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Neural, environmental and individual factors affecting cognition in Long Covid: what are the LINCS?

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Neural, environmental and individual factors affecting cognition in Long Covid: what are the LINCS?

Abstract

Objective. To explore the lived experiences and extent of cognitive symptoms in Long Covid (LC). *Design.* Eight focus group discussions were held with people with Long Covid. Qualitative data was analysed using the Framework Analysis to reveal the experiences and impact of cognitive symptoms. A self-report questionnaire assessed the perceived change and extent of symptomology post-Covid.

Participants. 25 people with Long Covid living in the UK participated in the study. Participants were aged 19 to 76 years (M = 43.6 years, SD = 14.7) and included 17 females and 8 males.

Setting. Focus groups were conducted in April 2023 online via Zoom and in-person at the University of Leeds, UK.

Results. Reduced cognitive ability was among the most prevalent symptoms reported by participants. Three key themes were identified from the qualitative data: (i) rich accounts of cognitive symptoms, (ii) the impact on physical and psychological functioning, and (iii) symptom management. Descriptions of cognitive symptoms included impairments in memory, attention, language, executive function and processing speed. Cognitive symptoms had a profound impact on physical functioning and psychological wellbeing, including reduced ability to work and complete activities of daily living. Strategies used for symptom management varied in effectiveness and were tedious to implement.

Conclusion. Cognitive dysfunction in LC appears to be exacerbated by vicious cycle of withdrawal from daily life including loss of employment, physical inactivity and social isolation driving low mood, anxiety and poor cognitive functioning. Previous evidence has revealed the anatomical and physiological biomarkers in the brain affecting cognition in LC. To synthesise these contributing factors, we propose the Long-covid Interacting Network of factors affecting Cognitive Symptoms (LINCS) Model to inform future interventions to take a comprehensive approach, targeting the neural, environmental and individual factors, with an aim of improving cognitive function in LC.

Keywords

Long COVID; COVID-19; cognitive symptoms; qualitative research; mixed methods

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Strengths and limitations of this study

- This study used a mixed-methods approach, combining qualitative and quantitative methods of data collection to capture the experiences of LC and the severity of cognitive dysfunction among other symptoms in LC.
- The research team was interdisciplinary and interprofessional, combining expertise from Long Covid Rehabilitation, Neurology, Cognitive Psychology and Qualitative Methods.
- This study may be limited by a self-selecting, potentially biased sample consisting of mostly female, middle-aged participants.
- The use of multiple facilitators in discussions may have resulted in different focuses of conversation. However, one member of the research team coded and analysed the data to ensure consistency.

Introduction

Post-Acute Covid-19 Syndrome, also known as Long Covid (LC), is the continuation or development of new symptoms three months after the initial SARS-CoV-2 infection, with symptoms lasting for at least two months (1). In 2023, an estimated 2 million people living in private households in the UK (3.1% of the population) were experiencing self-reported LC (2) with common symptoms including fatigue, breathlessness, muscle ache, general malaise and cognitive dysfunction (3). The Office for National Statistics (2) reported that the second most common symptom following fatigue was difficulty concentrating, reported by 52% of respondents. Furthermore, cognitive dysfunction was found to be one of the most common symptoms in a multinational survey of 3762 people with Long Covid, reported in ~88% of individuals (4).

Neuropsychological assessments and subjective reports have shown cognitive impairments in memory, attention, executive function and verbal fluency following SARS-CoV-2 infection in comparison to individuals without infection (5, 6). A UK Biobank study found poorer cognitive accuracy in working memory, attention, reasoning and motor control in those who had been infected with SARS-CoV-2 than controls, with the largest deficits found in individuals with ≥12 weeks of symptoms, continuing to 2 years in some individuals (7). Persistent cognitive impairment in LC is associated with anatomical and physiological biomarkers. Magnetic resonance images (MRI) and objective cognitive tests recorded before and after SARS-CoV-2 infection have revealed reduced grey matter in the orbitofrontal cortex and parahippocampal gyrus and reduced global brain size correlated with impaired cognitive performance in those who had been infected than controls (8). On a cellular level, SARS-COV-2 infection is associated with tau pathology in the brain (9), and the virus sequence can code for cytotoxic amyloid proteins with comparable toxicity to proteins found in Alzheimer's disease (10). Further biomarkers associated with LC include chronic neuroinflammation associated with a cascade of neurotoxic events (11, 12) and hypoxia (13, 14). LC is associated with accelerated cognitive aging and an increased risk of dementia (15).

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Previous qualitative studies have reported the profound negative impact of LC on daily functioning and quality of life including high prevalence of mental health problems, change or loss of occupational status, difficulty accessing and navigating healthcare services, feelings of isolation, stigma, shame and loss of personal identity (16). One previous qualitative study has reported the experiences of 'brain fog' in COVID-19 long haulers (17), a colloquial term describing a state of confusion, forgetfulness and slowing of mental abilities (18, 19). However, focus group discussions conducted by Callan et al. (17) were held early in the COVID-19 pandemic in 2020, and to our knowledge no further studies have investigated the qualitative experiences of cognitive symptoms in Long Covid. Given the heightened risk of neurodegeneration and dementia, and detrimental impact on daily life associated with LC, it is

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crucial to have a current understanding of the impact of cognitive impairment on the lives of people with LC. By combining qualitative and quantitative methods, this study aimed to capture both in-depth experiences and quantify the extent of cognitive symptoms. This mixed-methods approach was used to enhance the validity and triangulation of the research, to inform a comprehensive understanding of cognitive symptoms in LC. In this study, people with LC completed focus group discussions and a Post COVID-19 Syndrome Questionnaire. The following questions were explored. 1) What is the prevalence of cognitive symptoms in LC? 2) What is the lived experience of cognitive symptoms in LC?

Methods

Participants

Participants included 25 adults with LC, aged 19 to 76 years (M = 43.6 years, SD = 14.7; 17 females and 8 males), see Table 1. Participants were eligible if they had self-reported LC and lived in the UK. One participant did not return the Post-Covid Questionnaire so were removed from the analysis. 92% (22/24) of participants had a clinical diagnosis of Long Covid. The duration of symptoms experienced varied between 4 months to 2.8 years (M = 77.96 weeks, SD = 32.58). Twenty one participants had British nationality, 1 French, 1 Finnish and 1 Chinese. Participants were recruited via social media advertisement on Facebook, Instagram, LinkedIn and NextDoor, via advertisement in the Chronic Pain & Fatigue Network at the University of Leeds and English National Opera Breathe Programme for Long Covid, and by word-of-mouth. Participants were reimbursed with a £20 Love2Shop voucher. All participants provided written informed consent. The study was approved by the University of Leeds Psychology Ethics Committee on 3rd January 2023 (PSC710), and was conducted in accordance with the BPS Code of Ethics (20) and the Declaration of Helsinki (21).

Quantitative Data Collection

The Post (Long) Covid-19 Syndrome Questionnaire was adapted from previous NHS questionnaires measuring symptoms in LC (available at <u>https://ardenhousemedicalpractice.co.uk/navigator/post-long-covid-19-syndrome-questionnaire/</u>) in the validated Patient Health Questionnaire format (PHQ-9). This questionnaire measured participant's perceived health in: breathing, mobility, energy, mood, mental ability and physical health (see Supplementary Materials). The questionnaire assessed the severity of symptoms using mixture of binary questions with "yes" or "no" responses, and scaled questions in which the rating scale comprised: normal functioning [0] Normal [1] Mild [2] Moderate, and [3] Severe. Participants rated their self-perceived change in symptom severity on 0 – 10 point Likert scales for before and after they contracted Long Covid.

Qualitative Data Collection

Eight exploratory focus groups were conducted in April 2023 in person (50%) and online via Zoom in the School of Psychology, University of Leeds, UK. Discussions were audio-recorded and lasted

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 approximately 2 hours. Each group contained two to five participants and one of four facilitators who informally followed guidance questions intended to encourage discussion around the main symptoms and experiences (see Supplementary Information).

Data management and analysis

Qualitative data were analysed according to the Framework Analysis developed by Ritchie and Spencer (22). Following data transcription and familiarisation, data were 'open coded' and a framework was developed and refined within the research team. Manual coding was performed in NVivo (R14.23.1, QSR International) using the framework. Double-coding of 25% of the data was performed by a second analyst to assess the quality of the coding. The results were reviewed by an interdisciplinary research team, combining expertise from Cognitive Psychology and Qualitative Methods.

Patient or Public Involvement

Participants were invited to review the manuscript prior to submission to ensure the findings accurately represented their views and experiences.

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Participant Number	Age (vears)	Gender	Nationality		Disease Duration
		Gender	Duitie		
1	52	M	British	Yes	76
2	52	F	British	Yes	120
3	33	М	British	Yes	28
4	41	Μ	British	Yes	68
5	29	F	British	Yes	72
6	48	F	French	Yes	68
7	19	F	British	Yes	78
8	30	F	British	Yes	146
9	26	F	Chinese	No	52
10	47	F	British	Yes	60
11	64	F	British	Yes	64
12	60	М	British	Yes	120
13	43	М	British	No	60
14	38	F	British	Yes	72
15	50	F	British	Yes	130
16	62	Ē	British	Yes	126
17	21	F	British	Yes	130
18	24	М	British	Yes	86
19	50	F	British	Yes	80
20	54	F	British	Yes	104
21	76	F	British	Yes	19
22	45	М	Finnish	Yes	60
23	33	F	British	Yes	52
24	51	М	British	Yes	52

Table 1. Participant demographic information. Abbreviations; male (M), female (F), Long Covid (LC).

Results

Quantitative Results

Results from the Post Long Covid-19 Questionnaire showed that participants experienced wide ranging symptoms following the development of LC, see Figure 1 and Figure 2. The most severe symptoms, with the greatest change after disease contraction, were decreases in energy, mobility, breathing and mental ability.

In terms of cognition; 87.50% (21/24) of participants reported that their ability to concentrate had worsened, 83.33% (20/24) reported that their short-term memory had declined, 75.00% (18/24) reported that they or their family had identified a difference in the way they communicated. Participants reported a 10-fold increase in concern about their cognition following LC (M = 5.83, SEM = 0.61) compared to before LC (M = 0.54, SEM = 0.27).

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Almost all participants reported that their illness and cognition affected their ability to work (95.65%; 22/23; 1 participant was retired). All participants (24/24) requested to be informed of future LC research opportunities showing clear motivation to advance understanding and treatment for persistent symptoms.



Figure 1. Participant self-reported ratings of symptom severity across health domains. High scores indicate greater severity of symptoms. [0] Normal [1] Mild [2] Moderate, and [3] Severe. Error bars show standard error (SEM). N = 24.

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Qualitative Results

Summary

Data from the focus group discussions were categorised into three interconnected themes, see Figure 3. Theme 1) Rich accounts of cognitive symptoms. Theme 2) Impact of physical function and psychological wellbeing. Theme 3) Symptom management. Participants experienced various cognitive impairments (theme 1) which impacted daily functioning and psychological wellbeing (theme 2). Participants attempted to manage the symptoms and impact on their daily life (themes 1 & 2) using strategies (theme 3). Oftentimes these strategies (theme 3) were tedious to implement or ineffective, further exacerbating the impact on physical and psychological functioning (theme 2). See theme descriptions for further details.



Figure 3. A map of the relationships between themes.

Theme 1) Rich accounts of cognitive symptoms

Participants described experiences of a range of cognitive symptoms. The most reported symptoms were difficulties with memory and language, followed by attention, executive function and reduced processing speed. Participants consistently used the term 'brain fog' to describe their symptoms.

Memory

Participants described experiences of memory deficits which were consistent with definitions of working memory, long term memory (declarative and non-declarative memory) and prospective memory. Participants were concerned about the consequences of these memory impairments on their safety. For example, Participant 1 was forgetting to take their medication and reported '*I could be overdosing and I've no idea'*. Other participants were worried about the impact of their memory difficulties on their perceived image, as Participant 18 described '*it makes you look stupid*' after missing appointments. Participants described a need to review information multiple times before they could process, retain and remember it:

'I'll go back to the book and think I don't remember this bit at all and be going back a chapter... not necessarily reading it in detail, but scanning through and it will kind of prompt me.' Participant 14.

Occasional lapses in memory lead to experiences of disorientation and confusion. Participant 23 described the experience as a 'full blank moment' and as 'disconcerting'.

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Language

Impairments in language affected word finding, reading comprehension and writing. Participant 14 described making errors in writing and proof-reading at work which they didn't do before, 'I would read it and think this is great letter and then actually there'd be, like, a word missing.' Issues with communication included difficultly following conversations or abruptly deviating from the topic of conversation. A feeling of 'disconnection in the brain' was frequently described:

'I'm often looking for words when I'm speaking and I think of a word, but I can't find it, like I know what it means and I know what I want to say, but it's like it's just disappeared from my brain.' Participant 17.

