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Short Communication

Prevalence and co-occurrence of cognitive impairment in children and young people up to 12-months post infection with SARS-CoV-2 (Omicron variant)

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ABSTRACT

Background: Cognitive impairment is often reported after SARS-CoV-2 infection, yet evidence gaps remain. We aimed to (i) report the prevalence and characteristics of children and young people (CYP) reporting "brain fog" (i.e., cognitive impairment) 12-months post PCR-proven SARS-CoV-2 infection and determine whether differences by infection status exist and (ii) explore the prevalence of CYP experiencing cognitive impairment over a 12-month period post-infection and investigate the relationship between cognitive impairment and poor mental health and well-being, mental fatigue and sleep problems.

Methods: The Omicron CLoCk sub-study, set up in January 2022, collected data on first-time PCR-test-positive and PCR-proven reinfected CYP at time of testing and at 3-, 6- and 12-months post-testing. We describe the prevalence of cognitive impairment at 12-months, indicating when it was first reported. We characterise CYP experiencing cognitive impairment and use chi-squared tests to determine whether cognitive impairment prevalence varied by infection status. We explore the relationship between cognitive impairment and poor mental health and well-being, mental fatigue and trouble sleeping using validated scales. We examine associations at 3-, 6- and 12-months post-testing by infection status using Mann-Whitney U and chi-square tests.

Results: At 12-months post-testing, 7.0 % (24/345) of first-positives and 7.5 % (27/360) of reinfected CYP experienced cognitive impairment with no difference between infection-status groups ($p = 0.78$). The majority of these CYP experienced cognitive impairment for the first time at either time of testing or 3-months post-test (no difference between the infection-status groups; $p = 0.60$). 70.8 % of first-positives experiencing cognitive impairment at 12-months, were 15-to-17-years-old as were 33.3 % of reinfected CYP experiencing cognitive impairment ($p < 0.01$). Consistently at all time points post-testing, CYP experiencing cognitive impairment were more likely to score higher on all Strengths and Difficulties Questionnaire subscales, higher on the Chalder Fatigue sub-scale for mental fatigue, lower on the Short Warwick-Edinburgh Mental Wellbeing Scale and report more trouble sleeping.

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Conclusions: CYP have a fluctuating experience of cognitive impairment by 12-months post SARS-CoV-2-infection. Cognitive impairment is consistently correlated with poorer sleep, behavioural and emotional functioning over a 12-month period. Clinicians should be aware of cognitive impairment post-infection and its co-occurring nature with poorer sleep, behavioural and mental health symptoms.

1. Introduction

Post-COVID condition (PCC) is a difficult but important area of research (Pan & Pareek, 2023). PCC is highly prevalent and can have debilitating consequences for individuals suffering from it. For example, approximately 45 % of those infected with COVID-19 experience symptoms 4-months post-SARS-CoV-2 infection (O'Mahoney et al., 2023). In particular, in children and young people (CYP), 13·3% of 12–17-year-olds with prior symptomatic infection had persistent symptoms for 3-months or more following COVID-19, with one in nine reporting a large impact on their ability to carry out day-to-day activities (Atchison et al. (2023)).

