grounded approaches.

Overall it was found that the participants experienced and are still experiencing cognitive and emotional troubles. Both the COVID-encephalopathy participants and the COVID participants who were absent of encephalopathy experienced this. This is in line with many findings from studies on COVID-19 which show that the virus affects the brain and can leave long lasting challenges for patients physically, cognitively and emotionally (Almeria et al., 2020; Nalleballe et al., 2020; Niazkar et al., 2020; Sun et al., 2021; Wilson et al., 2020). Additionally, these findings correspond to reports of cognitive and affective disturbances in encephalopathy in other contexts (Roos, 2014).

Participants reported deficits in their concentration when it came to driving, reading a book, doing their work, watching TV and having conversation with others. Attention deficits were noted by Bajaj (2010) to be one of the more severe deficits in encephalopathy patients' neuropsychology profile. Therefore, encephalopathy patients are known to have deficits in their concentration, and this suggests that qualitative reports of attention difficulties in this COVID-encephalopathy sample correspond with quantitative reports in prior studies.

Participants also found that their language was affected and that they often could not express themselves or find the words they were looking for. This is consistent with findings by Grønkjær et al. (2018) who found that hepatic encephalopathy patients struggled with communication. Howoever, communication difficulties do not directly imply a language disorder. In neuropsychological classification, a language disorder (aphasias) are diagnosed in terms of controlled attention, complex working memory, fluid reasoning, and language knowledge in long-term memory (Gillam et al., 2019). Not all of these symptoms were found in the current cohort. Thus, it is likely that communication in the current sample was hampered by other factors such as fatigue, lack of concentration, or problems with memory and executive functioning (Khatoonabadi et al., 2020). Although, has been found that many COVID-encephalopathy patients tend to have language disorders such as aphasia, however in studies by Pensato et al. (2020) and Muccioli et al. (2020), these disorders were attributed more to global brain dysfunction where it is not possible to diagnose specific neuropsychological syndromes. Therefore, this study can illustrate that COVID-encephalopathy patients do have problems with communication but findings did not suport the presence of aphasia.

In prior studies of cognitive difficulties in COVID-19 survivors, memory deficits are consistently reported (Almeria et al., 2020; Koçak et al., 2021; Logue et al., 2021; Wilson et al., 2020; Yang et al., 2020). In keeping with this trend, all participants here reported difficulties with their memory and high levels of forgetfulness. This is consistent with findings from Wilson et al. (2020) who reported significant problems of processing information and memory failure in COVID victims, such as forgetting appointments or taking their medication. In the same way that communication challenges do not necessarily imply language disorders, forgetfulness and problems with memory do not imply an actual axial amnesia where we would expect damage in the hippocampus and medial temporal lobes of the brain (Ponsford & Donnan, 1980). Studies on forgetfulness in encephalopathy patients do not often clearly differentiate between difficulties with recall versus recognition and prompting, making it difficult to interpret whether patients show encoding or solely retrieval problems (Blahak et al., 2015; Vedes et al., 2012). However, one of the most sensitive areas of the brain to hypoxia is the hippocampus (Ponsford & Donnan, 1980). Therefore, future research should be conducted on how to classify the memory loss that COVID-encephalopathy patients describe and additionally, what can cause it.

Another cognitive deficit that participants from this study report is problems that correspond most closely to executive functioning which is in line with many studies on encephalopathy and also severe COVID-19 (Almeria et al., 2020; Grønkjær et al., 2018; Koçak et al., 2021; Logue et al., 2021; Roos, 2014; Wilson et al., 2020; Yang et al., 2020). Participants reported that their illness has left them with slow thinking and an inability to make judgements and discernments. All these cognitive deficits were further exhibited in the scores that the participants achieved on their cognitive tests. While this study found that COVID-encephalopathy patients experiences cognitive challenges, it cannot comment on the reasons behind these difficulties. Other authors have speculated that executive deficits in

COVID-19 and encephalopathy may be explained by increased inflammation and immune activation, respectively (Hellmuth et al., 2021).