Attention

Participants described impaired attention, particularly divided attention (multitasking) and maintaining selective/sustained attention, and the impact of this on daily life. Participant 6 described difficulty talking whilst driving and *'could* [only] *retrieve the information'* once *'stopped at the traffic lights'*. Participant 17 described the frustration of losing their attention, *'I used to be able to sit down and watch films and things. Now, I find myself sometimes flicking the TV over because I can't, like, concentrate on stuff.'*

Executive Functioning

Executive dysfunction included difficulties with planning, decision-making and mental flexibility. For example, Participant 11 found difficulty following 'a *logical train of thought*' and 'getting things done around the house'. The term 'decision fatigue' was used by participants 12 and 13 to describe the exhaustion associated making a choice out of many options, such as selecting a programme on the TV.

Processing speed

Accounts of cognitive dysfunction included descriptions of the delay involved in completing tasks or retrieving information, suggesting participants were experiencing reduced processing speed.

'When I'm doing patients notes have to go over them like up to 10 times maybe, word by word to make sure I've put the correct word. People used to comment how quick I could, like, type and do the notes. Now it's taking me a lot longer'. Participant 15.

Contributing factors

For many participants, fatigue, poor sleep and headaches exacerbated their cognitive symptoms. Participant 4 explained that tiredness makes their brain feel '*jumbled*'. Other participants described continuous cognitive symptoms, independent of other factors.

Theme 2) Impact on physical function and psychological wellbeing

Participants described profound impacts on their employment, daily functioning and psychological wellbeing. Several participants were unable to return to work, had reduced working hours or adapted roles due to the self-perceived inability to uphold the cognitive demands and high responsibility of their previous roles. Participants were concerned about when or if their cognitive abilities would return and this was associated with a loss of professional identity.

'Throughout my career has involved writing and also proofreading and copy editing. And I had to give that up for two years, and I was so scared that my ability would never come back... I've always seen myself as someone who works with words'. Participant 9.

'I've actually changed jobs at work, changing jobs on Monday, because the job I do requires a lot of concentration and I was just making so many mistakes. I've kind of taken a sideways step.'

Participant 24.

Some participants felt they had lost confidence in their ability to carry out activities of daily living including cooking and driving, which they were previously proficient in or enjoyed:

'The odd time I have actually forgotten to turn the cooker off as well. So I'm not, like, keen to cook a lot these days either, which I've always enjoyed cooking.' Participant 17.

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Psychological impacts included a loss of personal identity in relation to impaired cognitive abilities. Several participants reported feelings of accelerated ageing beyond their years and anxiety about whether this reflected the development of age-related neurodegenerative diseases:

'A few weeks into having Covid I felt like I'd aged 20 years and lost 20 IQ points....It makes you worried that there are other things, I think, oh my God have I actually got Alzheimer's, you know? Because I could tick most of the boxes.' Participant 12.

Overall, the experiences of cognitive impairment contributed to low mood, stress and anxiety. Participant 16 described the experience of losing their memory abilities as 'stressful' and feeling 'so down'.

Theme 3) Symptom management

Participants reported strategies they had tried to manage their cognitive symptoms, with variable success. Some participants described simplifying daily life by reducing demands or decision-making: *'I find decisions tiring... So I've just eliminated that, I just wear the same coloured clothes every day* [and] cook the same meals' Participant 13.

Strategies for recording information and setting reminders were described, including making to-do lists, setting alarms to take medication or remember dates and appointments. Descriptions showed these strategies were mostly ineffective. Participant 19 attempted to use pill boxes and phone notifications to reminder them to take their medication, however they explained *'I would still forget... I'll see the notification, and I think right, I'll do that in a minute and then I'll get distracted and I'll forget about it'.*

Regular rest and breaks were required, particularly throughout the working day. Participant 4 took regular breaks whilst working from home, and explained '*if I didn't do that, I won't be able to continue for my day'*.

Descriptions of strategy use were often associated with feelings of frustration and tediousness over the increased time or effort required implement these strategies in order to complete tasks:

'I just have to stop organising [meetings] any time after about 2 o'clock because I then I can't find

the words that I'm trying to say and it sounds like ridiculous... That's really, really frustrating'

Participant 23.

Some participants attempted to regain their pre-Covid-19 cognitive function by challenging themselves in progressive increments, with some success:

'I struggled to even just reading a page of a book... I've progressed again over kind over the last few months, really just by setting myself the kind of challenge or time to just read one chapter or a few pages of the book every day'. Participant 14.

Discussion

This study investigated the lived experiences of cognitive symptoms in LC. The majority of participants in this study reported a decline in cognitive ability. Cognitive symptoms were among the most common symptoms reported alongside low energy, immobility and breathlessness. Impairments were reported in memory, attention, language, executive function and processing speed. Cognitive symptoms had profound negative effects on participants' ability to work, complete activities of daily living, their psychological wellbeing and self-image, in some cases for >2 years after the initial infection. Participants attempted to manage their cognitive symptoms using strategies to reduce decision making and mental load, facilitate memory and improve energy levels. However, the strategies were described as tedious to implement and mostly ineffective. By combining quantitative and qualitative methods, this study revealed that cognitive symptoms are among the most prevalent and severe symptoms in LC with significant negative impacts on the wellbeing, functioning and daily life of people with LC.

The findings of this study reflect previous reports of 'brain fog' and cognitive impairment in LC (5, 6, 17) as well as negative impacts of LC including loss of full-time employment and unemployment (23), impaired ability to complete activities of daily living (24), high rates of mood disorders (25) and living an altered lifestyle (26). The novel findings of this study are the interactions found between the experiences of cognitive impairment, physical and psychological functioning and self-management of cognitive symptoms. Poor memory, attention and executive functioning affected many areas of daily functioning and contributed to a loss of self-worth and identity and reduced psychological wellbeing. Strategies used for self-management of cognitive symptoms involved living an altered lifestyle by reducing daily demands, activities, exercise and decision making and implementing 'reminders' for tasks and regular rest, most of which added further distraction and frustration to daily life. This may reflect a vicious cycle of withdrawal from daily life, low mood and hopelessness that essentially exacerbates cognitive impairment.

The high incidence of breathlessness, fatigue, depression, anxiety and cognitive symptoms in LC found this study and previous studies may reflect an interacting symptom network (27). We propose a conceptual model, the Long-covid Interacting Network of factors affecting Cognitive Symptoms (LINCS) model to describe the interrelated neural, environmental and individual factors shaping actual and self-perceived cognitive dysfunction in LC, see Figure 4. Neural factors include the anatomical and physiological biomarkers associated with LC including brain atrophy (8), tau pathology (9), risk of

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cytotoxic amyloid protein aggregation (10), chronic neuroinflammation (11, 12) and hypoxia (13, 14). Environmental factors describe the reduced cognitive and physical engagement from withdrawing from activities of daily life including physical inactivity, gaps in employment, working reduced hours and social withdrawal. Individual factors include attempts to recover, implement strategies, fatigue, perceived energy levels, mood disorders, learned helplessness and fear. Previous evidence shows many of these factors are linked and likely contribute to the cognitive symptoms in LC. Fatigue and depression have been found to contribute towards impairments in cognitive function in chronic fatigue syndrome and multiple sclerosis (28, 29). Withdrawal from activities of daily living (ADL) was described by participants as a mechanism to manage their symptoms, however a lack of cognitive, physical and social engagement has been associated with accelerated cognitive decline in mid and later adulthood (30, 31, 32). This withdrawal from ADL might be explained by Learned Helplessness theory. Learned Helplessness, first proposed by Seligman and Maier (33), is a psychological state where an individual feels they have no control over a situation following repeated exposure to a stressor and is commonly associated with poorly managed chronic health conditions (34, 35). These individual and environmental factors may exacerbate neural and cognitive challenges in LC. Systematic review evidence has revealed links between depression and grey matter atrophy in frontal and hippocampal regions, responsible for memory and cognitive functioning (36). Furthermore, sedentary behaviours and a lack of cognitive engagement are associated with neuroinflammation and heightened dementia risk (37). Therefore, LC presents a complex array of interacting factors and symptoms which without treatment, exacerbate cognitive dysfunction.

Given the evidence of accelerated cognitive ageing and dementia risk in LC (8, 9, 15), this clinical population of an estimated 2 million people in the UK (2) may be the next generation at risk of developing age-related neurodegenerative diseases, fuelling a future epidemic of dementia in the UK. Currently, there is no approved treatment for LC (38) and the findings of this study highlight the vital need for an intervention to tackle the cognitive symptoms in LC, with aims to improve quality of life and reduce dementia risk. We propose that the LINCS Model should be used to inform a comprehensive biopsychosocial approach to intervention development, by addressing the network of neural, environmental and individual factors contributing to cognitive dysfunction. Instead of limiting ADL to manage symptoms, people with LC should be supported to gradually increase activity levels. Frequent and vigorous exercise, social activity and housework in middle-age has been found to offer neuroprotective effects by significantly lowering risk of developing dementia over 10 years (39). Possible interventions for LC could include occupational reintegration, cognitive skill training, and socialisation for mental stimulation; psychological resistance training, occupational therapy and

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cognitive behavioural therapy CBT for emotional and psychological support; and possible drug therapies to tackle the neural challenges.





The term 'brain fog' was used by most participants in this study to describe their cognitive symptoms, however previous evidence suggests the term lacks specificity and may not capture the severity cognitive symptoms experienced in LC (17). The term 'fog' implies a perceptual deficit or 'clouding' of cognitive processes, whereas in this study, participants reported reduced processing speed, increased cognitive effort and a feeling of disconnection in the brain. Without the development of appropriate terminology to define these symptoms and lack of recognition of the specific impairments to cognitive functioning, there is a barrier for medical diagnosis and the development of targeted cognitive interventions. An alternative code name has been proposed to described the accelerated process of cognitive decline in pre-existing dementia following COVID-19, termed FADE-IN-MEMORY i.e. Fatigue, decreased Fluency, Attention deficit, Depression, Executive dysfunction, slowed INformation processing speed, and subcortical MEMORY impairment (40). The findings of this study show that FADE-IN-MEMORY might also be an appropriate term to describe the experience of cognitive symptoms in LC.

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The strengths of this study include the rigorous and well-established methods to analyse the focus group data, and the use of quantitative data collection to supplement the qualitative responses. Specifically, the questionnaire data allowed us to measure the self-perceived quantitative change in cognitive abilities following LC, and compare the severity of cognitive symptoms with other symptoms. However, the questionnaire rating scales were arbitrary and the self-report nature of the questionnaire may not reflect an objective measure of cognitive functioning. One possibility would be to administer a brief test of global cognitive function, such as the Montreal Cognitive Assessment (MoCA; 41), to measure participants' individual global cognitive function on the day of the focus group discussions. However, tests of global cognitive function primarily measure working memory, therefore may not capture the impairments in other cognitive domains participants reported in this study. Furthermore, the self-report nature of the questionnaire complimented the qualitative data in which the overall aim was to investigate the lived experience of cognitive symptoms from the participants' perspective, rather than to obtain an objective measurement of cognitive functioning. This study may be limited by the biased sample of mostly female and middle-aged participants, which prevented comparison of possible age and gender differences in the experience of LC symptoms.

This study found that cognitive dysfunction in LC severely affects daily life and functioning, with limited options for symptom management and treatment. Interventions that take into account the multiple interacting factors contributing to cognitive symptoms are greatly needed. Without an effective intervention, people with LC are at a greater risk of accelerated cognitive ageing and dementia.

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Author Statement

Melanie Rose Burke, Manoj Sivan and Rumana Chowdhury gained funding for the study. Amy Miller and Melanie Rose Burke conceived the idea and conducted the study. Ning Song informed the methods for qualitative data analysis. Amy Miller conducted the transcription, data analysis and wrote the first draft of the manuscript. All authors contributed towards the refinement of the manuscript.

Patient and public involvement

Participants were invited to review the manuscript prior to journal submission.

Data Availability Statement

Data are available on reasonable request.

Conflicts of Interest

The authors disclose no competing interests.

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Figure 1. Participant self-reported ratings of symptom severity across health domains. High scores indicate greater severity of symptoms. [0] Normal [1] Mild [2] Moderate, and [3] Severe. Error bars show standard error (SEM). N = 24.

127x76mm (150 x 150 DPI)



Figure 2. Participant self-reported symptom change before and after contracting Long Covid (LC). High scores indicate greater symptom severity. Error bars show SEM. N = 24.

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Supplementary Information Guided Questions followed by Facilitators What symptoms post covid are most distressing for you? What can you not do now that you could do before Long Covid? How has Long Covid affected your quality of life? What can clinical services provide to help with your everyday functioning? What services can society provide to help with your symptoms? What self-help strategies have worked for you? What research would most help pwLC get back to ot oper terien ont normal functioning?

