THE AMERICAN JOURNAL of MEDICINE®

Post-Traumatic Stress Disorder and Complex Post-Traumatic Stress Disorder in People with Long COVID, ME/CFS, and Controls

Nilihan E.M. Sanal-Hayes, PhD,[a,b] Lawrence D. Hayes, PhD,[b] Marie Mclaughlin, PhD,[b,c] Ethan C.J. Berry, BSc, (Hons),[b] Nicholas F. Sculthorpe, PhD[b]

[a]School of Health and Society, University of Salford, Salford, UK; [b]Sport and Physical Activity Research Institute, School of Health and Life Sciences, University of the West of Scotland, Glasgow, UK; [c]School of Sport, Exercise & Rehabilitation Sciences, University of Hull, Hull, UK.

ABSTRACT

BACKGROUND: Prevalences of post-traumatic stress disorder (PTSD) and complex post-traumatic stress disorder (CPTSD) have not previously been compared between individuals with long coronavirus disease (COVID) and individuals with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), and healthy age-matched controls. For these reasons, this study aimed to determine the prevalence of PTSD and CPTSD in individuals with long COVID (n = 21) and ME/CFS (n = 20) and age-matched controls (n = 20).

METHODS: A case-case-control approach was employed; participants completed the International Trauma Questionnaire, a self-report measure of the International Classification of Diseases of PTSD and CPTSD consisting of 18 items. Scores were calculated for each PTSD and Disturbances in Self-Organization (DSO) symptom cluster and summed to produce PTSD and DSO scores. PTSD was diagnosed if the criteria for PTSD were met but not DSO, and CPTSD was diagnosed if the criteria for PTSD and DSO were met. Moreover, each cluster of PTSD and DSO were compared among individuals with long COVID, ME/CFS, and healthy controls.

RESULTS: Individuals with long COVID (PTSD = 5%, CPTSD = 33%) had more prevalence of PTSD and CPTSD than individuals with ME/CFS (PTSD = 0%, CPTSD = 20%) and healthy controls (PTSD = 0%, CPTSD = 0%). PTSD and CPTSD prevalence was greater in individuals with long COVID and ME/CFS than controls. Individuals with long COVID had greater values controls for all PTSD values. Moreover, individuals with long COVID had greater values than controls for all DSO values. Individuals with ME/CFS had greater values than controls for all DSO values. Both long COVID and ME/CFS groups differed in overall symptom scores compared with controls.

CONCLUSION: Findings of this study demonstrated that individuals with long COVID generally had more cases of PTSD and CPTSD than individuals with ME/CFS and healthy controls.

 • The American Journal of Medicine (2023) 000:1–9

KEYWORDS: Chronic fatigue syndrome; Complex post-traumatic stress disorder; Long COVID; Myalgic encephalomyelitis; Post-traumatic stress disorder; Trauma

Funding: This work was supported by grants from The Chief Scientist Office for Scotland (COV/LTE/20/08) and the National Institute for Health and Care Research (COV-LT2-0010).

Conflicts of Interest: All co-authors have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Authorship: Conceptualization: NEMS-H, LDH, ECB, MM, and NFS; Methodology: NEMS-H, LDH, MM, and NFS; Software: NEMS-H, LDH, ECB, MM, and NFS; Validation: NEMS-H, LDH, ECB, MM, and NFS; Formal analysis: NEMS-H; Investigation: NEMS-H, LDH, MM, ECB, and NFS; Resources: LDH, and NFS; Data curation: NEMS-H, LDH, ECB, and MM; Writing—original draft preparation: NEMS-H; Writing—review and editing: NEMS-H, LDH, MM, ECB, and NFS; Visualization: NEMS-H, and LDH; Supervision: NFS; Project administration: NEMS-H, LDH, MM, ECB, and NFS; Funding acquisition: LDH and NFS. All authors have read and agreed to the published version of the manuscript.

Requests for reprints should be addressed to Lawrence D. Hayes, PhD, School of Health and Life Sciences, University of the West of Scotland, Glasgow, UK, G72 0LH.