In this study, emotional trauma emerged as a dominant theme in interviews. This is consistent with a large number of studies on COVID-19 survivors which show that psychological trauma was experienced due to what patients had gone through in hospital and how their functioning had changed (Lei & Klopack, 2020; Sun et al., 2021). Trauma is also speculated to play a role in mood disturbances. In this cohort, it appeared that participants emotional trauma was also linked to their cognitive difficulties. Almeria et al. (2020) found in their study on the effects of COVID-19 that cognitive deficits were associated with anxiety and depression. According to Rabinowitz & Arnett (2013) and Di Cara et al. (2020), neurological damage and mood interacts. Rabinowitz and Arnett (2013) found that the rate of depression and apathy in neurological patients is notably higher than the rate of incidence found in the general population. The degree of cognitive deficits found in patients may affect motivation and cause anxiety (Di Cara et al., 2020). There is clearly a link between neurological difficulties and mood, however to what extent cannot be said based on the current design and further large-scale quantitative investigations using brain scanning approached in conjunction with psychometric testing is needed on this topic.

Nevertheless, this study provides important insights into the nature of trauma experienced by COVID-encephalopathy patients. In this study, a link was indeed found between the two and themes of emotional trauma also included guilt, hospital negligence, motivation, social support and resilience. Participants in this study reported frustration, worry and depression due to not being able to do what they used to. The participants were also left with guilt from seeing other patients die in front of them and were wondering why they survived as also found in other studies by Miranda et al. (2021).

Participants were worried that the doctors and nurses who were treating them were negligent. Many reported that they have still not been able to work through this trauma and that they still think about it often, even after seeking help from a psychologist. The emotional trauma the participants experienced led to a decrease in motivation and the feeling that they would never recover, a hopelessness. This was also found in a study by Ortelli et al. (2021). However, this was tied to a resilience that had now developed in the participants as well as a need to find out who they are after their illness. This is similar to findings by PeConga et al. 2020 but differed from the results of Killgore et al. (2020). Therefore, future studies should conduct further research on resilience in COVID and COVID-encephalopathy patients.

Both the COVID-encephalopathy participants and the COVID participants who were absent of encephalopathy experienced these cognitive and emotional deficits. However, the COVID-encephalopathy participants reported more cognitive deficits which was supported by their test scores, which showed they were severely impaired. This is unlike the COVID participants, of which two of the participants scored normally and the third’s test scores were classified as mildly impaired. As a result, not only do COVID-encephalopathy patients experience the same cognitive deficits and psychological problems, but they also experience the deficits associated with just acquiring encephalitis as reported by Grønkjær et al. (2018), Hopkins et al. (2004) and Iwashyna et al. (2010). As encephalopathy is an inflammation of the brain parenchyma it results in cognitive dysfunction (Ellul et al., 2020). These increased deficits have also heightened the emotional challenges experienced by COVID-encephalopathy patients when compared to the emotional challenges of COVID patients absent of encephalopathy.

Limitations and Recommendations

As this study focused on a specific population, the number of eligible participants were limited and this led to difficulty in finding participants. Participants needed to be referred by a doctor, which resulted in only 3 COVID-encephalopathy participants being interviewed alongside 3 COVID participants. However, due to the sample holding prolific and detailed information, a lower number of participants was deemed acceptable (Malterud et al., 2016). Additionally, the sample size was practicable for the researcher due to the limited time frame provided for research to be conducted in. Interviews were conducted in a face-to-face setting and therefore the researcher's identity may have influenced what the participants felt comfortable to share. However, this was considered in reflexivity. As thematic analysis was used to analyse the data, the emphasis was placed on shared experiences between the participants. Experiences that were not shared were considered outliers and therefore may have been excluded. In the future, similar studies should focus on only COVID-encephalopathy patients on a wider scale, and participants from lower income areas. It would also be interesting to interview the same participants from this study a year later to ascertain if they are still experiencing the same cognitive and emotional challenges.