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	Part	icipant Detai	ils	
Name:		D	ate of Birth:	
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Can we contact you in the futu intervention study on people v	ure for taking p with Long Covi	oart in an d? <u>[YE</u>	s / NO]	
Do you have an official Diagno	osis of Long Cov	/id? [YE	S / NO]	
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	NORMAI	MILD	MODERATE	SEVERE
Is your Breathing back to norn [NB: Circle the answer that b describes you]	mal? Normal best	Not normal but can do everything	, Breathless on hills/stairs	Stops me doing som things, breathless a rest/mild activity.
On a scale of 0-10, with 0 be not breathless at all, and 10 b extremely breathless, how breathless are you:	eing Bef being w	ore COVID	Af	ter COVID
Is your Mobility/Activity leve back to normal?	els Normal	Nearly back to normal	Having to move more slowly, but doing everything	Struggling with som activities, barely getting around.
On a scale of 0-10, with 0 be very active, and 10 being completely inactive, how act are you:	eing Bef S tive	ore COVID	After COVID	
Are your Energy Levels back normal?	to Normal	Feeling tired but doing all normal	Needing to rest frequently and some restriction	Significant tirednes cannot do usual tasl or fatigue is

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On a scale of 0-10, with 0 being full of energy, and 10 being constantly tired, how fatigued are you:	Before COVID		After COVID		
Is your Mood back to normal?	Normal	l have brief occasional moments of low mood.	l suffer most days with low mood or anxiety.	I struggle to think and remember, or I feel hopeless and suicidal.	
On a scale of 0-10, with 0 being not atall depressed, and 10 being very depressed/suicidal, how would you rate your mood:	Before COVID		After COVID		
On a scale of 0-10, with 0 being not atall anxious, and 10 being anxious all the time, how would you rate your anxiety:	Before COVID		After COVID		
Are your Mental ability levels back to normal?	Normal	I have the odd lapse in concentration and memory	d My brain is working much n slower than it . used to.	My mental capacity is significantly affecting my day-to-day functioning.	
On a scale of 0-10, with 0 very alert, and 10 being very limited on thinking and memory, how would you rate your mental capacity:	Be	fore COVID	Aft	er COVID	
ls your overall health (physical N and mental) back to normal?	lormal mi wi	I have only inor concerns th my health.	My physical and/or mental health is worse than it was, but is manageable.	My physical and mental health is a huge concern, and I am struggling to function independently.	
	Further	Cognitive Qu	estions		
Cognition is our ability to think, plan and process things. Ha CONCENTRATION worsened since	rememb as your your illn	er, ess?	YES	NO	

Has your SHORT-TERM MEMORY worsened since your illness?	YES	NO
On a scale of 0-10, with 0 being not atall concerned, and 10 very concerned, how would you rate your concern about your cognition:	Before COVID	After COVID
Have you or your family identified a difference in the way you COMMUNICATE putting thoughts into words/difficulty reading/communicating?	YES	NO
Has your illness/cognition affected your ability to work?	YES	NO
On a scale of 0-10, with 0 being not atall affected my work, and 10 can no longer work, how would you rate your working ability:	Before COVID	After COVID

THANK-YOU FOR YOUR TIME IN COMPLETEING THIS QUIZ !!

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Exploring the Experiences of Cognitive Symptoms in Long COVID: A Mixed-Methods Study in the UK

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Exploring the Experiences of Cognitive Symptoms in Long COVID: A Mixed-Methods Study in the UK Amy Miller^{a, 1} Ning Song^b Manoj Sivan^c Rumana Chowdhury^d Melanie Rose Burke^a ^a School of Psychology, University of Leeds, Woodhouse, Leeds, UK ^b Leeds Institute of Health Sciences, University of Leeds, Woodhouse, Leeds, UK ^c Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, UK ^d The Leeds Teaching Hospitals, NHS Trust, UK ¹Corresponding author e-mail address: ps16am@leeds.ac.uk Word count: 5606 Number of figures & tables: 5 Source of support: This study was supported by the Wellcome Institutional Translational Partnership Award, Grant Number: 219420/Z/19/Z. Disclaimer: This article reflects the views of the authors only, not the institutions or funders.

Exploring the Experiences of Cognitive Symptoms in Long COVID: A Mixed-Methods Study in the UK

Abstract

Objective. To explore the lived experiences and extent of cognitive symptoms in long COVID (LC).

Design. This study implemented a mixed-methods design. Eight focus groups were conducted to collect qualitative data, and the Framework Analysis was used to reveal the experiences and impact of cognitive symptoms. A self-report questionnaire was used to collect the quantitative data to assess the perceived change and extent of symptomology post COVID-19.

Participants. 25 people with LC living in the UK participated in the study. Participants were aged 19 to 76 years (M = 43.6 years, SD = 14.7) and included 17 females and 8 males.

Setting. Focus groups were conducted in April 2023 online via Zoom and in-person at the University of Leeds, UK.

Results. Reduced cognitive ability was among the most prevalent symptoms reported by participants. Three key themes were identified from the qualitative data. (i) Rich accounts of cognitive symptoms. (ii) The impact on physical and psychological functioning. (iii) Symptom management. Descriptions of cognitive symptoms included impairments in memory, attention, language, executive function and processing speed. Cognitive symptoms had a profound impact on physical functioning and psychological wellbeing, including reduced ability to work and complete activities of daily living. Strategies used for symptom management varied in effectiveness and were tedious to implement.

Conclusion. Cognitive dysfunction in LC appears to be exacerbated by vicious cycle of withdrawal from daily life including loss of employment, physical inactivity and social isolation driving low mood, anxiety and poor cognitive functioning. Previous evidence has revealed the anatomical and physiological biomarkers in the brain affecting cognition in LC. To synthesise these contributing factors, we propose the Long-COVID

Interacting Network of factors affecting Cognitive Symptoms (LINCS). This framework is designed to inform clinicians and researchers to take a comprehensive approach towards rehabilitation, targeting the neural, individual and lifestyle factors, with an aim of improving cognitive function in LC.

Keywords

Long COVID; COVID-19; cognitive symptoms; qualitative research; mixed-methods

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Strengths and limitations of this study

- This study used a mixed-methods approach, combining qualitative and quantitative methods of data collection to capture the experiences of LC and the severity of cognitive dysfunction among other symptoms in LC.
- The research team was interdisciplinary and interprofessional, combining expertise from Long Covid Rehabilitation, Neurology, Cognitive Psychology and Qualitative Methods.
- This study may be limited by a self-selecting, potentially biased sample consisting of mostly female, middle-aged participants.
- The involvement of multiple facilitators may have led to different areas of focus during the discussions.

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Introduction

Post-Acute Covid-19 Syndrome, also known as long COVID (LC), is the continuation or development of new symptoms three months after the initial SARS-CoV-2 infection, with symptoms lasting for at least two months [1]. In 2024, an estimated 2 million people living in private households in the UK (3.3% of the population) were experiencing self-reported LC [2] with common symptoms including fatigue, breathlessness, muscle ache, general malaise and cognitive dysfunction [3]. The Office for National Statistics [2] reported that the second most common symptom following fatigue was difficulty concentrating, reported by 52% of respondents. Furthermore, cognitive dysfunction was found to be one of the most common symptoms in a multinational survey of 3762 people with Long Covid, reported in ~88% of individuals [4].

Neuropsychological assessments and subjective reports have shown cognitive impairments in memory, attention, executive function and verbal fluency following SARS-CoV-2 infection in comparison to individuals without infection [5, 6]. Objectively measured memory deficits following COVID-19 infection, have been found to increase in severity, in line with the severity of self-reported ongoing symptoms [7]. A UK Biobank study found poorer cognitive accuracy in working memory, attention, reasoning and motor control in those who had been infected with SARS-CoV-2 than controls, with the largest deficits found in individuals with ≥ 12 weeks of symptoms, continuing to 2 years in some individuals [8]. Persistent cognitive impairment in LC is associated with anatomical and physiological biomarkers. Magnetic resonance images (MRI) and objective cognitive tests recorded before and after SARS-CoV-2 infection, have revealed reduced grey matter in the orbitofrontal cortex and parahippocampal gyrus and reduced global brain size correlated with impaired cognitive performance in those who had been infected than controls [9]. On a cellular level, SARS-COV-2 infection has been linked to tau pathology in the brain [10], and the viral sequence is capable of coding for cytotoxic amyloid proteins with comparable toxicity to proteins found in Alzheimer's disease [11]. Further biomarkers associated with LC include chronic neuroinflammation associated with a cascade of neurotoxic events [12, 13] and hypoxia [14, 15]. Collectively, these factors contribute to accelerated cognitive aging and a heightened risk of dementia in individuals with LC [16].

Previous qualitative studies have reported the profound, negative impact of LC on daily functioning and quality of life including high prevalence of mental health problems, change or loss of occupational status, difficulty accessing and navigating healthcare services, feelings of isolation, stigma, shame and loss of personal identity [17]. One previous qualitative study has reported the experiences of 'brain fog' in COVID-19 long haulers [18], a colloquial term describing a state of confusion, forgetfulness and slowing of mental abilities [19, 20]. However, focus group discussions conducted by Callan et al. [18] were held early in the COVID-19 pandemic in 2020, and to our knowledge no further studies have investigated the qualitative experiences of cognitive symptoms in Long Covid. Given the heightened risk of neurodegeneration and dementia [16], and detrimental impact on daily life associated with LC [17], it is crucial to have a current understanding of the impact of cognitive impairment on the lives of people with LC. By combining qualitative and quantitative methods, this study aimed to capture both in-depth experiences and quantify the extent of cognitive symptoms. This mixed-methods approach was used to enhance the validity and triangulation of the research, to inform a comprehensive understanding of cognitive symptoms in LC. In this study, people with LC took part in focus group discussions and a Post COVID-19 Syndrome Questionnaire. The following questions were explored. 1) What is the prevalence of cognitive symptoms in LC? 2) What is the lived experience of cognitive symptoms in LC?

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Methods

Study Design

The study implemented a mixed-methods design to explore the experiences of cognitive symptoms in LC. Eight exploratory focus groups were conducted in April 2023 to collect the qualitative data. Four of the groups were held in person in the School of Psychology, University of Leeds (UK) and four were held online via Zoom. The online discussions were held to make the study more accessible, allowing participation from individuals living outside the region or those with mobility impairments. Participants completed a Post (Long) Covid-19 Syndrome Questionnaire, detailed below, providing a quantitative measure of symptom prevalence and severity. A mixed methods approach was employed to capture both the quantitative nature of symptoms and the qualitative insights into the subjective

impacts on daily life. This combined approach provides a comprehensive understanding of the complex nature of cognitive symptoms and their effects.

Participants

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Participants included 25 adults with LC. Eligibility criteria included individuals with selfreported LC who lived in the UK. One participant did not return the Post-Covid-19 Syndrome Questionnaire so were removed from the analysis. The final sample size of 24 participants was sufficient to reach data saturation, where no additional codes or insights emerged from further discussions, ensuring the themes were rich and fully addressed the research question. Participants were recruited via social media advertisement on Facebook, Instagram, LinkedIn and NextDoor, via advertisement in the Chronic Pain & Fatigue Network at the University of Leeds and English National Opera Breathe Programme for Long Covid, and by word-of-mouth. Participants were reimbursed with a £20 Love2Shop voucher. All participants provided written informed consent. The study was approved by the University of Leeds Psychology Ethics Committee on 3rd January 2023 (PSC710) and was conducted in accordance with the BPS Code of Ethics [21] and the Declaration of Helsinki [22].

Quantitative Data Collection

The Post (Long) Covid-19 Syndrome Questionnaire was adapted from previous NHS LC questionnaires symptoms (available measuring in at https://ardenhousemedicalpractice.co.uk/navigator/post-long-covid-19-syndromequestionnaire/) in the validated Patient Health Questionnaire format (PHQ-9). This questionnaire measured participant's perceived health in: breathing, mobility, energy, mood, mental ability and physical health [23] (see Supplementary Materials). The questionnaire assessed the severity of symptoms using mixture of binary questions with "yes" or "no" responses, and scaled questions in which the rating scale comprised: (0) Normal, (1) Mild, (2) Moderate, and (3) Severe. Participants rated their selfperceived change in symptom severity on 0 - 10 point Likert scales for before and after they contracted Long Covid.

Qualitative Data Collection

The focus group discussions were audio-recorded and lasted approximately 2 hours. Participants were informed that the discussions were recorded and that any information they gave was confidential and would be anonymised. There were 8

groups each containing two to five participants and one of four facilitators. These groups sizes were selected as previous evidence has shown that a larger number of groups containing fewer participants can yield more information than fewer groups with more participants per group [24]. Facilitators informally followed guidance questions to encourage discussions around the main symptoms and experiences (see Table 1). The guided questions were intentionally broad to encourage participants to explore various aspects of their experiences with LC. We intended to refine the analysis from this broader discussion to focus on key topics of particular relevance and importance. The questions were used to guide the sessions whilst the content of the discussions was self-directed by the participants in the focus groups.

Guided Discussion Questions

What symptoms post COVID are most distressing for you?

What can you not do now that you could do before long COVID?

How has long COVID affected your quality of life?

What can clinical services provide to help with your everyday functioning?

What services can society provide to help with your symptoms?

What self-help strategies have worked for you?

What research would most help pwLC get back to normal functioning?

Table 1. Guided discussion questions followed by facilitators. The questions were intended to guide broad discussions around the experiences of LC. The analysis focused on key themes of relevance and importance, in this case, the experiences of cognitive symptoms.