E-mail address: lawrence.hayes@uws.ac.uk

https://doi.org/10.1016/j.amjmed.2023.12.006

INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic had a profound impact on global public health.[1-4] An emerging and dynamic finding is the presence of symptoms such as anxiety, depression, insomnia, and trauma-related symptoms seen in COVID-19 survivors (individuals who tested positive for coronavirus or who were later confirmed to have had the virus by testing positive for antibodies), as documented in numerous studies.[5-8] The long-term course of the symptoms such as anxiety, depression, insomnia, and trauma-related symptoms in COVID-19 survivors reveals a trajectory characterized by exacerbation over time, particularly in the case of conditions associated with post-traumatic stress disorder (PTSD).[6] Individuals who have faced a fear of survival remain vulnerable to post-traumatic stress symptoms (PTSS), and hospitalization during COVID-19 is a well-recognized risk factor for PTSD.[9-12] Several studies have documented a rapid onset of severe PTSS in COVID-19 survivors following hospital discharge.[10,13-16] Mazza et al[10] documented the rapid onset of severe PTSS in COVID-19 survivors, typically within 1 month following hospital discharge. Matalon et al[13] revealed a direct association between higher levels of anxiety and depression during the first week of hospitalization, social isolation, and prolonged hospital stays with higher post-traumatic stress symptoms 1 month after discharge. Tu et al[14] reported the persistence of PTSS in COVID-19 survivors from Wuhan, extending to 3 and 6 months post-discharge. Neuroimaging studies indicate larger gray matter volumes and increased functional activities in the bilateral hippocampus and amygdala of COVID-19 survivors, 2 regions associated with the pathophysiology of PTSS.[15] Cao and colleagues[16] demonstrated that 1 year on after COVID-19, the prevalence of possible post-traumatic stress disorder was 12.4%, and this finding seemed to match up with sociodemographic factors.

Only 1 in 3 people fully recover from COVID-19 a year after hospital discharge.[17] Individuals that have persistent symptoms lasting over 12 weeks after the acute phase of the COVID-19 infection are known to suffer from long COVID. Long COVID shares similarities and several overlapping symptoms with another condition known as myalgic encephalomyelitis (ME), chronic fatigue syndrome (CFS), or ME/CFS.[18,19] Individuals with long COVID are reported to experience new and worsening mental health symptoms. Most frequently reported were depression, anxiety, PTSS, and insomnia.[20] Moreover, it has been revealed that there is a link between childhood trauma exposure and an increased risk of long COVID, possibly attributed to immune responses, peripheral dysfunction, and central sensitization.[21] Nishimi et al[22] reported that higher psychological resilience to trauma reduced the risk of COVID-19 infection but was not associated with COVID-19 severity or long COVID. In terms of the association between PTSD and CFS, Simani et al[23] found no association between PTSD and risk of CFS in COVID-19 patients.

CLINICAL SIGNIFICANCE

- People with long COVID and myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) exhibit higher prevalence of post-traumatic stress disorder (PTSD) and complex post-traumatic stress disorder (CPTSD) than controls.
- Prevalence of PTSD and CPTSD puts these groups at greater risk of employment and activities of daily living challenges.
- As a result of the above, rehabilitation programs should be implemented, or accommodations for activities of daily living and employment should be made for people with long COVID and ME/CFS.

Taken together, past research suggests a link between PTSS and COVID-19 survivors, especially in hospitalized cases. Specifically, one year after an acute COVID-19 infection, prevalence of possible PTSD has been demonstrated to be approximately 12.4%.[10,13-16] Given that some hospitalized COVID-19 survivors develop long COVID,[17,24] we sought to examine the prevalence of PTSD and complex post-traumatic stress disorder (CPTSD) in individuals with long COVID. Furthermore, given the considerable overlap between long COVID and ME/CFS, we sought to examine prevalence of PTSD and CPTSD in individuals with ME/CFS. For that reason, the objective of this case-control study was to investigate the prevalence of PTSD and CPTSD in individuals with long COVID, individuals with ME/CFS, and healthy age-matched controls. We hypothesized that individuals with long COVID would display higher prevalence and cluster scores of PTSD and CPTSD compared with the individuals with ME/CFS and age-matched healthy controls.

METHODS

Participants

Following institutional ethics approval, 61 participants—21 individuals with long COVID (aged M = 47 years, SD = 10 years, duration of illness; M = 16 years, SD = 6 months), 20 individuals with ME/CFS (aged M = 50 years, SD = 10 years, duration of illness; M = 16 years, SD = 11 years), and 20 healthy controls (aged M = 49 years, SD = 10 years, and no known illness)—were recruited via social media (eg, Twitter/X and Facebook/Meta) and attended the University of the West of Scotland Lanarkshire campus laboratories once between March 2022 and January 2023. This study was completed in accordance with the

Declaration of Helsinki. Written informed consent was obtained from all participants prior to study involvement.