One particular class of PCC-associated symptoms that has attracted the attention of neuropsychologists is cognitive impairment, colloquially referred to as 'brain fog'. While the term 'brain fog' lacks a universally agreed definition (Sia et al., 2023), it is commonly used by the general population to refer to a range of symptoms including confusion, poor concentration, slow mental processing, forgetfulness and lack of mental clarity as well as a range of cognitive impairments, such as difficulties in executive function, attention and speed of information processing(McWhirter et al., 2023; Ocon, 2013). Thus, 'brain fog' is characterised as deficits in various cognitive abilities involved in reasoning and memory and encompasses symptoms such as confusion, disorientation, forgetfulness and cognitive fatigue(Jennings et al., 2022; Nouraeinejad, 2022). In adults, cognitive impairment has been reported several months after SARS-CoV-2 infection, with reported deficits in verbal and executive function, attention, and memory(Becker et al. (2021); Graham et al., 2021; Hampshire et al., 2021; Jennings et al., 2022; Lamontagne et al., 2021; Miskowiak et al., 2021). Moreover, recent *meta*-analyses found the prevalence of cognitive symptoms in adults suffering from PCC to vary between 22–32 %(Ceban et al. (2022); Premraj et al., 2022). There is less research regarding the prevalence, duration, and characteristics of cognitive impairment in CYP suffering from PCC. Our previous *meta*-analysis on PCC in CYP found a prevalence estimate for cognitive symptoms of 26 %(Behnood et al. (2022)), while Zheng and colleagues (2023) reported a prevalence of neurological symptoms and concentration difficulties of 13.5 % and 11.4 %, respectively(Zheng et al. (2023)). Nonetheless, questions remain regarding the reporting of cognitive impairment over a long time-period post SARS-CoV-2 infection. Given that concentration difficulties are associated with anxiety and depression(APA. (2013)), it is also important to examine whether cognitive impairment co-occurs with poor mental health and well-being, mental fatigue and/or sleep problems.

Given the above identified literature gaps, we have two overarching aims in this short report. First, we aim to describe the prevalence and characteristics of CYP experiencing cognitive impairment at 12-months post-infection and to determine whether there are any differences by infection status (i.e., first-time PCR-test-positives vs PCR-proven reinfected). We hypothesise, based on previous findings(Stephenson et al., 2023), that reinfected CYP are more likely to experience cognitive impairment compared to first-positives. Second, in exploratory analyses, we explore the prevalence of CYP experiencing cognitive impairment at specific time points over the 12-month period after infection and investigate the relationship between cognitive impairment and poor mental health and well-being, psychological fatigue and sleep problems.

2. Method

The methodology of the CLoCk Omicron study has been previously described(Pinto Pereira et al., 2023). Briefly, 15,045 CYP who had a SARS-CoV-2 PCR test in January 2022 (of which 5,135 were first-time PCR positives and 4,507 were PCR-proven reinfected) were invited by mail to participate. First-positives (i.e., CYP who PCR tested positive for the first time during the period when the Omicron variant dominated) were matched, at study invitation, to PCR test-negatives by age (at last birthday), sex and geographical area (based on lower super output area – which is made up of between 400 and 1,200 households and have a usually resident population between 1,000 and 3,000 persons) using the national SARS-CoV-2 testing database held at the UK Health Security Agency (UKHSA). All reinfected CYP (i.e., CYP who PCR-tested positive both before and during Omicron dominance) were invited. Consenting CYP filled in an online questionnaire shortly after testing (i.e., at 0-months post-testing) and subsequently at 3-, 6- and 12-months post-testing. The questionnaires included demographics, elements of the International Severe Acute Respiratory and Emerging Infection Consortium questionnaire, 28 symptoms in the form of check boxes, including '"brain fog' (confusion/memory loss)" and "trouble sleeping". The questionnaire also included validated scales: the Strengths and Difficulty Questionnaire (SDQ)(Goodman (2001)), the Chalder Fatigue Scale (CFS)(Chalder et al., 1993), and the Short Warwick-Edinburgh Mental Wellbeing Scale (SWEMWBS)(Tennant et al. (2007)).

By March 2022, almost 82–99 % of 5-to-18-year-olds in the UK had SARS-CoV-2 antibodies(ONS. (2022)). Hence, it was near impossible to follow-up a comparator group of truly SARS-CoV-2 negative CYP. Thus, we focus here on examining the CYP who tested positive for the first time, and CYP who were reinfected, when the Omicron variant was prevalent. Hence, we analysed data from 345 first-positives and 360 reinfected CYP who responded to all questionnaires (at 0-, 3-, 6- and 12-months post-infection). We have previously shown that these participants are broadly similar to the target population, albeit with some differences (e.g., by region and levels of deprivation)(Pinto Pereira et al., 2024).