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Data Management and Analysis

Firstly, audio recordings were transcribed verbatim and anonymised. To maintain confidentiality, personal identifiers were removed from the data, and access was restricted to the individuals directly involved in the data analysis. Participants' names were replaced with pseudonyms for anonymity. The data was analysed according to the Framework Analysis proposed by Ritchie and Spencer [25]. The Framework Analysis provides a structured yet flexible approach to analysing qualitative data,

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facilitating the systematic organisation of large datasets and diverse participant experiences into themes. The Framework Analysis was selected over other qualitative methods, such as Grounded Theory and Interpretative Phenomenological Analysis (IPA), as the focus of this study was not to generate new theory or deeply analyse lived experiences, but to explore and categorise experiences within a broader thematic framework.

The Framework Analysis involved four stages: (a) the process of data familiarisation involved repeatedly reading the transcripts and listening to the audio recordings, which allowed for the identification of initial codes; (b) data were 'open coded' and a framework was developed and refined within the research team; (c) manual coding was performed in NVivo (R14.23.1, QSR International) to index the data according to the framework. A second analyst (S.M.) independently double-coded 25% of the data (2/8 transcripts) to assess the quality of the coding and to enhance the reliability and validity of the data analysis. Any differences in the coding were resolved by consensus and the framework was altered accordingly. Then the framework was applied to all remaining transcripts. To ensure consistency in the coding and reduce possible bias, the second analyst (S.M.) checked 20% of the coding. Data saturation was reached when no new codes were emerging from the analysis. The initial framework was developed from the broader discussions and from this framework we identified common codes which were relevant to the research question to develop into themes. (d) In the charting stage, the coded data were arranged in a system to organise the data into relevant themes. (e) Theme development involved mapping and interpreting codes, identifying relationships between them, and systematically grouping them into sub-themes. These sub-themes were then further refined and categorised into overarching themes that captured the key patterns and insights from the data. All stages of the data analysis, framework and theme development were reviewed by an interdisciplinary research team, combining expertise from Cognitive Psychology and Qualitative Methods. Discussions within the research team were held to inform the process. Whilst this analysis focused on investigating the experiences of cognitive symptoms, we have also reported on the broader perceived 'needs' of people with LC in our previous publication of this study [26].

Patient or Public Involvement

Participants were invited to review the manuscript prior to submission to ensure the findings accurately represented their views and experiences.

Results

Participants were aged 19 to 76 years (M = 43.6 years, SD = 14.7; 17 females and 8 males). Participants were eligible if they had self-reported LC and lived in the UK. 92% (22/24) of participants had a clinical diagnosis of LC. The duration of symptoms experienced varied between 4 months to 2.8 years (M = 77.96 weeks, SD = 32.58). Twenty one participants had British nationality, 1 French, 1 Finnish and 1 Chinese.

Quantitative Results

Results from the Post Long COVID-19 Questionnaire showed that participants experienced wide ranging symptoms following the development of LC, see Figure 1 and Figure 2. The most severe symptoms, with the greatest change after disease contraction, were decreases in energy, mobility, breathing and mental ability.

In terms of cognition; 87.50% (21/24) of participants reported that their ability to concentrate had worsened, 83.33% (20/24) reported that their short-term memory had declined, 75.00% (18/24) reported that they or their family had identified a difference in the way they communicated. Participants reported a 10-fold increase in concern about their cognition following LC (M = 5.83, SEM = 0.61) compared to before LC (M = 0.54, SEM = 0.27).

Almost all participants reported that their illness and cognition affected their ability to work (95.65%; 22/23; 1 participant was retired). All participants (24/24) requested to be informed of future LC research opportunities showing clear motivation to advance understanding and treatment for persistent symptoms.

Qualitative Results

Summary

Data from the focus group discussions were categorised into three interconnected themes, see Figure 3. Theme 1) Rich accounts of cognitive symptoms, theme 2) impact on physical function and psychological wellbeing; and theme 3) symptom management. Participants experienced various cognitive impairments (theme 1) which impacted daily functioning and psychological wellbeing (theme 2). Participants attempted to manage the symptoms and impact on their daily life (themes 1 & 2) using strategies (theme 3). Oftentimes these strategies (theme 3) were tedious to implement or ineffective, further exacerbating the impact on physical and psychological functioning (theme 2). See theme descriptions for further details.

Theme 1) Rich accounts of cognitive symptoms

The majority of participants (20/24) described experiences of cognitive symptoms associated with LC. The most commonly reported symptoms were difficulties with memory and language, followed by attention, executive function and reduced processing speed. Participants frequently used the term 'brain fog' to describe their symptoms.

Memory

Participants described experiences of memory deficits which were consistent with definitions of working memory, long term memory (declarative and non-declarative memory) and prospective memory. Participants were concerned about the consequences of these memory impairments on their safety. For example, Participant 1 was forgetting to take their medication and reported "*I could be overdosing and I've no idea*". Other participants were worried about the impact of their memory difficulties on their perceived image, as Participant 18 described "*it makes you look stupid*" after missing appointments. Participants described a need to review information multiple times before they could process, retain and remember it:

"I'll go back to the book and think I don't remember this bit at all and be going back a chapter... not necessarily reading it in detail, but scanning through and it will kind of prompt me." Participant 14.

Occasional lapses in memory lead to experiences of disorientation and confusion. Participant 23 described the experience as a "full blank moment" and as 'disconcerting'.

Language

Impairments in language affected word finding, reading comprehension and writing. Participant 14 described making errors in writing and proof-reading at work which they didn't do before, "*I would read it and think this is great letter and then actually there'd be, like, a word missing.*" Issues with communication included difficultly following conversations or abruptly deviating from the topic of conversation. A feeling of "disconnection in the brain", while trying to communicate, was described by participants:

"I'm often looking for words when I'm speaking and I think of a word, but I can't find it, like I know what it means and I know what I want to say, but it's like it's just disappeared from my brain." Participant 17.

Attention

Participants experienced impaired attention, particularly divided attention (multitasking) and maintaining selective/sustained attention, and the impact of this on daily life. Participant 6 described difficulty talking whilst driving and *"could* [only] *retrieve the information"* once *'stopped at the traffic lights'*. Participant 17 described the frustration of losing their attention, *"I used to be able to sit down and watch films and things. Now, I find myself sometimes flicking the TV over because I can't, like, concentrate on stuff."*

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Executive Functioning

Executive dysfunction included difficulties with planning, decision-making and mental flexibility. For example, Participant 11 found difficulty following "a logical train of thought" and "getting things done around the house". The term "decision fatigue" was used by participants 12 and 13 to describe the exhaustion associated making a choice out of many options, such as selecting a programme on the TV.

Processing speed

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Accounts of cognitive dysfunction included descriptions of the delay involved in completing tasks or retrieving information, suggesting participants were experiencing reduced processing speed.

"When I'm doing patients notes have to go over them like up to 10 times maybe, word by word to make sure I've put the correct word. People used to comment how quick I could, like, type and do the notes. Now it's taking me a lot longer". Participant

15.

Contributing factors

Fatigue, poor sleep and headaches were reported to exacerbate cognitive symptoms. Participant 4 explained that tiredness makes their brain feel *"jumbled*". Other participants described continuous cognitive symptoms, independent of other factors.

Theme 2) Impact on physical function and psychological wellbeing

Over half of participants (14/24) experienced negative impacts on their daily lives including employment, physical functioning and psychological wellbeing, as a direct result of their cognitive symptoms. Of these, ten participants reported a decline in their perceived work performance or changes in employment or education due to issues with their memory or concentration. This included being unable to return to their pre-COVID-19 careers, reducing working hours or adapting roles due to the self-perceived inability to uphold the cognitive demands and high responsibility of their previous roles. Participants were concerned about when or if their cognitive abilities would return and this was associated with a loss of professional identity:

"Throughout my career has involved writing and also proofreading and copy editing. And I had to give that up for two years, and I was so scared that my ability would never come back... I've always seen myself as someone who works with words". Participant 9.

"I've actually changed jobs at work, changing jobs on Monday, because the job I do requires a lot of concentration and I was just making so many mistakes. I've kind of taken a sideways step". Participant 24.

More than half of participants (14/24) described the challenges of carrying out activities of daily living including cooking, driving and shopping, that they were previously proficient in or enjoyed:

 "The odd time I have actually forgotten to turn the cooker off as well. So I'm not, like, keen to cook a lot these days either, which I've always enjoyed cooking." Participant 17.

Ten participants experienced psychological impacts as a result of their cognitive symptoms. Cognitive impairment contributed to low mood, stress and anxiety. Participant 16 described the experience of losing their memory abilities as "stressful" and feeling "so down". Participants reported concern about their cognitive health including experiencing a sense of accelerated ageing, and anxiety over whether these cognitive changes might signal the onset of age-related neurodegenerative diseases.

"A few weeks into having Covid I felt like I'd aged 20 years and lost 20 IQ points....It makes you worried that there are other things, I think, oh my God have I actually got Alzheimer's, you know? Because I could tick most of the boxes." Participant 12.

Theme 3) Symptom management

Half of participants (12/24) reported strategies they had tried to manage their cognitive symptoms, with variable success. Participants described simplifying daily life by reducing demands or decision-making:

"I find decisions tiring... So I've just eliminated that, I just wear the same coloured clothes every day [and] cook the same meals" Participant 13.

Strategies for recording information and setting reminders were reported, including making to-do lists, setting alarms to take medication or remember dates and appointments. The effectiveness of these strategies for improving cognitive function was varied, with at least five participants reporting continued difficulties with memory and forgetfulness despite using strategies. Participant 19 attempted to use pill boxes and phone notifications to reminder them to take their medication, however they explained *"I would still forget… I'll see the notification, and I think right, I'll do that in a minute and then I'll get distracted and I'll forget about it"*.

Regular rest and breaks were required, particularly throughout the working day. Participant 4 took regular breaks whilst working from home, and explained *"if I didn't do that, I won't be able to continue with my day".*

Several participants (7/24) described feelings of frustration and tediousness over the increased time or effort required implement these strategies in order to complete tasks:

"I just have to stop organising [meetings] *any time after about 2 o'clock because I then I can't find the words that I'm trying to say and it sounds like ridiculous... That's really, really frustrating"* Participant 23.

One participant attempted to regain their pre-Covid-19 cognitive function by challenging themselves in progressive increments, with some success:

"I struggled to even just reading a page of a book... I've progressed again over kind over the last few months, really just by setting myself the kind of challenge or time to just read one chapter or a few pages of the book every day". Participant 14.

Discussion

This mixed-methods study aimed to explore the lived experiences of cognitive symptoms in LC. The majority of participants in this study reported a decline in cognitive ability and concern about this change. Cognitive symptoms were among the most common symptoms reported alongside low energy, immobility and breathlessness. The experiences of subjective cognitive impairments included difficulties with memory, attention, language, executive function, and processing speed. Cognitive symptoms had profound negative effects on participants' ability to work, complete activities of daily living, their psychological wellbeing and self-image, in some cases for >2 years after the initial infection. Participants attempted to manage their cognitive symptoms using strategies to reduce decision making and mental load, facilitate memory and improve energy levels. However, the strategies were described as tedious and frustrating to implement, with mixed effectiveness. By combining quantitative and qualitative methods, this study found that cognitive symptoms are among the most prevalent symptoms in LC with considerable negative impacts on the wellbeing, functioning and daily lives of people with LC.

The findings of this study are consistent with previous research on both objective measures of cognitive impairment [5, 6] and the lived experiences of LC [17, 18]. Our findings strongly align with those of Callan et al. [18], showing the experiences of subjective cognitive impairments, altered self-identity and the challenges of managing ongoing symptoms. Similar to previous studies, we found cognitive impairment in LC impacted occupational status, including reducing working hours, changing job roles and loss of pre-COVID-19 employment [27]. Additionally, participants reported difficulties in completing activities of daily living, which reflects previous research

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highlighting the functional limitations caused by cognitive decline in LC [28]. High rates of mood disorders, such as anxiety and depression, were also prevalent among participants, reinforcing existing evidence that emotional and mental health challenges often accompany cognitive dysfunction in LC [29]. Furthermore, many participants described living an altered lifestyle, consistent with prior findings that LC can affect individuals' ability to engage in social, professional, and personal activities [30]. These results contribute the growing literature documenting the far-reaching impact of ongoing cognitive impairment in LC. The novel findings of this study are the interactions found between the experiences of cognitive impairment, physical and psychological functioning and self-management of cognitive symptoms. Poor memory, attention and executive functioning affected many areas of daily functioning and contributed to a loss of self-worth and identity and reduced psychological wellbeing. Strategies used for self-management of cognitive symptoms involved living an altered lifestyle by reducing daily demands, activities, exercise and decision making and implementing 'reminders' for tasks and regular rest, most of which added further distraction and frustration to daily life. This may reflect a vicious cycle of withdrawal from daily life, low mood and poor self-coping strategies that essentially exacerbates cognitive impairment.