Materials and Apparatus

Participants completed the English version of the International Trauma Questionnaire (ITQ), this 18-question self-report measure that focuses on core features of PTSD and CPTSD consistent with the International Classification of Diseases, 11th Revision. The 18-item ITQ has 6 PTSD items, 6 Disturbances in Self-Organization (DSO) items, and 3 functional impairment items related to each symptom cluster.

The first section of the 18-item ITQ is dedicated to 3 PTSD symptom clusters (P.1-P.6): re-experiencing of the trauma (P1-P.2), avoidance of internal or external trauma reminders (P.3-P.4), and a sense of current threat (P.5-P.6). These are measured by 2 items each. In this section, respondents reported how much they have been bothered by the symptoms in the past month. In the 3 functional impairment items related to PTSD (P.7-P.9), respondents reported how the above problems affected their relationship or social life, work or ability to work, and other important part of their life such as parenting or school or work, etc.

The second section consists of 3 main symptom clusters of DSO (C.1-C.6: affective dysregulation [C.1-C.2]), negative self-concept [C.3-C.4], and disturbances in relationships [C.5-C.6]). In the 3 functional impairment items (C.7-C.9), respondents reported how they typically felt about their relationships or social life, if work or ability to work had been affected, and how this affected other important parts of their lives such as parenting or school or work or other important activities.

All items are answered on a 5-point Likert scale, ranging from “not at all” (scored 0) to “extremely” (scored 4). Scores were calculated for each PTSD and DSO symptom cluster and summed to produce PTSD and DSO scores. PTSD was diagnosed if the criteria for PTSD, but not DSO, were met, and CPTSD was diagnosed if the criteria for PTSD and DSO were met. Criteria for PTSD was met if one of the 2 symptoms from the symptom clusters and at least one indicator of functional impairment associated with these symptoms were scored 2 or above. Criteria for CPTSD was met if one of the 2 symptoms from each of the 3 PTSD symptom clusters and one of the 2 symptoms for each of the 3 DSO, and at least one indicator of functional impairment related to PTSD and one indicator of functional impairment related to the DSO symptoms were scored 2 or above. Endorsement of a symptom or functional impairment item was therefore defined as a score ≥2. Thus, a person can be classified as having a score commensurate with PTSD *or* CPTSD, but not both.

PTSD.

If P1 or P2 ≥2
If P3 or P4 ≥2
If P5 or P6 ≥2
AND
At least one of P7, P8, or P9 ≥2

CPTSD.

If C1 or C2 ≥2
If C3 or C4 ≥2
If C5 or C6 ≥2
AND
At least one of C7, C8, or C9 ≥2

PTSD is diagnosed if the criteria for PTSD are met but not the criteria for DSO. CPTSD is diagnosed if the criteria for PTSD are met and the criteria for DSO are met.

Procedure

Participants were seated in front of a table that had one information sheet, a consent form, a demographic sheet, and the ITQ. Participants were instructed to read the information sheet, complete the consent form, complete the demographic form, and then complete the ITQ. Participants were informed that their answers were anonymous.

Statistical Analysis

All data were assessed for normal distribution and homogeneity of variance. To assess the differences in dependent variables, Welch’s one-way analyses of variance was performed with Games-Howell post hoc tests performed where necessary. The χ^2 test was performed to determine whether a difference in prevalence of PTSD and CPTSD existed among the 3 groups. Post hoc pairwise Fisher’s exact test tested for a difference in affected (PTSD or CPTSD) and not between groups. Data were analyzed using Jamovi (Version 2.3.21; available at https://www.jamovi.org). Data are presented without subjective terminology and alpha levels are reported as exact *P* values, without dichotomous interpretation of "significant" or "non-significant" as advised by the American Statistical Association.[25] Effect size for paired comparisons was conducted using Cohen’s *d*, whereby the difference in means between 2 samples was divided by the pooled standard deviation (SD). Thresholds of 0.2, 0.5, 0.8, and 1.2 for small, moderate, large, and very large effects, respectively, were used for Cohen’s *d*.[26] Figures were generated in GraphPad Prism (GraphPad Prism 8.4.3, GraphPad Software Inc., San Diego, Calif) and display grouped dot plots with mean and 95% confidence intervals as recommended by Drummond and Vowler.[27,28] Figures also display pairwise comparisons in the form of Games-Howell post hoc *P* values, and Cohen’s *d* values. Data are presented in text as mean ± SD.