We report the prevalence of cognitive impairment at 12-months post-infection, indicating when it was first experienced. We also characterise (via age, sex, ethnicity, and deprivation) the CYP experiencing cognitive impairment. We use chi-squared tests to determine whether the prevalence of cognitive impairment varied by infection status. To examine whether cognitive impairment co-occurs with poor mental health and well-being, mental fatigue and/or sleep problems we examine associations at 3-, 6- and 12-months post-testing by infection status, between cognitive impairment and emotional and behavioural difficulties (captured by the SDQ)(Goodman (2001)), poor well-being (captured by the SWEMWBS)(Tennant et al. (2007)), mental fatigue (captured by the mental fatigue sub-scale of the CFS)(Chalder et al., 1993) and trouble sleeping (reported by a binary response). We used Mann-Whitney U tests and (for trouble sleeping only) a chi-square test.

3. Results

At 12-months post-testing, 7.0 % (24/345) of first-positives and 7.5 % (27/360) of reinfected CYP experienced cognitive impairment (Table 1). Contrary to our original hypothesis, there was no evidence of difference between the infection-status groups ($p = 0.78$). The majority (62.7 %; 32/51) of these CYP experienced cognitive impairment for the first time at either time of testing or 3-months post-test, with no statistical difference between the infection-status groups ($p = 0.60$). There was a higher prevalence of females and white ethnicity in both infection-status groups reporting cognitive impairment at 12-months. Strikingly,

Table 1
Prevalence* and characteristics of first-positive and reinfected CYP reporting cognitive impairment at 12-months post-testing (N (%)).

	First-positives ($n = 24$)	Reinfected ($n = 27$)	p-value**
Prevalence	6.96 %	7.50 %	0.78
Time cognitive impairment first reported (post PCR-test)			0.60
0-months	4 (16.67)	9 (33.33)	
3-months	10 (41.67)	9 (33.33)	
6-months	2 (8.33)	2 (7.41)	
12-months	8 (33.33)	7 (25.93)	
Age at infection (years)			<0.01
11–14	7 (29.17)	18 (66.67)	
15–17	17 (70.83)	9 (33.33)	
Sex			0.51
Female	18 (75)	18 (66.67)	
Male	6 (25)	9 (33.33)	
Ethnicity			0.56
White	19 (79.17)	18 (66.67)	
Asian or Asian British	4 (16.67)	5 (18.52)	
Black, African or Caribbean	0 (0)	2 (7.41)	
Mixed	1 (4.17)	1 (3.70)	
Other	0 (0)	1 (3.70)	
Index of Multiple Deprivation quintile			0.40
1 (most deprived)	4 (16.67)	5 (18.52)	
2	2 (8.33)	8 (29.63)	
3	8 (33.33)	6 (22.22)	
4	5 (20.83)	4 (14.81)	
5 (least deprived)	5 (20.83)	4 (14.81)	

*there were 345 first-positive and 360 reinfected CYP in the analytical sample
**p-value from chi-squared test of association

for first-positives, most CYP (70.8 %) who were experiencing cognitive impairment at 12-months, were 15–17 years old. While for reinfected, most CYP (66.7 %) who were experiencing cognitive impairment at 12-months, were 11–14 year olds ($p < 0.01$).

Consistently at all time points post-testing (i.e., at 3-, 6- and 12-months), those who experienced cognitive impairment (regardless of infection status) were more likely to score higher on all SDQ subscales, higher on the mental fatigue sub-scale, lower on the SWEMBS and report more trouble sleeping (Table 2). A higher SDQ score indicates more problems; a higher fatigue score is more severe and a higher SWEMWBS score indicates better mental well-being. In contrast, those who did not experience cognitive impairment, had SDQ scores broadly in-line with normative data from 11-to-15-year-old British CYP pre-pandemic (i.e. mean (SD): hyperactivity = 3.8(2.2); emotional symptoms = 2.8 (2.1); peer problems = 1.5(1.4); conduct problems = 2.2(1.7))(Meltzer et al. (2003)). Likewise, the SWEMWBS score among those who did not experience cognitive impairment was similar to those reported pre-pandemic in 10-to-16-year-old Danish school children (mean = 23.33 (SD = 3.78))(Hauch et al. (2023)).