Building on the findings of this study and prior research, we propose a new framework to conceptualise the factors contributing to cognitive impairment in LC, which appear to reflect an interacting symptom network [31]. The Long-COVID Interacting Network of factors affecting Cognitive Symptoms (LINCS) framework integrates the findings of this study and previous research showing the neural, lifestyle and individual factors shaping actual and self-perceived cognitive dysfunction in LC (see figure 4). The possible interplay between psychological, physical, and social factors, and the contribution of this to ongoing cognitive dysfunction following COVID-19, has previously been suggested by Callan et al. [18]. The need for this framework stems from the lack of evidence-based recommendations for clinicians regarding LC treatment [32]. Furthermore, patients with LC have reported the challenging experiences of accessing primary care such as receiving inconsistent advice from healthcare professionals, difficulty accessing and navigating services and a lack of understanding the complexity of cognitive dysfunction in LC patients, which

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emphasises the multifaceted nature of the condition and may inform a more holistic approach to treatment by considering biological mechanisms, internal and external factors. The aim of presenting the LINCS framework is to guide future research and clinical practice towards more personalised, integrated and multi-disciplinary care strategies for managing cognitive symptoms in LC, in line with previously published recommendations [33-35].

The LINCS framework also highlights neuroinflammatory processes and brain structural changes as primary biological drivers of cognitive impairment in LC. Previous reviews have reported on the current understanding of the neurobiology of LC [12, 36]. The COVID-19 infection triggers an inflammatory response in the respiratory system, which can spread to the central nervous system (CNS). Within the CNS, cytokines, chemokines, and activated microglial cells disrupt various neural cell types. This disruption interferes with the maintenance of myelin, impairs neuroplasticity, and hinders hippocampal neurogenesis. It can also initiate neurotoxic responses in astrocytes, leading to a breakdown in neural circuits and cognitive impairment [13]. COVID-19 infection can trigger anti-neural autoantibodies and T cells to provoke an autoimmune response, potentially leading to autoimmune encephalitis and contributing to continued neural damage [37]. In more severe cases of COVID-19, nervous system injury can also result from hypoxia, further aggravating neuroinflammation [14, 15]. Structural changes to the brain following COVID-19 infection include reduced global brain size and grey matter thickness in the orbitofrontal cortex and parahippocampal gyrus [9]. Several studies have highlighted the risks of developing abnormal tau pathology and cytotoxic amyloid protein aggregation in LC [10, 11], which may indicate a future trajectory toward neurodegeneration.

Lifestyle factors also play a significant role in the cognitive impairment associated with LC. In a previous publication, we reported on the experiences and needs of individuals with LC and found that many participants experienced symptoms that significantly impacted their daily lives [26]. Participants commonly reported challenges such as impaired physical mobility, cognitive dysfunction, and social withdrawal. These difficulties often led to changes in employment, including reduced working hours, adjusting their role or being unable to return to work. Additionally, social withdrawal was frequently driven by a lack of understanding and support from family, friends, and

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society, which contributed to feelings of shame and isolation. These changes in an individual's engagement with their surroundings may reduce mental stimulation, further accelerating cognitive decline. Notably, both physical and social withdrawal, along with increased sedentary behaviour, are well-documented risk factors for the development of Dementia [38, 39], highlighting the need to address these lifestyle factors when considering interventions for cognitive symptoms in LC patients.

The findings of the current study, in line with existing research, enhance our understanding of the individual factors that exacerbate cognitive symptoms in LC. Participants reported their efforts to recover by implementing coping strategies, and managing fatigue and energy levels, whilst also dealing with the high prevalence of mood disorders. Prior evidence highlights the interconnectedness of these factors, suggesting they may collectively contribute to cognitive impairment in LC. For instance, fatigue and depression have been shown to impair cognition in conditions such as chronic fatigue syndrome and multiple sclerosis [40, 41], and major depressive disorder (MDD) is associated with reduced brain grey matter volume [42]. Participants also described withdrawing from activities of daily living (ADL) as a way to manage symptoms. However, reduced cognitive, physical, and social engagement, along with prolonged absence from work, have been associated with accelerated cognitive decline in mid to later adulthood [43, 44, 45]. These findings emphasise the importance of addressing both the physical and psychological components in managing cognitive dysfunction in LC.

Given the evidence of accelerated cognitive ageing and dementia risk in LC [9, 10, 16], this clinical population of an estimated 2 million people in the UK [2] may be the next generation at risk of developing age-related neurodegenerative diseases, fuelling a future epidemic of dementia in the UK. Currently there is no approved treatment for LC [46], and the findings of this study highlight the vital need for an intervention to tackle the cognitive symptoms in LC, with aims to improve quality of life and reduce possible dementia risk. A recent scoping review evaluated treatments for cognitive impairment in LC and provided key recommendations for primary care management [32]. The authors emphasised that a multidisciplinary, patient-centred approach is appropriate for addressing the cognitive symptoms. One of the main recommendations was for patients to adopt a healthy lifestyle, incorporating a balanced diet including key vitamins, micronutrients and probiotics, sufficient sleep, stress-reduction

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techniques, and appropriate physical activity. The World Health Organization selfmanagement booklet on LC provides a comprehensive strategy for returning to physical activity using a cautious pacing approach to mitigate overexertion [35]. This approach contrasts with graded exercise therapy (GET), which has been shown to potentially cause harm and worsen post-exertional malaise (PEM) in various chronic health conditions, including LC [33]. Behavioural interventions were also identified, including cognitive training, mind-body interventions, music therapy and meditation [32]. Overall this scoping review underscored the importance of tailoring care plans to each individual, combining lifestyle modifications with medical and psychological interventions to create a comprehensive and adaptive treatment strategy for cognitive impairment [32]. These recommendations align with the LINCS framework by advocating for a multidisciplinary and individualised approach to addressing the various factors which appear to exacerbate cognitive symptoms in LC. LC is a relatively new condition, and as such, the underlying pathology of cognitive impairment remains poorly understood and there is a current lack of high-quality evidence supporting targeted interventions for managing cognitive deficits in LC patients [32]. Future research should prioritize identifying the precise mechanisms driving cognitive impairment in LC, including neuroinflammatory processes, neural dysregulation, and neurovascular dysfunction [36]. Additionally, there is a need for large-scale, highquality, longitudinal studies to evaluate the effectiveness of both pharmacological and non-pharmacological interventions, such as cognitive rehabilitation and lifestyle modifications, in improving cognitive function. Developing standardised assessment tools and outcome measures will also be crucial to ensure consistency across studies and provide clearer guidance for clinical practice [32].

The term 'brain fog' was used by some participants in this study to describe their cognitive symptoms, however previous evidence suggests the term lacks specificity and may not capture the severity of cognitive symptoms experienced in LC [18]. The term 'fog' implies a perceptual deficit or 'clouding' of cognitive processes, whereas in this study, participants reported reduced processing speed, increased cognitive effort and a feeling of disconnection in the brain. Without the development of appropriate terminology to define these symptoms and lack of recognition of the specific impairments to cognitive functioning, there is a barrier for medical diagnosis and the development of targeted cognitive interventions. An alternative code name has been

proposed to described the accelerated process of cognitive decline in pre-existing dementia following COVID-19, termed FADE-IN-MEMORY i.e. Fatigue, decreased Fluency, Attention deficit, Depression, Executive dysfunction, slowed INformation processing speed, and subcortical MEMORY impairment [47]. The findings of this study show that FADE-IN-MEMORY might also be an appropriate term to describe the experience of cognitive symptoms in LC.

The strengths of this study include the rigorous and well-established methods to analyse the focus group data. The Framework Analysis [25] is data analysis technique that provides a structured yet flexible approach to processing qualitative data. By organising, coding, and conducting thematic analysis in a systematic manner, this method allows for efficient analysis of qualitative research while strengthening the credibility of the research process [48]. The Framework Analysis is increasing used in the analysis of qualitative data in multi-disciplinary health research [48]. The use of quantitative data collection to supplement the qualitative responses in this study, allowed us to quantify the self-perceived change in cognitive abilities following LC, and compare the severity of cognitive symptoms with other symptoms. However, the questionnaire rating scales were arbitrary, and the self-report nature of the questionnaire may not reflect an objective measure of cognitive functioning. Having said that, the extent of memory deficits following COVID-19 infection has been found to increase with the severity of self-reported ongoing symptoms [7], demonstrating the link between objective and subjective cognitive measures. One possibility for related future research would be to administer a brief test of global cognitive function, such as the Montreal Cognitive Assessment (MoCA) [49], to measure participants' individual global cognitive function on the day of the focus group discussions. However, tests of global cognitive function primarily measure working memory, therefore may not capture the impairments in other cognitive domains participants reported in this study. There are also concerns that global screening tools, developed for identifying dementia and mild cognitive impairment, may lack sensitivity in reliability detecting cognitive deficits in LC [50]. Furthermore, in this study, the self-report nature of the questionnaire complimented the qualitative data in which the overall aim was to investigate the lived experience of cognitive symptoms from the participants' perspective, rather than to obtain an objective measurement of cognitive functioning. This study may be limited by the biased sample of mostly female and middle-aged

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participants, which prevented comparison of possible age and gender differences in the experience of LC symptoms.

This mixed-methods study found that cognitive dysfunction was commonly reported by participants and had a significant impact on daily life and overall functioning. Participants were concerned about their cognitive decline and the limited options available for symptom management and treatment. There is a clear need for interventions that address the complex, multifactorial nature of cognitive impairment in LC. Without such targeted strategies, individuals with LC face an increased risk of accelerated cognitive aging and the potential onset of dementia. This study introduced the LINCS framework, designed to provide a structured approach for clinicians to assess and manage the array of factors contributing to cognitive dysfunction in LC. By integrating multiple dimensions of cognitive health, the LINCS framework offers a valuable tool for both clinical practice and future research, which could be used to inform the development of interventions that are tailored to the needs of LC patients. Future high-quality, large-scale intervention studies are essential to identify effective treatments for cognitive dysfunction in individuals affected by LC.

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Contributors

Melanie Rose Burke, Manoj Sivan and Rumana Chowdhury gained funding for the study. Amy Miller and Melanie Rose Burke conceived the idea and conducted the study. Ning Song informed the methods for qualitative data analysis. Amy Miller conducted the transcription, data analysis and wrote the first draft of the manuscript. All authors contributed towards the refinement of the manuscript. Amy Miller is the guarantor.

Patient and public involvement

Participants were invited to review the manuscript prior to journal submission.

Data Availability Statement

Data are available on reasonable request.

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Figure Legends

Figure 1. Participant self-reported ratings of symptom severity across health symptoms. High scores indicate greater severity of symptoms. [0] Normal [1] Mild [2] Moderate, and [3] Severe. Error bars show standard error (SEM). N = 24.

Figure 2. Participant self-reported symptom change before and after contracting Long Covid (LC). High scores indicate greater symptom severity. Error bars show SEM. N = 24.

Figure 3. A map of the relationships between themes.

Figure 4. A conceptual framework of the Long-COVID Interacting Network of factors affecting Cognitive Symptoms (LINCS).

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Figure 1. Participant self-reported ratings of symptom severity across health symptoms. High scores indicate greater severity of symptoms. (0) Normal, (1) Mild, (2) Moderate, and (3) Severe. Error bars show standard error (SEM). N = 24.

130x90mm (300 x 300 DPI)

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Figure 2. Participant self-reported symptom change before and after contracting Long Covid (LC). High scores indicate greater symptom severity. Error bars show SEM. N = 24.

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Figure 3. A map of the relationships between themes.

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Supplementa	ary Information

Participant Questionnaire

Post (Long) COVID-19 Syndrome Questionnaire

	Pari	ticipant Det	ails	
Name:	Date of Birth:			
Email Address:				
Gender:			Nationalit	y:
Can we contact you in the future for intervention study on people with	or taking p Long Covi	bart in an d? [`	(ES / NO]	
Do you have an official Diagnosis of Long Covid?		vid? [`	[YES / NO]	
How long have you had Long Covid	sympton	ns? [Weeks]	
	Gener	al Question	naire	
	Gener	un gueboron		
	NORMA	L MILD	MODERATE	SEVERE
Is your Breathing back to normal? [NB: Circle the answer that best describes you]	Normal	Not norm but can o everythi	al, Breathless on do hills/stairs ng	Stops me doing some things, breathless at rest/mild activity.
On a scale of 0-10, with 0 being not breathless at all, and 10 being extremely breathless, how breathless are you:	Bef 3	ore COVID	Af	ter COVID
Is your Mobility/Activity levels back to normal?	Normal	Nearly back to normal	Having to move more slowly, but doing everything	Struggling with some activities, barely getting around.
On a scale of 0-10, with 0 being very active, and 10 being completely inactive, how active are you:	Bef	ore COVID	Af	ter COVID
Are your Energy Levels back to normal?	Normal	Feeling tire but doing a normal activities.	d Needing to rest Il frequently and some restriction to activities.	Significant tiredness cannot do usual tasks or fatigue is debilitating.