Implications of the findings

The findings from this study can be used to facilitate rehabilitation programmes for COVID patients. Survivors of neurological injuries tend to isolate themselves from their friends, families and communities (Salas et al., 2018). By implementing rehabilitation programmes, patients can go to a safe space that is entirely focused on their recovery, they can disconnect from the outside world, and they can relate to other patients in these programmes who are going through similar experiences (Salas et al., 2018). This may prove to be vital to adjusting back to life after illness. It may be suggested that hospitals implement rehabilitation centres and change policies to make rehabilitation mandatory. Health policies should change to advocate for these types of programmes. This study should also create awareness in healthcare workers on the impact they can have on patients and how to improve their interactions with patients. Lastly, this research can be used to facilitate further research on COVID and COVID-encephalopathy patients.

Conclusion

This study overall aimed to document the qualitative experiences of cognitive and emotional changes that took place in COVID-encephalopathy patients during the acute and subacute phases of the virus. Additionally, a comparison of the changes in COVID-encephalopathy patients and COVID patients absent of encephalopathy was made. The literature on cognitive and emotional deficits in COVID-encephalopathy patients is limited and is mostly quantitative. The findings from this study, however, were consistent with previous studies on the experiences of COVID patients. Two main themes were concluded after thematic analysis, being cognitive deficits and emotional trauma. These themes were interpreted using the theoretical framework and principles that govern modern clinical neuropsychology. The data was analysed by looking at how the brain and behaviour interacts, which results in an effect on cognition. Signs of cognitive deficits included problems with processing of information, memory, concentration, language and executive functioning. The emotional trauma led to emotional difficulties for patients which presented itself in the forms of guilt, hospital mistreatment, motivation, resilience and social support. When comparing COVID-encephalopathy participants and COVID participants absent of encephalopathy, it was found that they all experience cognitive and emotional challenges, however the challenges faced by COVID-encephalopathy participants were much harder to deal with and overcome. Future research should focus on conducting COVID-encephalopathy studies on a wider scale with follow up studies interviewing the same participants to see if they still are experiencing the same cognitive and emotional challenges.

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Appendix A

Informed Consent Form – COVID-encephalopathy participant

UNIVERSITY OF CAPE TOWN

DEPARTMENT OF PSYCHOLOGY

Personal Experiences and Observations of Mental Changes During the Course of Illness in Survivors of COVID-19.

1. Invitation and Purpose

You have been invited today to take part in this research study because we are hoping to understand more about your experiences of changes in thinking, memory and emotions since you were diagnosed with encephalopathy due to COVID-19. I am a research student from the Psychology department at the University of Cape Town.

2. Procedure

- If you decide to participate in this study, I will interview you on your experiences of emotional and cognitive changes that have taken place due to your positive diagnosis of encephalopathy due to COVID-19. I will ask you to share your experiences from when you got sick up until the present day. By interviewing you, I hope to find out what changes you have experienced mentally. For example, changes in your memory, how long you can focus on something, your mood, and your daily routine.

- The interview will take about an hour and will be audio recorded. This will be followed by 3 exercises that assess certain types of attention, memory and thinking.

3. Risks, Discomforts & Inconveniences

- This study poses minimal risk to you, however, given that the session will take place in a public venue, there is a chance you could get re-infected with the COVID-19 virus by meeting with me. All COVID-19 safety protocols will be followed, and every precaution will be taken to minimise the chances of re-infection.

- Potentially, through sharing your experiences with me, it could be emotionally distressing. However, you are not in any way obligated to share anything you do not feel comfortable sharing and you can decide what to share with me. At any time, you may withdraw from the study with no consequences.

- If you feel like you need to speak to a counsellor to further discuss your experiences, I will refer you to the Psychiatry unit at Groote Schuur Hospital with your permission.

4. Benefits

By voicing your experiences, you will be creating awareness, especially in healthcare workers and family members, of the difficulties you and patients like you face on a daily basis. This data will also further inform rehabilitation programmes for patients like you.

5. Costs

There are no costs that you will have to pay. You will receive R50 in compensation for your travel arrangements.

6. Privacy and Confidentiality

- Interviews will occur in a private room.

- Anything you say to me or share with me is strictly confidential. Throughout the research process you will remain anonymous, and you have the right to request to withdraw any information that you have shared with me so that it is removed from the study.