4. Discussion

We have three important findings in this short report. First, in line with our previous report (Pinto Pereira et al., 2023), 7–8 % of first-positive and reinfected CYP experienced cognitive impairment at 12-months post-infection. Importantly, only 2.4 % of included CYP experienced cognitive impairment consistently at 3-, 6- and 12-months suggesting that for most CYP who have this symptom, it is transient. Second, more females than males experienced cognitive impairment at 12-months post-testing. This is in line with our previous work on other symptoms such as fatigue and shortness of breath (Nugawela et al., 2022; Stephenson et al., 2022) and the literature more widely (Avittan and Kustovs (2023); Nouraeinejad, 2022). Notably however, for the older age group, a higher proportion of first-positives compared to reinfected CYP experienced cognitive impairment at 12-months. In contrast, for the younger age group, a higher proportion of reinfected CYP (compared to first-positives) experienced cognitive impairment at 12-months. Third, consistently at all time-points, CYP experiencing cognitive impairment had worse mental health, were more mentally fatigued, had poorer well-being and more trouble sleeping compared to those who did not experience cognitive impairment. Of course, these difficulties are inter-related, and it is likely that these factors influence each other.

These findings highlight that several (potentially distinct) behavioural (e.g., trouble sleeping) and mental health symptoms (e.g., poor well-being) co-occur with cognitive impairment. Corresponding treatments/interventions should thus be multi-disciplinary. Further research is required to elucidate the temporal nature of these associations. For

Table 2
Validated scales for mental health (SDQ), fatigue (CFS) and well-being (SWEMWBS) and trouble sleeping at 3-, 6- and 12-months post-testing by cognitive impairment and infection status (First-positives ($n = 345$), reinfected ($n = 360$); Mean (SD)).

	3-months post-testing				6-months post-testing				12-months post-testing			
	First-positives Cognitive impairment?		Reinfected		First-positives Cognitive impairment?		Reinfected		First-positives Cognitive impairment?		Reinfected	
	No ($n = 317$)	Yes ($n = 28$)	No ($n = 334$)	Yes ($n = 26$)	No ($n = 318$)	Yes ($n = 27$)	No ($n = 335$)	Yes ($n = 25$)	No ($n = 321$)	Yes ($n = 24$)	No ($n = 333$)	Yes ($n = 27$)
SDQ												
Hyperactivity	3.55 (2.54)	5.75 (2.58)***	3.56 (2.56)	6.23 (2.12)***	3.69 (2.59)	5.33 (2.51)**	3.61 (2.50)	6.12 (2.54)***	3.77 (2.64)	5.29 (2.65)**	3.80 (2.76)	5.67 (2.37)***
Emotional symptoms	3.31 (2.41)	6.89 (2.23)***	2.94 (2.40)	5.73 (2.25)***	3.46 (2.51)	5.85 (2.66)***	2.90 (2.36)	6.2 (2.48)***	3.45 (2.58)	6.21 (2.83)***	3.16 (2.42)	5.19 (2.70)***
Peer problems	2.19 (1.94)	3.54 (2.13)**	1.77 (1.75)	3.04 (2.36)**	2.16 (1.90)	3.67 (1.82)***	1.60 (1.60)	3.28 (2.07)***	2.38 (1.82)	3.75 (2.64)*	1.88 (1.93)	2.81 (2.04)**
Conduct problems	1.53 (1.57)	2.43 (1.97)**	1.69 (1.56)	2.27 (1.54)*	1.54 (1.58)	2.93 (2.20)***	1.69 (1.56)	2.56 (2.43)	1.55 (1.63)	2.79 (2.55)*	1.66 (1.68)	2.67 (2.02)**
CFS Mental Fatigue	4.49 (1.66)	7.43 (2.63)***	4.23 (1.65)	7.50 (2.37)***	4.49 (1.80)	6.96 (2.19)***	4.22 (1.66)	7.20 (2.40)***	4.50 (1.63)	7.25 (3.03)***	4.35 (1.59)	6.81 (2.97)***
SWEMWBS	21.79 (4.08)	17.99 (3.57)***	22.50 (4.18)	19.13 (3.00)***	21.91 (4.14)	19.01 (3.64)***	22.57 (4.18)	18.35 (3.66)***	21.89 (4.47)	18.65 (5.26)***	22.51 (4.61)	18.50 (3.78)***
Trouble sleeping (N(%))	75 (23.66 %)	18 (64.29 %)***	77 (23.05 %)	20 (76.92 %)***	76 (23.90 %)	19 (70.37 %)***	64 (19.10 %)	18 (72.00 %)***	78 (24.30 %)	17 (70.83 %)***	82 (24.62 %)	20 (74.07 %)***