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On a scale of 0-10, with 0 being full of energy, and 10 being constantly tired, how fatigued are you:	Be	fore COVID	Aft	er COVID
Is your Mood back to normal?	Normal	I have brief occasional moments of low mood.	l suffer most days with low mood or anxiety.	I struggle to think and remember, or I feel hopeless and suicidal.
On a scale of 0-10, with 0 being not atall depressed, and 10 being very depressed/suicidal, how would you rate your mood:	Be	fore COVID	Aft	er COVID
On a scale of 0-10, with 0 being not atall anxious, and 10 being anxious all the time, how would you rate your anxiety:	Be	fore COVID	Aft	er COVID
Are your Mental ability levels back to normal?	Normal	I have the odd lapse in concentratior and memory.	d My brain is working much n slower than it used to.	My mental capacity is significantly affecting my day-to-day functioning.
On a scale of 0-10, with 0 very alert, and 10 being very limited on thinking and memory, how would you rate your mental capacity:	Be	fore COVID	Aft	er COVID
Is your overall health (physical N and mental) back to normal?	lormal m w	I have only inor concerns ith my health.	My physical and/or mental health is worse than it was, but is manageable.	My physical and mental health is a huge concern, and I am struggling to function independently.
	Further	Cognitive Qu	estions	
Cognition is our ability to think, plan and process things. Ha CONCENTRATION worsened since	rememb is your your illn	ver, vess?	YES	NO

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Has your SHORT-TERM MEMORY worsened since your illness?	YES	NO
On a scale of 0-10, with 0 being not atall concerned, and 10 very concerned, how would you rate your concern about your cognition:	Before COVID	After COVID
Have you or your family identified a difference in the way you COMMUNICATE putting thoughts into words/difficulty reading/communicating?	YES	NO
Has your illness/cognition affected your ability to work?	YES	NO
On a scale of 0-10, with 0 being not atall affected my work, and 10 can no longer work, how would you rate your working ability:	Before COVID	After COVID

THANK-YOU FOR YOUR TIME IN COMPLETEING THIS QUIZ !!

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Exploring the experiences of cognitive symptoms in Long COVID: a mixed-methods study in the UK

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Exploring the experiences of cognitive symptoms in Long COVID: a mixed-methods study in the UK

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Abstract

Objective: To explore the lived experiences and extent of cognitive symptoms in Long COVID (LC) in a UK-based sample.

Design: This study implemented a mixed-methods design. Eight focus groups were conducted to collect qualitative data, and the Framework Analysis was used to reveal the experiences and impact of cognitive symptoms. A self-report questionnaire was used to collect the quantitative data to assess the perceived change and extent of symptomology post COVID-19.

Setting: Focus groups were conducted in April 2023 online via Zoom and in-person at the University of Leeds, UK.

Participants: 25 people with LC living in the UK participated in the study. Participants were aged 19 to 76 years (M = 43.6 years, SD = 14.7) and included 17 females and 8 males.

Results: Reduced cognitive ability was among the most prevalent symptoms reported by the study participants. Three key themes were identified from the qualitative data. (i) Rich accounts of cognitive symptoms. (ii) The impact on physical and psychological functioning. (iii) Symptom management. Descriptions of cognitive symptoms included impairments in memory, attention, language, executive function and processing speed. Cognitive symptoms had a profound impact on physical functioning and psychological wellbeing, including reduced ability to work and complete activities of daily living. Strategies used for symptom management varied in effectiveness

Conclusion: Cognitive dysfunction in LC appears to be exacerbated by vicious cycle of withdrawal from daily life including loss of employment, physical inactivity and social isolation driving low mood, anxiety and poor cognitive functioning. Previous evidence has revealed the anatomical and physiological biomarkers in the brain affecting cognition in LC. To synthesise these contributing factors, we propose the Long-COVID Interacting Network of factors affecting Cognitive Symptoms (LINCS). This framework is designed to inform clinicians and researchers to take a comprehensive approach towards LC rehabilitation, targeting the neural, individual and lifestyle factors.
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Keywords

Long COVID; COVID-19; cognitive symptoms; qualitative research; mixed-methods

Strengths and limitations of this study

- This study used a mixed-methods approach, combining qualitative and quantitative methods of data collection to capture the experiences of Long COVID (LC) and the severity of cognitive dysfunction among other symptoms in LC.
- The research team was interdisciplinary and interprofessional, combining expertise from LC Rehabilitation, Neurology, Cognitive Psychology and Qualitative Methods.
- This study may be limited by a self-selecting, potentially biased sample consisting of mostly female, middle-aged participants.
- The involvement of multiple facilitators may have led to different areas of focus during the discussions.



INTRODUCTION

Post-Acute Covid-19 Syndrome, also known as Long COVID (LC), is the continuation or development of new symptoms three months after the initial SARS-CoV-2 infection, with symptoms lasting for at least two months [1]. In 2024, an estimated 2 million people living in private households in the UK (3.3% of the population) were experiencing self-reported LC [2] with common symptoms including fatigue, breathlessness, muscle ache, general malaise and cognitive dysfunction [3]. The Office for National Statistics [2] reported that the second most common symptom following fatigue was difficulty concentrating, reported by 52% of respondents. Furthermore, cognitive dysfunction was found to be one of the most common symptoms in a multinational survey of 3762 people with LC, reported in ~88% of individuals [4].

Neuropsychological assessments and subjective reports have shown cognitive impairments in memory, attention, executive function and verbal fluency following SARS-CoV-2 infection in comparison to individuals without infection [5, 6]. Objectively measured memory deficits following COVID-19 infection, have been found to increase in severity, in line with the severity of self-reported ongoing symptoms [7]. A UK Biobank study found poorer cognitive accuracy in working memory, attention, reasoning and motor control in those who had been infected with SARS-CoV-2 than controls, with the largest deficits found in individuals with ≥ 12 weeks of symptoms, continuing to 2 years in some individuals [8]. Persistent cognitive impairment in LC is associated with anatomical and physiological biomarkers. Magnetic resonance images (MRI) and objective cognitive tests recorded before and after SARS-CoV-2 infection, have revealed reduced grey matter in the orbitofrontal cortex and parahippocampal gyrus and reduced global brain size correlated with impaired cognitive performance in those who had been infected than controls [9]. On a cellular level, SARS-COV-2 infection has been linked to tau pathology in the brain [10], and the viral sequence is capable of coding for cytotoxic amyloid proteins with comparable toxicity to proteins found in Alzheimer's disease [11]. Further biomarkers associated with LC include chronic neuroinflammation associated with a cascade of neurotoxic events [12, 13] and hypoxia [14, 15]. Collectively, these factors contribute to accelerated cognitive aging and a heightened risk of dementia in individuals with LC [16].

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Previous qualitative studies have reported the profound, negative impact of LC on daily functioning and quality of life including high prevalence of mental health problems, change or loss of occupational status, difficulty accessing and navigating healthcare services, feelings of isolation, stigma, shame and loss of personal identity [17]. One previous qualitative study has reported the experiences of 'brain fog' in COVID-19 long haulers [18], a colloquial term describing a state of confusion, forgetfulness and slowing of mental abilities [19, 20]. However, focus group discussions conducted by Callan et al. [18] were held early in the COVID-19 pandemic in 2020, and to our knowledge no further studies have directly investigated the qualitative experiences of cognitive symptoms in LC. Given the heightened risk of neurodegeneration and dementia [16], and detrimental impact on daily life associated with LC [17], it is crucial to have a current understanding of the impact of cognitive impairment on the lives of people with LC. By combining qualitative and quantitative methods, this study aimed to capture both in-depth experiences and quantify the extent of cognitive symptoms. This mixed-methods approach was used to enhance the validity and triangulation of the research, to inform a comprehensive understanding of cognitive symptoms in LC. In this study, people with LC living in the UK took part in focus group discussions and a Post COVID-19 Syndrome Questionnaire. The following questions were explored. 1) What is the extent of cognitive symptoms in LC? 2) What is the lived experience of cognitive symptoms in LC?

METHODS

Study design

The study implemented a mixed-methods design to explore the experiences of cognitive symptoms in LC. Eight exploratory focus groups were conducted in April 2023 to collect the qualitative data. Four of the groups were held in person in the School of Psychology, University of Leeds (UK) and four were held online via Zoom. The online discussions were held to make the study more accessible, allowing participation from individuals living outside the region or those with mobility impairments. Participants completed a Post (Long) COVID-19 Syndrome Questionnaire, detailed below, providing a quantitative measure of symptom prevalence and severity. A mixed methods approach was employed to capture both the quantitative nature of symptoms and the qualitative insights into the subjective

impacts on daily life. This combined approach provides a comprehensive understanding of the complex nature of cognitive symptoms and their effects.

Participants

Participants included 25 adults with LC. Eligibility criteria included individuals with selfreported LC who lived in the UK. One participant did not return the Post-Covid-19 Syndrome Questionnaire so were removed from the analysis. The final sample size of 24 participants was sufficient to reach data saturation, where no additional codes or insights emerged from further discussions, ensuring the themes were rich and fully addressed the research question. Participants were recruited via social media advertisement on Facebook, Instagram, LinkedIn and NextDoor, via advertisement in the Chronic Pain & Fatigue Network at the University of Leeds and English National Opera Breathe Programme for LC, and by word-of-mouth. Participants were reimbursed with a £20 Love2Shop voucher. All participants provided written informed consent. The study was approved by the University of Leeds Psychology Ethics Committee on 3rd January 2023 (PSC710) and was conducted in accordance with the BPS Code of Ethics [21] and the Declaration of Helsinki [22].

Quantitative data collection

The Post (Long) Covid-19 Syndrome Questionnaire was adapted from previous NHS LC questionnaires symptoms measuring in (available at https://ardenhousemedicalpractice.co.uk/navigator/post-long-covid-19-syndromequestionnaire/) in the validated Patient Health Questionnaire format (PHQ-9). This questionnaire measured participant's perceived health in: breathing, mobility, energy, mood, mental ability and physical health [23] (see Supplementary Materials). The questionnaire assessed the severity of symptoms using mixture of binary questions with "yes" or "no" responses, and scaled questions in which the rating scale comprised: (0) Normal, (1) Mild, (2) Moderate, and (3) Severe. Participants rated their selfperceived change in symptom severity on 0 - 10 point Likert scales for before and after they contracted LC.

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Qualitative data collection

The focus group discussions were audio-recorded and lasted approximately 2 hours. Participants were informed that the discussions were recorded and that any information they gave was confidential and would be anonymised. There were 8

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groups each containing two to five participants and one of four facilitators. These groups sizes were selected as previous evidence has shown that a larger number of groups containing fewer participants can yield more information than fewer groups with more participants per group [24]. Facilitators informally followed guidance questions to encourage discussions around the main symptoms and experiences (see Table 1). The guided questions were intentionally broad to encourage participants to explore various aspects of their experiences with LC. We intended to refine the analysis from this broader discussion to focus on key topics of particular relevance and importance. The questions were used to guide the sessions whilst the content of the discussions was self-directed by the participants in the focus groups.

Guided discussion questions

What symptoms post COVID are most distressing for you?

What can you not do now that you could do before long COVID?

How has long COVID affected your quality of life?

What can clinical services provide to help with your everyday functioning?

What services can society provide to help with your symptoms?

What self-help strategies have worked for you?

What research would most help pwLC get back to normal functioning?

Table 1. Guided discussion questions followed by facilitators. The questions were intended to guide broad discussions around the experiences of LC. The analysis focused on key themes of relevance and importance, in this case, the experiences of cognitive symptoms.

Data management and analysis

Firstly, audio recordings were transcribed verbatim and anonymised. To maintain confidentiality, personal identifiers were removed from the data, and access was restricted to the individuals directly involved in the data analysis. Participants' names were replaced with pseudonyms for anonymity. The data was analysed according to the Framework Analysis proposed by Ritchie and Spencer [25]. The Framework Analysis provides a structured yet flexible approach to analysing qualitative data,

facilitating the systematic organisation of large datasets and diverse participant experiences into themes. The Framework Analysis was selected over other qualitative methods, such as Grounded Theory and Interpretative Phenomenological Analysis (IPA), as the focus of this study was not to generate new theory or deeply analyse lived experiences, but to explore and categorise experiences within a broader thematic framework.

The Framework Analysis involved four stages: (a) the process of data familiarisation involved repeatedly reading the transcripts and listening to the audio recordings, which allowed for the identification of initial codes; (b) data were 'open coded' and a framework was developed and refined within the research team; (c) manual coding was performed in NVivo (R14.23.1, QSR International) to index the data according to the framework. A second analyst (S.M.) independently double-coded 25% of the data (2/8 transcripts) to assess the quality of the coding and to enhance the reliability and validity of the data analysis. Any differences in the coding were resolved by consensus and the framework was altered accordingly. Then the framework was applied to all remaining transcripts. To ensure consistency in the coding and reduce possible bias, the second analyst (S.M.) checked 20% of the coding. Data saturation was reached when no new codes were emerging from the analysis. The initial framework was developed from the broader discussions and from this framework we identified common codes which were relevant to the research question to develop into themes. (d) In the charting stage, the coded data were arranged in a system to organise the data into relevant themes. (e) Theme development involved mapping and interpreting codes, identifying relationships between them, and systematically grouping them into sub-themes. These sub-themes were then further refined and categorised into overarching themes that captured the key patterns and insights from the data. All stages of the data analysis, framework and theme development were reviewed by an interdisciplinary research team, combining expertise from Cognitive Psychology and Qualitative Methods. Discussions within the research team were held to inform the process. Whilst this analysis focused on investigating the experiences of cognitive symptoms, we have also reported on the broader perceived 'needs' of people with LC in our previous publication of this study [26].

Patient and public involvement

Participants were invited to review the manuscript prior to submission to ensure the findings accurately represented their views and experiences.