RESULTS

Descriptive Statistics and Prevalence

Prevalence of PTSD and CPTSD in the 3 groups are displayed in the Table. The χ^2 test resulted in a difference in prevalence of PTSD and CPTSD among the 3 groups (P = .038). Fisher's exact test identified no difference in prevalence of PTSD *or* CPTSD between the long-COVID and ME/CFS groups (P = .3058). Fisher's exact test identified a greater prevalence of PTSD *or* CPTSD between the long-COVID and control groups (P = .003). Fisher's exact test identified no difference in prevalence of PTSD *or* CPTSD between the ME/CFS and control groups (P = .106).

Reasons for the Experience

For people with long COVID, 6 mentioned the experience of COVID (29%), 5 mentioned long COVID (24%), 3 mentioned health (14%), 2 mentioned fatigue (9%), 2 mentioned pain (9%), one mentioned brain fog (5%), one mentioned childbirth (5%), and one mentioned no reason for their experience (5%). For experience occurrence time, 10 mentioned 1 to 5 years ago (48%), 8 mentioned 6 to 12 months ago (38%), 2 mentioned <6 months ago (9%), and one did not specify time (5%). Among the 7 that met the criteria for CPTSD, 3 mentioned long COVID (43%), 2 mentioned COVID (29%), one mentioned health (14%), and one mentioned pain (14%) as their reason behind their experience. Among these, 2 mentioned that the experience of long COVID occurred 1 to 5 years ago (29%) and one mentioned it occurred 6 to 12 months ago (14%). Two mentioned that the experience of COVID occurred 1 to 5 years ago (29%), one mentioned experience of health occurred 6 to 12 months ago (14%), and one mentioned experience of pain occurred 6 to 12 months ago (14%). One person that met criteria for PTSD mentioned health as their reason behind their experience, and mentioned it occurred 6 to 12 months ago.

For people with ME/CFS, 10 mentioned ME/CFS (50%), 2 mentioned no reason for their experience (10%), 2 mentioned health (10%), one mentioned fatigue (5%), one mentioned illness (5%), one mentioned surgery (5%), one mentioned upbringing (5%), one mentioned work stress (5%), and one mentioned work dismissal (5%) as a reason behind their experience. For experience occurrence time, 6 mentioned it occurred 10 to 20 years ago (30%), 5 mentioned it occurred 5 to 10 years ago (25%), 3 mentioned it occurred more than 20 years ago (15%), 2 mentioned 1 to 5 years ago (10%), 2 mentioned no time (10%), one mentioned 6 to 12 months ago (5%), and one mentioned <6 months ago (5%). Among the 4 that met the criteria for CPTSD, 3 mentioned ME/CFS (75%), and one mentioned surgery (25%) as the reason behind their experience. Among these, 2 mentioned that their experience of ME/CFS occurred more than 20 years ago (50%), and one mentioned it occurred 1 to 5 years ago (25%). One mentioned that their experience of surgery occurred 5 to 10 years ago (25%).

Among the 20 healthy control participants, no one met the criteria for CPSTD or PTSD. For the reason behind the experience, 7 mentioned health (35%), 3 mentioned no reason (15%), 3 mentioned bereavement (15%), 2 mentioned flying (10%), one mentioned cancer diagnosis of family member (5%), one mentioned injury (5%), one mentioned giving birth (5%), one mentioned illness of family member (5%), and one mentioned premature birth of family member (5%). For experience occurrence time, 5 mentioned that it occurred 1 to 5 years ago (25%), 5 mentioned that it occurred 5 to 10 years ago (25%), 5 did not mention a time frame (25%), 3 mentioned 10 to 20 years ago (15%), one mentioned <6 months ago (5%), and one mentioned more than 20 years ago (5%).

PTSD and DSO

PTSD. The was an effect of group for re-experiencing in the here and now, avoidance, and sense of current threat, overall PTSD score, and PTSD impairment [$F(2,58) = 3.71$, $P = .03$; $F(2,58) = 6.77$, $P < .01$, $F(2,58) = 6.74$, $P < .01$; $F(2,58) = 6.61$, $P < .01$; and $F(2,58) = 17.87$, $P < .001$, respectively]. Pairwise comparisons (Games-Howell post hoc test P values and *Cohen's d* values) are presented in Figure 1.