- An audio recording will be taken during the interview. This will only be taken with your permission and will permanently be deleted upon conclusion of the study unless you give permission for them to be used at a later stage.

- All data collected will be stored on a password protected computer, separately from the consent forms. All data will only be accessible by the research team and will have no identifying details. Each participant's information will remain anonymous and be referred to via a randomly generated number. Data will be stored for a period of 5 years after which it will be permanently deleted.

7. Voluntary Participation

You may withdraw from the interview and the study at any time with no consequences. Your participation is completely voluntary and will have no effect on services received from Groote Schuur Hospital or any other hospital.

8. Questions and further information

Should you wish to ask questions about your rights as a study participant, make comments or lodge complaints about the study you can contact Rosalind Adams on 021 650 3417. Further information may be requested from us, or our supervisor. See section 8.

9. Contact details

If you have any further questions, concerns, or complaints about the study please contact:

- Raine Comninos (student researcher) on 061 435 8562
- Donné Minné (Supervisor) at the Department of Psychology, University of Cape Town (UCT) 021 650 3417

10. Signatures

{Subject's name} ________________ has been informed of the nature and purpose of the procedures described above including any risks involved in its performance. He or she has been given time to ask any questions and these questions have been answered to the best of the investigator's ability. A signed copy of this consent form will be made available to the subject.

_____________________ __________

Investigator's Signature Date

I have been informed about this research study and understand its purpose, possible benefits, risks, and discomforts. I agree to take part in this research as a participant. I know that I am free to withdraw this consent and quit this project at any time, and that doing so will not cause me any penalty or loss of benefits that I would otherwise be entitled to enjoy.

☐ I agree to have the interview audio recorded.

_____________________ __________

Subject's Signature Date

Appendix B

Informed Consent Form – COVID participant

UNIVERSITY OF CAPE TOWN

DEPARTMENT OF PSYCHOLOGY

Personal Experiences and Observations of Mental Changes During the Course of Illness in Survivors of COVID-19.

1. Invitation and Purpose

You have been invited today to take part in this research study because we are hoping to understand more about your experiences of changes in thinking, memory and emotions since you were diagnosed with COVID-19. I am a research student from the Psychology department at the University of Cape Town.

2. Procedure

- If you decide to participate in this study, I will interview you on your experiences of emotional and cognitive changes that have taken place due to your positive diagnosis of COVID-19. I will ask you to share your experiences from when you got sick up until the present day. By interviewing you, I hope to find out what changes you have experienced mentally. For example, changes in your memory, how long you can focus on something, your mood, and your daily routine.

- The interview will take about an hour and will be audio recorded. This will be followed by 3 exercises that assess certain types of attention, memory and thinking.

3. Risks, Discomforts & Inconveniences

- This study poses minimal risk to you, however, given that the session will take place in a public venue, there is a chance you could get re-infected with the COVID-19 virus by meeting with me. All COVID-19 safety protocols will be followed, and every precaution will be taken to minimise the chances of re-infection.

- Potentially, through sharing your experiences with me, it could be emotionally distressing. However, you are not in any way obligated to share anything you do not feel comfortable sharing and you can decide what to share with me. At any time, you may withdraw from the study with no consequences.

- If you feel like you need to speak to a counsellor to further discuss your experiences, I will refer you to the Psychiatry unit at Groote Schuur Hospital with your permission.

4. Benefits

By voicing your experiences, you will be creating awareness, especially in healthcare workers and family members, of the difficulties you and patients like you face on a daily basis. This data will also further inform rehabilitation programmes for patients like you.

5. Costs

There are no costs that you will have to pay. You will receive R50 in compensation for your travel arrangements.

6. Privacy and Confidentiality

- Interviews will occur in a private room.

- Anything you say to me or share with me is strictly confidential. Throughout the research process you will remain anonymous, and you have the right to request to withdraw any information that you have shared with me so that it is removed from the study.

- An audio recording will be taken during the interview. This will only be taken with your permission and will permanently be deleted upon conclusion of the study unless you give permission for them to be used at a later stage.