RESULTS

 Participants were aged 19 to 76 years (M = 43.6 years, SD = 14.7; 17 females and 8 males). Participants were eligible if they had self-reported LC and lived in the UK. 92% (22/24) of participants had a clinical diagnosis of LC. The duration of symptoms experienced varied between 4 months to 2.8 years (M = 77.96 weeks, SD = 32.58). Twenty one participants had British nationality, 1 French, 1 Finnish and 1 Chinese.

Quantitative results

Results from the Post Long COVID-19 Questionnaire showed that participants experienced wide ranging symptoms following the development of LC, see Figure 1 and Figure 2. The most severe symptoms, with the greatest change after disease contraction, were decreases in energy, mobility, breathing and mental ability.

In terms of cognition; 87.50% (21/24) of participants reported that their ability to concentrate had worsened, 83.33% (20/24) reported that their short-term memory had declined, 75.00% (18/24) reported that they or their family had identified a difference in the way they communicated. Participants reported a 10-fold increase in concern about their cognition following LC (M = 5.83, SEM = 0.61) compared to before LC (M = 0.54, SEM = 0.27).

Almost all participants reported that their illness and cognition affected their ability to work (95.65%; 22/23; 1 participant was retired). All participants (24/24) requested to be informed of future LC research opportunities showing clear motivation to advance understanding and treatment for persistent symptoms.

Qualitative results

Data from the focus group discussions were categorised into three interconnected themes, see Figure 3. Theme 1) Rich accounts of cognitive symptoms, theme 2) impact on physical function and psychological wellbeing; and theme 3) symptom management. Participants experienced various cognitive impairments (theme 1) which impacted daily functioning and psychological wellbeing (theme 2). Participants attempted to manage the symptoms and impact on their daily life (themes 1 & 2) using

 strategies (theme 3). Oftentimes these strategies (theme 3) were tedious to implement or ineffective, further exacerbating the impact on physical and psychological functioning (theme 2). See theme descriptions for further details.

Theme 1: Rich accounts of cognitive symptoms

The majority of participants (20/24) described experiences of cognitive symptoms associated with LC. The most commonly reported symptoms were difficulties with memory and language, followed by attention, executive function and reduced processing speed. Participants frequently used the term 'brain fog' to describe their symptoms.

Memory

Participants described experiences of memory deficits which were consistent with definitions of working memory, long term memory (declarative and non-declarative memory) and prospective memory. Participants were concerned about the consequences of these memory impairments on their safety. For example, Participant 1 was forgetting to take their medication and reported "*I could be overdosing and I've no idea*". Other participants were worried about the impact of their memory difficulties on their perceived image, as Participant 18 described "*it makes you look stupid*" after missing appointments. Participants described a need to review information multiple times before they could process, retain and remember it:

"I'll go back to the book and think I don't remember this bit at all and be going back a chapter... not necessarily reading it in detail, but scanning through and it will kind of prompt me." Participant 14.

Occasional lapses in memory lead to experiences of disorientation and confusion. Participant 23 described the experience as a "full blank moment" and as 'disconcerting'.

Language

Impairments in language affected word finding, reading comprehension and writing. Participant 14 described making errors in writing and proof-reading at work which they didn't do before, "*I would read it and think this is great letter and then actually there'd be, like, a word missing.*" Issues with communication included difficultly following conversations or abruptly deviating from the topic of conversation. A feeling of "disconnection in the brain", while trying to communicate, was described by participants:

"I'm often looking for words when I'm speaking and I think of a word, but I can't find it, like I know what it means and I know what I want to say, but it's like it's just disappeared from my brain." Participant 17.

Attention

Participants experienced impaired attention, particularly divided attention (multitasking) and maintaining selective/sustained attention, and the impact of this on daily life. Participant 6 described difficulty talking whilst driving and *"could* [only] *retrieve the information"* once *'stopped at the traffic lights'*. Participant 17 described the frustration of losing their attention, *"I used to be able to sit down and watch films and things. Now, I find myself sometimes flicking the TV over because I can't, like, concentrate on stuff."*

Executive functioning

Executive dysfunction included difficulties with planning, decision-making and mental flexibility. For example, Participant 11 found difficulty following "a logical train of thought" and "getting things done around the house". The term "decision fatigue" was used by participants 12 and 13 to describe the exhaustion associated making a choice out of many options, such as selecting a programme on the TV.

Processing speed

Accounts of cognitive dysfunction included descriptions of the delay involved in completing tasks or retrieving information, suggesting participants were experiencing reduced processing speed.

"When I'm doing patients notes have to go over them like up to 10 times maybe, word by word to make sure I've put the correct word. People used to comment how quick I could, like, type and do the notes. Now it's taking me a lot longer". Participant 15.

Contributing factors

Fatigue, poor sleep and headaches were reported to exacerbate cognitive symptoms. Participant 4 explained that tiredness makes their brain feel *"jumbled*". Other participants described continuous cognitive symptoms, independent of other factors.

Theme 2: Impact on physical function and psychological wellbeing

Over half of participants (14/24) experienced negative impacts on their daily lives including employment, physical functioning and psychological wellbeing, as a direct result of their cognitive symptoms. Of these, ten participants reported a decline in their perceived work performance or changes in employment or education due to issues with their memory or concentration. This included being unable to return to their pre-COVID-19 careers, reducing working hours or adapting roles due to the self-perceived inability to uphold the cognitive demands and high responsibility of their previous roles. Participants were concerned about when or if their cognitive abilities would return and this was associated with a loss of professional identity:

"Throughout my career has involved writing and also proofreading and copy editing. And I had to give that up for two years, and I was so scared that my ability would never come back... I've always seen myself as someone who works with words". Participant 9.

"I've actually changed jobs at work, changing jobs on Monday, because the job I do requires a lot of concentration and I was just making so many mistakes. I've kind of taken a sideways step". Participant 24.

More than half of participants (14/24) described the challenges of carrying out activities of daily living including cooking, driving and shopping, that they were previously proficient in or enjoyed:

"The odd time I have actually forgotten to turn the cooker off as well. So I'm not, like, keen to cook a lot these days either, which I've always enjoyed cooking." Participant

17.

Ten participants experienced psychological impacts as a result of their cognitive symptoms. Cognitive impairment contributed to low mood, stress and anxiety. Participant 16 described the experience of losing their memory abilities as "stressful" and feeling "so down". Participants reported concern about their cognitive health including experiencing a sense of accelerated ageing, and anxiety over whether these cognitive changes might signal the onset of age-related neurodegenerative diseases.

"A few weeks into having Covid I felt like I'd aged 20 years and lost 20 IQ points....It makes you worried that there are other things, I think, oh my God have I actually got Alzheimer's, you know? Because I could tick most of the boxes." Participant 12.

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Theme 3: Symptom management

Half of participants (12/24) reported strategies they had tried to manage their cognitive symptoms, with variable success. Participants described simplifying daily life by reducing demands or decision-making:

"I find decisions tiring... So I've just eliminated that, I just wear the same coloured clothes every day [and] cook the same meals" Participant 13.

Strategies for recording information and setting reminders were reported, including making to-do lists, setting alarms to take medication or remember dates and appointments. The effectiveness of these strategies for improving cognitive function was varied, with at least five participants reporting continued difficulties with memory and forgetfulness despite using strategies. Participant 19 attempted to use pill boxes and phone notifications to reminder them to take their medication, however they explained *"I would still forget… I'll see the notification, and I think right, I'll do that in a minute and then I'll get distracted and I'll forget about it"*.

Regular rest and breaks were required, particularly throughout the working day. Participant 4 took regular breaks whilst working from home, and explained "*if I didn't do that, I won't be able to continue with my day*".

Several participants (7/24) described feelings of frustration and tediousness over the increased time or effort required implement these strategies in order to complete tasks:

"I just have to stop organising [meetings] any time after about 2 o'clock because I then I can't find the words that I'm trying to say and it sounds like ridiculous... That's really, really frustrating" Participant 23.

One participant attempted to regain their pre-Covid-19 cognitive function by challenging themselves in progressive increments, with some success:

"I struggled to even just reading a page of a book... I've progressed again over kind over the last few months, really just by setting myself the kind of challenge or time to just read one chapter or a few pages of the book every day". Participant 14.

DISCUSSION

This mixed-methods study aimed to explore the extent and lived experiences of cognitive symptoms in LC. The majority of participants in this study reported a decline in cognitive ability and concern about this change. Cognitive symptoms were among

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the most common symptoms reported alongside low energy, immobility and breathlessness. The experiences of subjective cognitive impairments included difficulties with memory, attention, language, executive function, and processing speed. Cognitive symptoms had profound negative effects on participants' ability to work, complete activities of daily living, their psychological wellbeing and self-image, in some cases for >2 years after the initial infection. Participants attempted to manage their cognitive symptoms using strategies to reduce decision making and mental load, facilitate memory and improve energy levels. However, the strategies were described as tedious and frustrating to implement, with mixed effectiveness. By combining quantitative and qualitative methods, this study found that cognitive symptoms are among the most prevalent symptoms in LC with considerable negative impacts on the wellbeing, functioning and daily lives of people with LC.

The findings of this study are consistent with previous research on both objective measures of cognitive impairment [5, 6] and the lived experiences of LC [17, 18]. Our findings strongly align with those of Callan et al. [18], showing the experiences of subjective cognitive impairments, altered self-identity and the challenges of managing ongoing symptoms. Similar to previous studies, we found cognitive impairment in LC impacted occupational status, including reducing working hours, changing job roles and loss of pre-COVID-19 employment [27]. Additionally, participants reported difficulties in completing activities of daily living, which reflects previous research highlighting the functional limitations caused by cognitive decline in LC [28]. High rates of mood disorders, such as anxiety and depression, were also prevalent among participants, reinforcing existing evidence that emotional and mental health challenges often accompany cognitive dysfunction in LC [29]. Furthermore, many participants described living an altered lifestyle, consistent with prior findings that LC can affect individuals' ability to engage in social, professional, and personal activities [30]. These results contribute the growing literature documenting the far-reaching impact of ongoing cognitive impairment in LC. The novel findings of this study are the interactions found between the experiences of cognitive impairment, physical and psychological functioning and self-management of cognitive symptoms. Poor memory, attention and executive functioning affected many areas of daily functioning and contributed to a loss of self-worth and identity and reduced psychological wellbeing. Strategies used for self-management of cognitive symptoms involved living an altered

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lifestyle by reducing daily demands, activities, exercise and decision making and implementing 'reminders' for tasks and regular rest, most of which added further distraction and frustration to daily life. This may reflect a vicious cycle of withdrawal from daily life, low mood and poor self-coping strategies that essentially exacerbates cognitive impairment.

Building on the findings of this study and prior research, we propose a new framework to conceptualise the factors contributing to cognitive impairment in LC, which appear to reflect an interacting symptom network [31]. The Long-COVID Interacting Network of factors affecting Cognitive Symptoms (LINCS) framework integrates the findings of this study and previous research showing the neural, lifestyle and individual factors shaping actual and self-perceived cognitive dysfunction in LC (see figure 4). The possible interplay between psychological, physical, and social factors, and the contribution of this to ongoing cognitive dysfunction following COVID-19, has previously been suggested by Callan et al. [18]. The need for this framework stems from the lack of evidence-based recommendations for clinicians regarding LC treatment [32]. Furthermore, patients with LC have reported the challenging experiences of accessing primary care such as receiving inconsistent advice from healthcare professionals, difficulty accessing and navigating services and a lack of treatment options [33, 34]. This model provides a comprehensive framework for understanding the complexity of cognitive dysfunction in LC patients, which emphasises the multifaceted nature of the condition and may inform a more holistic approach to treatment by considering biological mechanisms, internal and external factors. The aim of presenting the LINCS framework is to guide future research and clinical practice towards more personalised, integrated and multi-disciplinary care strategies for managing cognitive symptoms in LC, in line with previously published recommendations [33-35].

The LINCS framework also highlights neuroinflammatory processes and brain structural changes as primary biological drivers of cognitive impairment in LC. Previous reviews have reported on the current understanding of the neurobiology of LC [12, 36]. The COVID-19 infection triggers an inflammatory response in the respiratory system, which can spread to the central nervous system (CNS). Within the CNS, cytokines, chemokines, and activated microglial cells disrupt various neural cell types. This disruption interferes with the maintenance of myelin, impairs

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neuroplasticity, and hinders hippocampal neurogenesis. It can also initiate neurotoxic responses in astrocytes, leading to a breakdown in neural circuits and cognitive impairment [13]. COVID-19 infection can trigger anti-neural autoantibodies and T cells to provoke an autoimmune response, potentially leading to autoimmune encephalitis and contributing to continued neural damage [37]. In more severe cases of COVID-19, nervous system injury can also result from hypoxia, further aggravating neuroinflammation [14, 15]. Structural changes to the brain following COVID-19 infection include reduced global brain size and grey matter thickness in the orbitofrontal cortex and parahippocampal gyrus [9]. Several studies have highlighted the risks of developing abnormal tau pathology and cytotoxic amyloid protein aggregation in LC [10, 11], which may indicate a future trajectory toward neurodegeneration.