DSO. The was an effect of group for affective dysregulation, negative self-concept, disturbances in relationship, overall DSO score, and DSO impairment [$F(2,58) = 10.99$, $P < .001$; $F(2,58) = 15.60$, $P < .001$; $F(2,58) = 16.77$, $P < .001$; $F(2,58) = 15.20$, $P < .001$; and $F(2, 58) = 15.36$, $P < .001$, respectively]. Pairwise comparisons (Games-Howell post hoc test P values and Cohen's d values) are presented in Figure 2.

Table Prevalence of PTSD and CTPSD in People with Long COVID, People with ME/CFS, and Controls

	Prevalence of Each Condition; n (%)		
	Long COVID (n = 21)	ME/CFS (n = 20)	Controls (n = 20)
PTSD	1 (5%)	0 (0%)	0 (0%)
CPTSD	7 (33%)	4 (20%)	0 (0%)
Neither PTSD nor CPTSD	13 (62%)	16 (80%)	20 (100%)

CFS = chronic fatigue syndrome; CPTSD = complex post-traumatic stress disorder; ME = myalgic encephalomyelitis; PTSD = post-traumatic stress disorder.

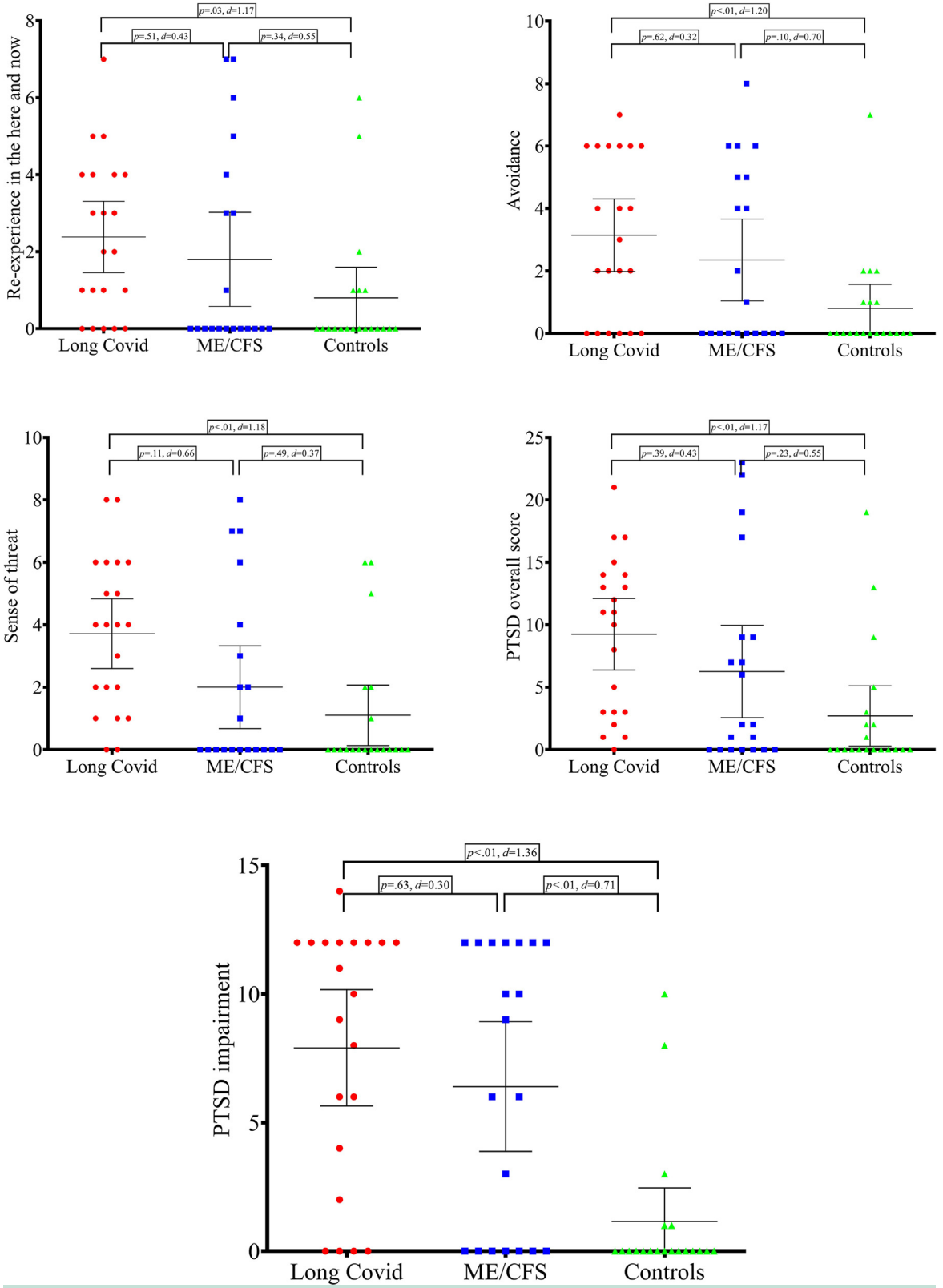

Figure 1 International Trauma Questionnaire (ITQ) results for the post-traumatic stress disorder (PTSD) items in people with long COVID (n = 21), ME/CFS (n = 20), and controls (n = 20). Data are presented as individual dot plots and means and 95% confidence intervals. *P* values are from Games-Howell post hoc tests and *d* values are Cohen's *d*.