- All data collected will be stored on a password protected computer, separately from the consent forms. All data will only be accessible by the research team and will have no identifying details. Each participant's information will remain anonymous and be referred to via a randomly generated number. Data will be stored for a period of 5 years after which it will be permanently deleted.

7. Voluntary Participation

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- Raine Comninos (student researcher) on 061 435 8562
- Donné Minné (Supervisor) at the Department of Psychology, University of Cape Town (UCT) 021 650 3417

10. Signatures

{Subject's name} ________________ has been informed of the nature and purpose of the procedures described above including any risks involved in its performance. He or she has been given time to ask any questions and these questions have been answered to the best of the investigator's ability. A signed copy of this consent form will be made available to the subject.

________________________ ____________

Investigator's Signature Date

I have been informed about this research study and understand its purpose, possible benefits, risks, and discomforts. I agree to take part in this research as a participant. I know that I am free to withdraw this consent and quit this project at any time, and that doing so will not cause me any penalty or loss of benefits that I would otherwise be entitled to enjoy.

☐ I agree to have the interview audio recorded.

________________________ ____________

Subject's Signature Date

Appendix C

Experiences of cognitive and emotional changes in COVID-encephalopathy patients and COVID patients absent of encephalopathy questionnaire.

1. I would like to know more about your experiences with the COVID-19 virus, maybe you could start by telling me about the time when you first got sick?
2. Do you recall your time in hospital? What was your stay in hospital like?
3. In terms of your memory and concentration, and things like that, can you tell me a bit more about how the virus was affecting you mentally during your hospital stay?
4. In what ways was your time in the hospital strange or unusual for you?
5. Can you tell me more about your mood and how you felt at the time?
6. What have people told you about how you were during your time in the hospital?
7. In what way has your life changed since COVID?
8. Can you tell me about the ways your memory might have changed since you got sick?
9. Can you describe your concentration before and after your illness?
10. Can you tell me about examples in your life when you feel confused?
11. In what ways do you think your level of intelligence has changed since being sick from COVID?
12. Can you describe your current motivation levels?
13. In what ways are your thoughts nowadays different to before you got Covid?
14. How have you been finding conversations with others?
15. Can you tell me about things that bring you joy nowadays or makes you laugh?
16. Can you tell me more about the kinds of challenges you now face in your life as a result of your COVID illness?
17. What has been hardest about adjusting back to life at home?
18. In what ways has your general sense of wellbeing or happiness changed?
19. Can you describe your emotional state on an average day?

20. Can you describe changes in your relationships since your illness?
21. Can you describe your sleep pattern?
22. Can you describe what everyday activities you might need help to do?
23. Can you give me any examples of how you might find it harder to hold back or control your emotions nowadays than before Covid?
24. How would you evaluate your overall functioning now compared to before your illness?
25. What has been your biggest source of strength?
26. Are there any other experiences related to how COVID has affected you that you would like to share with me?
27. Do you have any questions for me?

Social History Questions:

1. In what town and suburb do you live?
2. What gender do you identify as?
3. What is your age?
4. What is the highest level of education you have completed?
5. What race do you identify as?

Appendix D
Subjective Changes in Cognition Questionnaire (Adapted from Kim et al., 2011; Rabin et al., 2020)