SDQ = Strengths and Difficulties Questionnaire; CFS = Chalder Fatigue Scale; SWEMBS = Short Warwick-Edinburgh Mental Wellbeing Scale. A higher SDQ score indicates more problems; a higher fatigue (CFS) score is more severe and a higher SWEMWBS score indicates better mental well-being. Within infection-status, cognitive impairment group comparisons: *$p < .05$, **$p < .01$, ***$p < .001$ (Mann-Whitney U test or chi-square test (trouble sleeping)).

example, we do not yet know how much of the effect of SARS-CoV-2 infection on cognitive impairment is mediated by poor sleep routines. This is feasible because, for example, in adults with PCC, a review demonstrated the overall prevalence of sleep disturbance was 46 % (Chinvararak & Chalder, 2023). While contrasts with pre-pandemic norms are challenging for several reasons including a lack of comparable data, some observations are noteworthy. For example, we found that 12-months post-infection, 27.9 % of our sample reported 'trouble sleeping', while 21.1 % of pre-pandemic 13-to-15-year-olds reported trouble falling back asleep after nighttime awakening 'a good bit of the time'(Scott et al., 2019). Although the origins of cognitive dysfunction following SARS-CoV-2 infection has yet to be established, several hypotheses have been proposed that involve direct or indirect damage to the central nervous system by the virus, leading to chronic inflammation of brain tissues as well as neural injury via hypoxia or vascular dysfunction(Nouraeinejad, 2022). There is also an increasing literature highlighting increased brain injury after SARS-CoV-2 infection and abnormal brain imaging many months post-infection (Granholm, 2023). For example, 56 adult convalescent participants with neurological complications following COVID-19 showed elevated Glial Fibrillary Acidic Protein (a marker of astrocyte injury) and Neurofilament Light (a marker of axonal and dendritic injury) more than 6 weeks after their original infection (Michael et al., 2023). In 18 adults, longitudinal MRI data exploring brain structural changes of patients recovered from COVID-19 showed grey matter volume reduction persisted in the cerebellum, vermis, and right temporal lobe after two years (Du et al., 2023). Alternatively, the observed cognitive dysfunction could be, in part, due to indirect effects resulting from changes in CYP's daily life and routines during the pandemic. Deep phenotyping studies and neuroimaging of CYP might elucidate any underlying biological mechanisms. It should also be noted that pre-existing conditions could impact on reported cognitive impairment and emotional and behavioural difficulties. Relatedly, some subpopulations maybe more adversely affected e.g. CYP with central nervous system disorders/neurodevelopmental conditions and this warrants further exploration.

While our report is purely descriptive, a few findings are worth discussing. For example, that more females reported cognitive impairment compared to males is in line with the broader literature showing females are more affected than males by PCC(Nugawela et al., 2022). In contrast to previous observations demonstrating that on aggregate reinfected CYP have more symptoms(Stephenson et al., 2023), we did not find that reinfected CYP are more likely to experience cognitive impairment compared to first-positives. This suggests that heterogeneity in the prevalence of specific PCC symptoms warrants consideration.