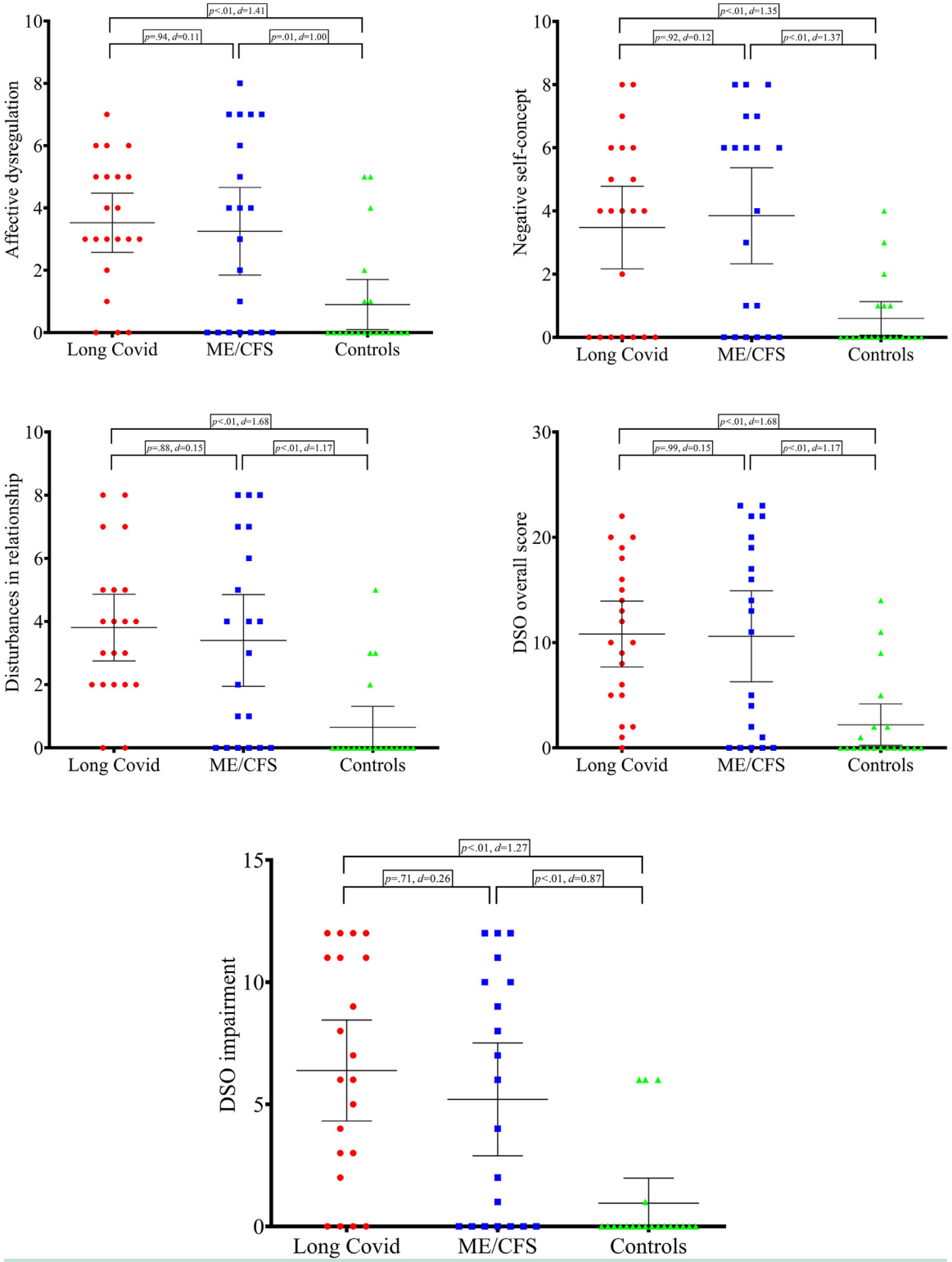

Figure 2 International Trauma Questionnaire (ITQ) results for the Disturbances in Self-Organization (DSO) items in people with long COVID (n = 21), ME/CFS (n = 20), and controls (n = 20). Data are presented as individual dot plots and means and 95% confidence intervals. *P* values are from Games-Howell post hoc tests and *d* values are Cohen's *d*.

Overall International Trauma Questionnaire (ITQ) Score

There was a main effect of group for overall ITQ score for CPSTD ($F(2,58) = 17.00$, $P < .001$). Individuals in the long COVID group (M = 34.33, SD = 19.30) scored higher ($P < .001$) than the healthy controls (M = 7.00, SD = 12.20). Individuals in the ME/CFS group (M = 28.45, SD = 24.90) scored higher ($P = .01$) than the healthy controls (M = 7.00, SD = 12.20).

DISCUSSION

The purpose of this study was to examine the prevalence of PTSD and CPSTD, and cluster of PTSD and DSO in people with long COVID, people with ME/CFS, and age-matched healthy controls. The main findings of the present investigation were that there was a difference in prevalence among individuals with long COVID, individuals with ME/CFS, and age-matched healthy controls. PTSD and CPTSD prevalence were greater in individuals with long COVID and individuals with ME/CFS compared with age-matched healthy controls. Individuals with long COVID had greater raw values than age-matched healthy controls for all PTSD values. Moreover, individuals with long COVID had greater raw values than age-matched healthy controls for all DSO values. Individuals with ME/CFS had greater values than age-matched healthy controls for all DSO values. Both long COVID and ME/CFS groups had higher symptom scores compared with controls.

The spread of data within each group was large, evidenced by the individual dot plots and large confidence intervals, suggesting considerable within-group heterogeneity. However, our findings were partially in line with our hypothesis of higher prevalence of PTSD and CPTSD, and cluster scores of PTSD and DSO in individuals with long COVID compared with individuals with ME/CFS and controls. This difference was not as apparent between individuals with long COVID and ME/CFS, although there was a very large difference between individuals with long COVID and control participants, and a moderate difference between individuals with ME/CFS and control participants, for PTSD impairment. In the DSO cluster, the difference between long COVID and control participants was very large, and the difference between the ME/CFS and control group was large.