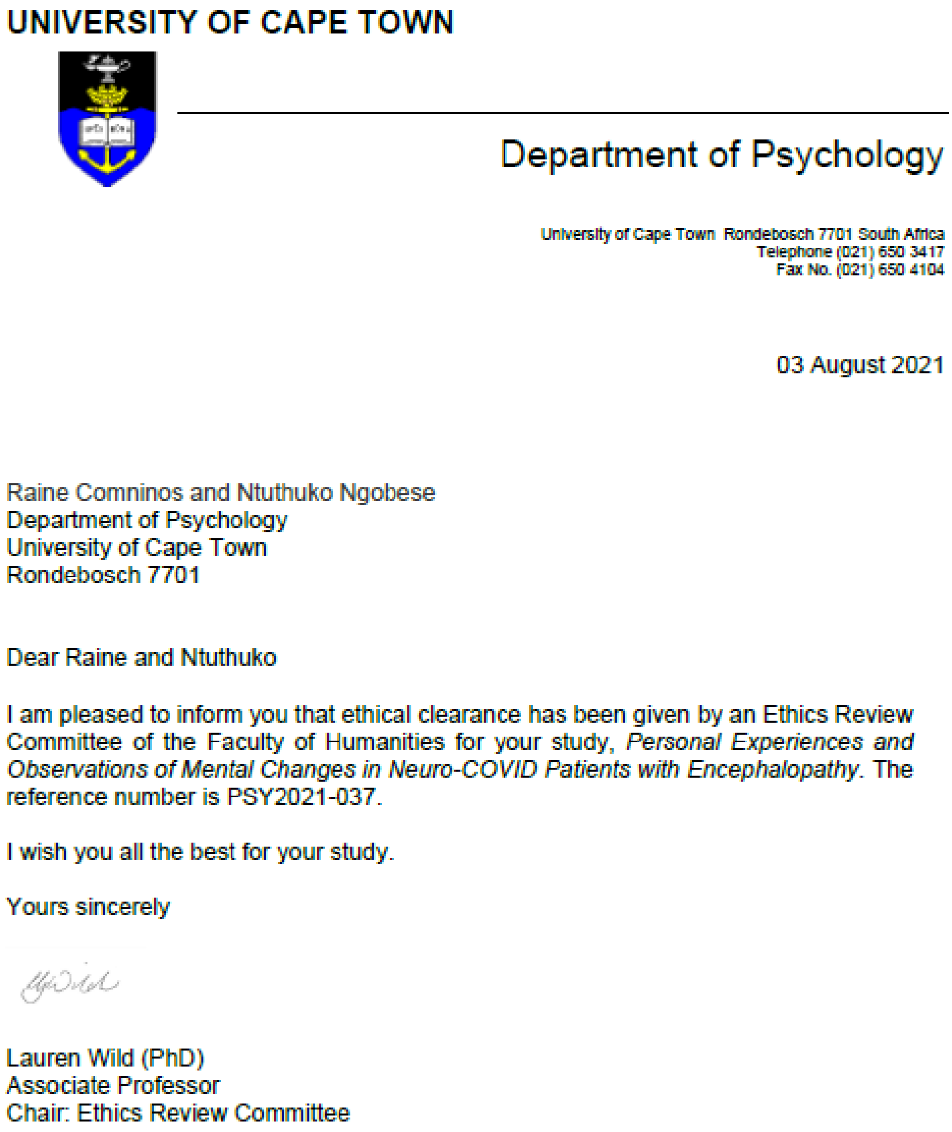
Subjective Changes in Cognition Questionnaire

Cognitive Domain	**Item Question**	**Response Choices/(Score)**
Language	Do others often have difficulty understanding what he/she is speaking about?	Yes (1)/No (0)/Don't know
Language	Does he/she experience difficulty finding the words they want to use in normal conversation?	Yes (1)/No (0)/Don't know
Memory	Does he/she struggle to remember recent events?	Yes (1)/No (0)/Don't know
Memory	Does he/she tend to repeat stories and/or questions?	Yes (1)/No (0)/Don't know
Attention	Is he/she able to focus on one thing at a time?	Yes (1)/No (0)/Don't know
Attention	Does he/she become easily distracted from the topic of an ongoing conversation?	Yes (1)/No (0)/Don't know
Executive Functioning	Does he/she have trouble performing a basic household	Yes (1)/No (0)/Don't know

	task (e.g., putting dishes away, making a cup of tea)?	
Executive Functioning	Does he/she have trouble using basic household appliances (e.g., kettle, TV, vacuum cleaner)?	Yes (1)/No (0)/Don’t know
Visuo-spatial Functioning	Is he/she prone to getting lost in familiar environments (e.g., local neighbourhoods or shopping centres)?	Yes (1)/No (0)/Don’t know
Visuo-spatial Functioning	Does he/she struggle to find the bedroom or bathroom in his/her home or familiar homes (relatives or close friends)?	Yes (1)/No (0)/Don’t know
General Cognitive Functioning	Does he/she experience any additional cognitive difficulties?	Yes (1)/No (0)/Don’t know