We have previously acknowledged study limitations (Pinto Pereira et al., 2024). Specifically, our questionnaire comprised a single item, asking only about the presence/absence of 'brain fog' and thus we are unable to examine change in severity over time. Furthermore, our single-item question, provided only a brief explanation of "confusion/memory loss" and may not fully capture the complexity of cognitive impairment that has been shown in adults with 'brain fog' after SARS-CoV-2 infection (e.g., Jennings et al., 2022; Hampshire et al., 2024). This may also explain why we did not observe a dose effect relationship between viral infections (reinfection vs first-positives) and their downstream effects on the brain. An objective assessment of cognitive functioning would allow for a more nuanced understanding of the link between brain fog and everyday functioning as measured by questionnaires such as the SDQ. Importantly, we are uncertain that the concept of 'brain fog' existed pre-pandemic, or if it did what it was called, and the corresponding pre-pandemic prevalence. Similarly, we are unaware of pre-pandemic normative data on the mental fatigue sub-scale of the CFS. Other limitations include that our analytical sample is drawn from the population when Omicron was dominant. While we cannot say with certainty that results would be similar for other variants, evidence suggests that, regarding PCC, there is little difference between variant (Pinto Pereira et al., 2024).

To conclude, this short report draws attention to the experience of brain fog over 12-months post SARS-CoV-2-infection and to the correlation between self-reported brain fog and behavioural and emotional functioning in everyday life settings (assessed via validated scales e.g. SDQ, the mental fatigue sub-scale, SWEMBS and a single item on trouble sleeping). Considering the substantial burden that cognitive impairment can represent for CYP in crucial domains such as education, it is hoped that this short report will help increase awareness of the co-occurring nature of such impairments with poorer health in CYP infected with SARS-CoV-2.

CRediT authorship contribution statement

Paul Foret-Bruno: Conceptualization, Formal analysis, Writing – original draft. **Roz Shafran:** Conceptualization, Funding acquisition, Investigation, Project administration, Resources, Supervision, Writing – review & editing. **Terence Stephenson:** Conceptualization, Funding acquisition, Investigation, Methodology, Writing – review & editing. **Manjula D Nugawela:** Data curation, Project administration, Software. **Dennis Chan:** Investigation, Writing – review & editing. **Shamez Ladhani:** Resources, Writing – review & editing. **Kelsey McOwat:** Data curation, Resources, Writing – review & editing. **Anna Mensah:** Data curation, Project administration. **Ruth Simmons:** Data curation, Project administration. **Lana Fox Smith:** Project administration, Writing – review & editing. **Anaïs D'oelsnitz:** Project administration. **Laila Xu:** Project administration. **Emma Dalrymple:** Resources, Writing – review & editing. **Isobel Heyman:** Writing – review & editing. **Tamsin Ford:** Writing – review & editing. **Terry Segal:** Writing – review & editing. **Trudie Chalder:** Writing – review & editing. **Natalia Rojas:** Writing – review & editing. **Snehal M Pinto Pereira:** Data curation, Formal analysis, Methodology, Supervision, Writing – review & editing, Conceptualization.

Declaration of Competing Interest

Terence Stephenson is Chair of the Health Research Authority and therefore recused himself from the Research Ethics Application. Tamsin Ford's research group receives funds for research consultancy to Place2Be, a third sector organisation providing mental health training and interventions to schools. TC is part-funded by the National Institute for Health Research (NIHR) Biomedical Research Centre at South London and Maudsley NHS Foundation Trust, King's College London. TC is the author of several self-help books on chronic fatigue for which she has received royalties; has received ad hoc payments for workshops carried out in long-term conditions; is on the Expert Advisory Panel for Covid-19 Rapid Guidelines; has received travel expenses and accommodation costs of attending Conferences; is in receipt of grants from Guy's and St Thomas' Charity, NIHR and UKRI. The remaining authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available upon resonable request.

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