Lifestyle factors also play a significant role in the cognitive impairment associated with LC. In a previous publication, we reported on the experiences and needs of individuals with LC and found that many participants experienced symptoms that significantly impacted their daily lives [26]. Participants commonly reported challenges such as impaired physical mobility, cognitive dysfunction, and social withdrawal. These difficulties often led to changes in employment, including reduced working hours, adjusting their role or being unable to return to work. Additionally, social withdrawal was frequently driven by a lack of understanding and support from family, friends, and society, which contributed to feelings of shame and isolation. These changes in an individual's engagement with their surroundings may reduce mental stimulation, further accelerating cognitive decline. Notably, both physical and social withdrawal, along with increased sedentary behaviour, are well-documented risk factors for the development of Dementia [38, 39], highlighting the need to address these lifestyle factors when considering interventions for cognitive symptoms in LC patients.

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The findings of the current study, in line with existing research, enhance our understanding of the individual factors that exacerbate cognitive symptoms in LC. Participants reported their efforts to recover by implementing coping strategies, and managing fatigue and energy levels, whilst also dealing with the high prevalence of mood disorders. Prior evidence highlights the interconnectedness of these factors, suggesting they may collectively contribute to cognitive impairment in LC. For instance, fatigue and depression have been shown to impair cognition in conditions

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such as chronic fatigue syndrome and multiple sclerosis [40, 41], and major depressive disorder (MDD) is associated with reduced brain grey matter volume [42]. Participants also described withdrawing from activities of daily living (ADL) as a way to manage symptoms. However, reduced cognitive, physical, and social engagement, along with prolonged absence from work, have been associated with accelerated cognitive decline in mid to later adulthood [43, 44, 45]. These findings emphasise the importance of addressing both the physical and psychological components in managing cognitive dysfunction in LC.

Given the evidence of accelerated cognitive ageing and dementia risk in LC [9, 10, 16], this clinical population of an estimated 2 million people in the UK [2] may be the next generation at risk of developing age-related neurodegenerative diseases, fuelling a future epidemic of dementia in the UK. Currently there is no approved treatment for LC [46], and the findings of this study highlight the vital need for an intervention to tackle the cognitive symptoms in LC, with aims to improve quality of life and reduce possible dementia risk. A recent scoping review evaluated treatments for cognitive impairment in LC and provided key recommendations for primary care management [32]. The authors emphasised that a multidisciplinary, patient-centred approach is appropriate for addressing the cognitive symptoms. One of the main recommendations was for patients to adopt a healthy lifestyle, incorporating a balanced diet including key vitamins, micronutrients and probiotics, sufficient sleep, stress-reduction techniques, and appropriate physical activity. The World Health Organization selfmanagement booklet on LC provides a comprehensive strategy for returning to physical activity using a cautious pacing approach to mitigate overexertion [35]. This approach contrasts with graded exercise therapy (GET), which has been shown to potentially cause harm and worsen post-exertional malaise (PEM) in various chronic health conditions, including LC [33]. Behavioural interventions were also identified, including cognitive training, mind-body interventions, music therapy and meditation [32]. Overall this scoping review underscored the importance of tailoring care plans to each individual, combining lifestyle modifications with medical and psychological interventions to create a comprehensive and adaptive treatment strategy for cognitive impairment [32]. These recommendations align with the LINCS framework by advocating for a multidisciplinary and individualised approach to addressing the various factors which appear to exacerbate cognitive symptoms in LC. LC is a

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relatively new condition, and as such, the underlying pathology of cognitive impairment remains poorly understood and there is a current lack of high-quality evidence supporting targeted interventions for managing cognitive deficits in LC patients [32]. Future research should prioritize identifying the precise mechanisms driving cognitive impairment in LC, including neuroinflammatory processes, neural dysregulation, and neurovascular dysfunction [36]. Additionally, there is a need for large-scale, highquality, longitudinal studies to evaluate the effectiveness of both pharmacological and non-pharmacological interventions, such as cognitive rehabilitation and lifestyle modifications, in improving cognitive function. Developing standardised assessment tools and outcome measures will also be crucial to ensure consistency across studies and provide clearer guidance for clinical practice [32].

The term 'brain fog' was used by some participants in this study to describe their cognitive symptoms, however previous evidence suggests the term lacks specificity and may not capture the severity of cognitive symptoms experienced in LC [18]. The term 'fog' implies a perceptual deficit or 'clouding' of cognitive processes, whereas in this study, participants reported reduced processing speed, increased cognitive effort and a feeling of disconnection in the brain. Without the development of appropriate terminology to define these symptoms and lack of recognition of the specific impairments to cognitive functioning, there is a barrier for medical diagnosis and the development of targeted cognitive interventions. An alternative code name has been proposed to described the accelerated process of cognitive decline in pre-existing dementia following COVID-19, termed FADE-IN-MEMORY i.e. Fatigue, decreased Fluency, Attention deficit, Depression, Executive dysfunction, slowed INformation processing speed, and subcortical MEMORY impairment [47]. The findings of this study show that FADE-IN-MEMORY might also be an appropriate term to describe the experience of cognitive symptoms in LC.

The strengths of this study include the rigorous and well-established methods to analyse the focus group data. The Framework Analysis [25] is data analysis technique that provides a structured yet flexible approach to processing qualitative data. By organising, coding, and conducting thematic analysis in a systematic manner, this method allows for efficient analysis of qualitative research while strengthening the credibility of the research process [48]. The Framework Analysis is increasing used in the analysis of qualitative data in multi-disciplinary health research [48]. The use of

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quantitative data collection to supplement the qualitative responses in this study, allowed us to quantify the self-perceived change in cognitive abilities following LC, and compare the severity of cognitive symptoms with other symptoms. However, the questionnaire rating scales were arbitrary, and the self-report nature of the questionnaire may not reflect an objective measure of cognitive functioning. Having said that, the extent of memory deficits following COVID-19 infection has been found to increase with the severity of self-reported ongoing symptoms [7], demonstrating the link between objective and subjective cognitive measures. One possibility for related future research would be to administer a brief test of global cognitive function, such as the Montreal Cognitive Assessment (MoCA) [49], to measure participants' individual global cognitive function on the day of the focus group discussions. However, tests of global cognitive function primarily measure working memory, therefore may not capture the impairments in other cognitive domains participants reported in this study. There are also concerns that global screening tools, developed for identifying dementia and mild cognitive impairment, may lack sensitivity in reliability detecting cognitive deficits in LC [50]. Furthermore, in this study, the self-report nature of the questionnaire complimented the qualitative data in which the overall aim was to investigate the lived experience of cognitive symptoms from the participants' perspective, rather than to obtain an objective measurement of cognitive functioning. This study may be limited by the biased sample of mostly female and middle-aged participants, which prevented comparison of possible age and gender differences in the experience of LC symptoms.

This mixed-methods study found that cognitive dysfunction was commonly reported by participants and had a significant impact on daily life and overall functioning. Participants were concerned about their cognitive decline and the limited options available for symptom management and treatment. There is a clear need for interventions that address the complex, multifactorial nature of cognitive impairment in LC. Without such targeted strategies, individuals with LC face an increased risk of accelerated cognitive aging and the potential onset of dementia. This study introduced the LINCS framework, designed to provide a structured approach for clinicians to assess and manage the array of factors contributing to cognitive dysfunction in LC. By integrating multiple dimensions of cognitive health, the LINCS framework offers a valuable tool for both clinical practice and future research, which

could be used to inform the development of interventions that are tailored to the needs of LC patients. Future high-quality, large-scale intervention studies are essential to identify effective treatments for cognitive dysfunction in individuals affected by LC.

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Contributors

Melanie Rose Burke, Manoj Sivan and Rumana Chowdhury gained funding for the study. Amy Miller and Melanie Rose Burke conceived the idea and conducted the study. Ning Song informed the methods for qualitative data analysis. Amy Miller conducted the transcription, data analysis and wrote the first draft of the manuscript. All authors contributed towards the refinement of the manuscript. Amy Miller is the guarantor. This article reflects the views of the authors only, not their institutions or the study funders.

Data availability statement

Data are available on reasonable request.

Competing Interests

The authors disclose no competing interests.

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FIGURE LEGENDS

Figure 1. Participant self-reported ratings of symptom severity across health symptoms. High scores indicate greater severity of symptoms. [0] Normal [1] Mild [2] Moderate, and [3] Severe. Error bars show standard error (SEM). N = 24.

Figure 2. Participant self-reported symptom change before and after contracting Long Covid (LC). High scores indicate greater symptom severity. Error bars show SEM. N = 24.

Figure 3. A map of the relationships between themes.

Figure 4. A conceptual framework of the Long-COVID Interacting Network of factors affecting Cognitive Symptoms (LINCS).



Figure 1. Participant self-reported ratings of symptom severity across health symptoms. High scores indicate greater severity of symptoms. (0) Normal, (1) Mild, (2) Moderate, and (3) Severe. Error bars show standard error (SEM). N = 24.

130x90mm (300 x 300 DPI)





Figure 2. Participant self-reported symptom change before and after contracting Long Covid (LC). High scores indicate greater symptom severity. Error bars show SEM. N = 24.

130x90mm (300 x 300 DPI)



Figure 3. A map of the relationships between themes.

146x90mm (300 x 300 DPI)

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107x90mm (300 x 300 DPI)

	Part	icinant Deta	ils			
Name:		D	ate of Birth:			
Email Address:						
Gender:			Nationality:			
Can we contact you in the future for taking part in ar intervention study on people with Long Covid?			n [YES / NO]			
Do you have an official Diagnosis	of Long Cov	/id? [YE	S / NO]			
How long have you had Long Covi	d symptom	ıs? [Weeks]			
	Genera	al Questionn	aire			
	NORMAL	. MILD	MODERATE	SEVERE		
	Normal Not normal but can do everything		Prootblace on	Stong ma daing com		
Is your Breathing back to normal [NB: Circle the answer that best describes you]	? Normal	Not normal but can do everything	hills/stairs	things, breathless a rest/mild activity.		
Is your Breathing back to normal [NB: Circle the answer that best describes you] On a scale of 0-10, with 0 being not breathless at all, and 10 bein extremely breathless, how breathless are you:	? Normal 	Not normal but can do everything ore COVID	hills/stairs	things, breathless a rest/mild activity.		
Is your Breathing back to normal [NB: Circle the answer that best describes you] On a scale of 0-10, with 0 being not breathless at all, and 10 bein extremely breathless, how breathless are you: Is your Mobility/Activity levels back to normal?	? Normal Bef	Not normal but can do everything ore COVID Nearly back to normal	Having to move more slowly, but doing everything	things, breathless a rest/mild activity. ter COVID Struggling with som activities, barely getting around.		
Is your Breathing back to normal [NB: Circle the answer that best describes you] On a scale of 0-10, with 0 being not breathless at all, and 10 bein extremely breathless, how breathless are you: Is your Mobility/Activity levels back to normal? On a scale of 0-10, with 0 being very active, and 10 being completely inactive, how active are you:	Pormal Bef	Not normal but can do everything ore COVID Nearly back to normal ore COVID	Having to move more slowly, but doing everything	stops me doing som things, breathless a rest/mild activity. ter COVID Struggling with som activities, barely getting around. ter COVID		

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On a scale of 0-10, with 0 being full of energy, and 10 being constantly tired, how fatigued are you:	Before COVID		Aft	After COVID	
Is your Mood back to normal?	Normal	I have brief occasional moments of low mood.	l suffer most days with low mood or anxiety.	I struggle to think and remember, or I feel hopeless and suicidal.	
On a scale of 0-10, with 0 being not atall depressed, and 10 being very depressed/suicidal, how would you rate your mood:	Before COVID		After COVID		
On a scale of 0-10, with 0 being not atall anxious, and 10 being anxious all the time, how would you rate your anxiety:	Be	fore COVID	Aft	er COVID	
Are your Mental ability levels back to normal?	Normal	I have the od lapse in concentration and memory	d My brain is working much n slower than it . used to.	My mental capacity is significantly affecting my day-to-day functioning.	
On a scale of 0-10, with 0 very alert, and 10 being very limited on thinking and memory, how would you rate your mental capacity:	Be	fore COVID	Aft	er COVID	
Is your overall health (physical N and mental) back to normal?	lormal m wi	I have only inor concerns ith my health.	My physical and/or mental health is worse than it was, but is manageable.	My physical and mental health is a huge concern, and I am struggling to function independently.	
	Further	Cognitive Qu	estions		
Cognition is our ability to think, plan and process things. Ha CONCENTRATION worsened since	rememb as your your illn	er, ess?	YES	NO	

Has your SHORT-TERM MEMORY worsened since your illness?	YES	NO
On a scale of 0-10, with 0 being not atall concerned, and 10 very concerned, how would you rate your concern about your cognition:	Before COVID	After COVID
Have you or your family identified a difference in the way you COMMUNICATE putting thoughts into words/difficulty reading/communicating?	YES	NO
Has your illness/cognition affected your ability to work?	YES	NO
On a scale of 0-10, with 0 being not atall affected my work, and 10 can no longer work, how would you rate your working ability:	Before COVID	After COVID

THANK-YOU FOR YOUR TIME IN COMPLETEING THIS QUIZ !!