Appendix E

Ethical Clearance from the Ethics Review Committee of the Faculty of Humanities



UNIVERSITY OF CAPE TOWN

Department of Psychology

University of Cape Town Rondebosch 7701 South Africa
Telephone (021) 650 3417
Fax No. (021) 650 4104

03 August 2021

Raine Comninos and Ntuthuko Ngobese
Department of Psychology
University of Cape Town
Rondebosch 7701

Dear Raine and Ntuthuko

I am pleased to inform you that ethical clearance has been given by an Ethics Review Committee of the Faculty of Humanities for your study, *Personal Experiences and Observations of Mental Changes in Neuro-COVID Patients with Encephalopathy*. The reference number is PSY2021-037.

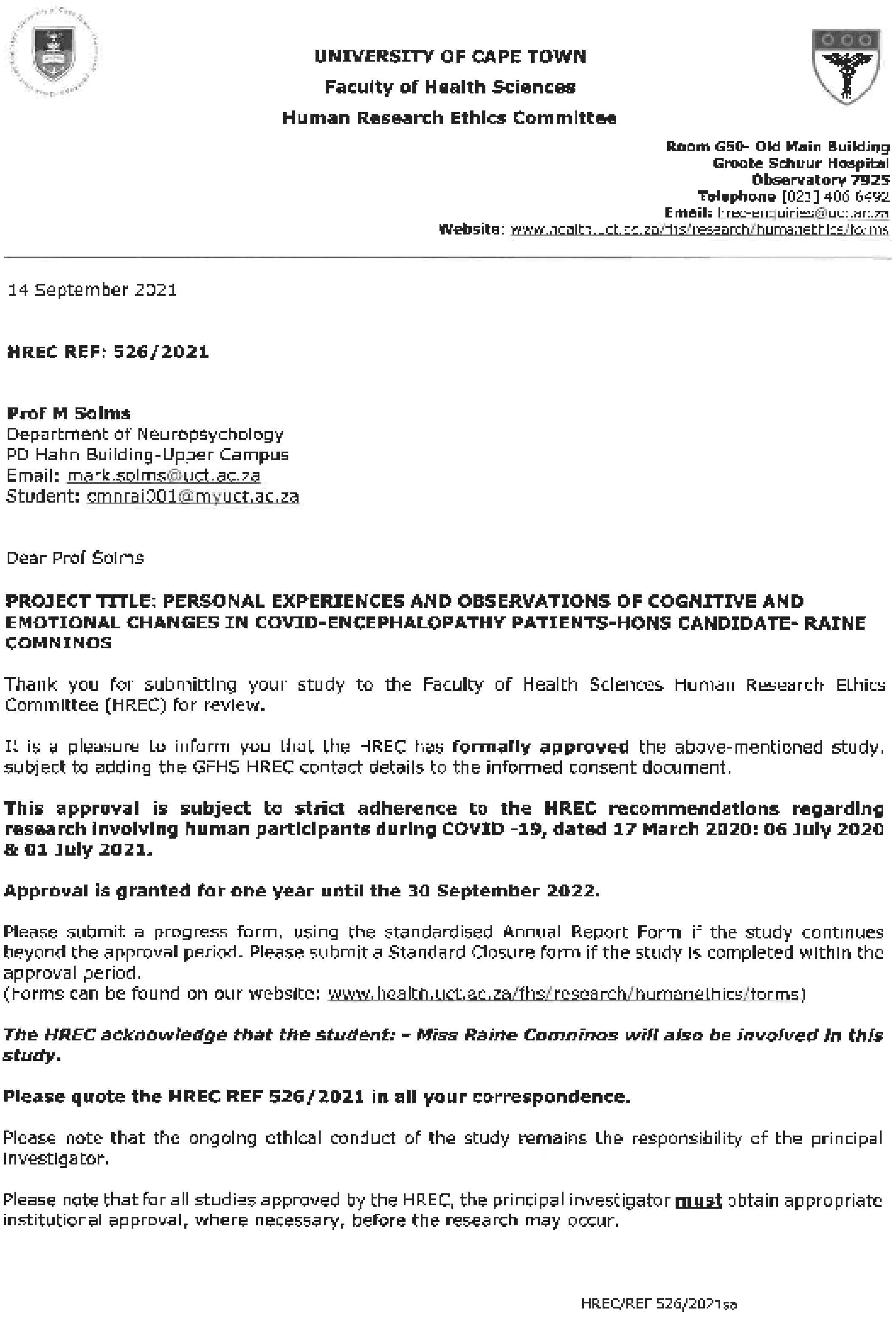
I wish you all the best for your study.