Individuals with long COVID reported experience occurrence time to be fewer in years compared with the individuals with ME/CFS. For example, 10 mentioned 1 to 5 years ago (48%), 8 mentioned 6 to 12 months ago (38%), 2 mentioned <6 months ago (9%), and one did not specify time (5%) in individuals with long COVID. Whereas 6 mentioned it occurred 10 to 20 years ago (30%), 5 mentioned it occurred 5 to 10 years ago (25%), 3 mentioned it occurred more than 20 years ago (15%), 2 mentioned 1 to 5 years ago (10%), 2 mentioned no time (10%), one mentioned 6 to 12 months ago (5%), and one mentioned <6 months ago (5%) in individuals with ME/CFS. This suggests that individuals with ME/CFS have been suffering from the post-viral symptoms longer than individuals with long COVID and may explain the larger differences from controls in the long COVID group compared with the ME/CFS group. There might be other contextual differences among these groups in terms of acceptance of condition, letting go of past events, and dealing better with current symptoms due to greater experience of similar symptoms over time, etc. Individuals with long COVID lived through the stressors of a pandemic while dealing with their own symptoms, and COVID survivors may have been hospitalized and seen passing of lives in hospitals.

Past research suggests that individuals that have faced a fear of survival remain vulnerable to PTSS, and hospitalization is a well-recognized risk factor for PTSD, with a rapid onset of severe PTSS within 1 month following hospital discharge; this has been reported to extend to 3 and 6 months post-discharge.[6,9-12,14] The longest duration of post-discharge that has been examined is 1 year on after COVID-19; PTSD was reported to be 12.4% and there was an interplay with sociodemographic factors.[16] The current study was conducted 2 years after the COVID-19 pandemic started, but our entire sample were not hospitalized prior and have developed long COVID. Past research on long COVID and PTSS suggest new and worsening mental health symptoms among individuals with long COVID; most frequently reported were PTSS, among a few others such as depression and anxiety, etc.[20] However, this study does not explain how these mental health symptoms change over time in individuals with long COVID; thus, a study examining these changes could be beneficial in creating awareness around mental health issues within the long COVID population to better support them.