Yours sincerely

Lauren Wild (PhD)
Associate Professor
Chair: Ethics Review Committee

Appendix F

Ethical Clearance from the Human Research Ethics Committee of the Faculty of Health Sciences



UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room G50- Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6492
Email: hrec-enquiries@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

14 September 2021

HREC REF: 526/2021

Prof M Solms
Department of Neuropsychology
PD Hahn Building-Upper Campus
Email: mark.solms@uct.ac.za
Student: cmnrai001@myuct.ac.za

Dear Prof Solms

PROJECT TITLE: PERSONAL EXPERIENCES AND OBSERVATIONS OF COGNITIVE AND EMOTIONAL CHANGES IN COVID-ENCEPHALOPATHY PATIENTS-HONS CANDIDATE- RAINE COMNINOS

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee (HREC) for review.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study, subject to adding the GFHS HREC contact details to the informed consent document.

This approval is subject to strict adherence to the HREC recommendations regarding research involving human participants during COVID -19, dated 17 March 2020: 06 July 2020 & 01 July 2021.

Approval is granted for one year until the 30 September 2022.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

The HREC acknowledge that the student: - Miss Raine Comninos will also be involved in this study.

Please quote the HREC REF 526/2021 in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval, where necessary, before the research may occur.

HREC/REF 526/2021sa

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, FACULTY OF HEALTH SCIENCES HUMAN RESEARCH ETHICS COMMITTEE
Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938
NHREC-registration number: REC-210208-007

This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use: Good Clinical Practice (ICH GCP), South African Good Clinical Practice Guidelines (DoH 2006), based on the Association of the British Pharmaceutical Industry Guidelines (ABPI), and Declaration of Helsinki (2013) guidelines. The Human Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

Appendix G

Support Resources Flyer

Thank you for participating in our study

If you are needing a referral to a psychologist, psychiatrist or support group, we encourage you to call The South African Depression and Anxiety Group (SADAG) on 011 234 4837 or 0800 20 50 26 and speak to a trained counsellor who can assist you further. Or alternatively email Zane on zane@sadag.org

You are also encouraged to email one of the Principal Investigators in this study, Dr Donné Minné, who is a registered neuropsychologist with the HPCSA and who will be able to provide you with a consultation should you be requiring one.
Donneminne.za@gmail.com
(PS 0150380)

We would also like to draw your attention to a number of other mental health support resources available to you:

Dr Reddy's Help Line
0800 21 22 23

Cipla 24hr Mental Health Helpline
0800 456 789

Pharmadynamics Police &Trauma Line
0800 20 50 26

Adcock Ingram Depression and Anxiety Helpline
0800 70 80 90

ADHD Helpline
0800 55 44 33

Department of Social Development Substance Abuse Line 24hr helpline
0800 12 13 14
SMS 32312

Suicide Crisis Line
0800 567 567

SADAG Mental Health Line
011 234 4837

Akeso Psychiatric Response Unit 24 Hour
0861 435 787

Cipla Whatsapp Chat Line
(9am-4pm, 7 days a week)
076 882 2775

24 hour Healthcare Workers Care Network Helpline
0800 21 21 21
SMS 43001

NPOWERSA Helpline
0800 515 515
SMS 43010

For affordable counselling, please contact the Counselling Hub

021 462-3902 (landline) or 067 235-0019 (mobile)
For non-appointment enquiries please email info@counsellinghub.org.za