Limitations

This study presents a few limitations, which we must acknowledge. Firstly, the sample size was relatively small, and therefore we encourage readers to consider effect sizes in addition to *P* values to contextualize findings. Secondly, findings may not be generalizable to the wider population of people with long COVID (or ME/CFS), particularly those who are unable to attend a laboratory (ie, those most severely affected). We are aware this is not entirely inclusive for people with long COVID and ME/CFS as, according to the National Institute for Health and Care Excellence, 25% of people with ME/CFS are bedbound or housebound, meaning that visiting a laboratory is impossible. Therefore, the magnitude of differences in psychological well-being presented herein likely underestimates the true effect due to the nature of recruitment bias. Finally, the study did not assess hospitalization or the impact of hospitalization on mental health.

CONCLUSION

In conclusion, findings of this study demonstrate that people with long COVID had greater prevalence of PTSD and

CPTSD than people with ME/CFS and controls. Individuals with long COVID demonstrate higher scores in PTSD and DSO clusters compared with controls, but no differences at the $P < .05$ level existed for PTSD and DSO clusters between the long COVID and the ME/CFS groups. Both the long COVID and ME/CFS groups differed in overall symptom scores compared with the control group, but magnitudes were heterogenous. Future research should focus on examining this relationship with a larger sample, and on developing mental health support strategies to aid individuals suffering with a post-viral condition.

CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

Nilihan E.M. Sanal-Hayes: Writing − review & editing, Writing − original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Lawrence D. Hayes:** Writing − review & editing, Writing − original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Marie Mclaughlin:** Writing − review & editing, Writing − original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Ethan C.J. Berry:** Writing − review & editing, Writing − original draft, Methodology, Investigation. **Nicholas F. Sculthorpe:** Writing − review & editing, Writing − original draft, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

References

1. McLaughlin M, Cerexhe C, Macdonald E, et al. A cross-sectional study of symptom prevalence, frequency, severity, and impact of long-COVID in Scotland: part I [online ahead of print]. *Am J Med* 2023. https://doi.org/10.1016/j.amjmed.2023.07.004. [Jul 20:S0002-9343(23)00460-6.
2. McLaughlin M, Cerexhe C, Macdonald E, et al. A cross-sectional study of symptom prevalence, frequency, severity, and impact of long-COVID in Scotland: part II [online ahead of print]. *Am J Med* 2023. https://doi.org/10.1016/j.amjmed.2023.07.009. [Jul 20:S0002-9343(23)00461-8.
3. Hayes LD, Ingram J, Sculthorpe NF. More than 100 persistent symptoms of SARS-CoV-2 (long COVID): a scoping review. *Front Med (Lausanne)* 2021;8:750378.
4. Anjum S, Ullah R, Rana MS, et al. COVID-19 pandemic: a serious threat for public mental health globally. *Psychiatr Danub* 2020;32 (2):245–50.
5. Xiao X, Yang X, Zheng W, et al. Depression, anxiety and post-traumatic growth among COVID-19 survivors six-month after discharge. *Eur J Psychotraumatol* 2022;13(1):2055294.
6. Kyzar EJ, Purpura LJ, Shah J, Cantos A, Nordvig AS, Yin MT. Anxiety, depression, insomnia, and trauma-related symptoms following COVID-19 infection at long-term follow-up. *Brain Behav Immun Health* 2021;16:100315.
7. Yuan Y, Liu ZH, Zhao YJ, et al. Prevalence of post-traumatic stress symptoms and its associations with quality of life, demographic and clinical characteristics in COVID-19 survivors during the post-COVID-19 era. *Front Psychiatry* 2021;12:665507.
8. Bridgland VME, Moeck EK, Green DM, et al. Why the COVID-19 pandemic is a traumatic stressor. *PLoS One* 2021;16(1):e0240146.
9. Zhou Y, Sun Z, Wang Y, et al. The prevalence of PTSS under the influence of public health emergencies in last two decades: a systematic review and meta-analysis. *Clin Psychol Rev* 2021;83:101938.
10. Mazza MG, De Lorenzo R, Conte C, et al. Anxiety and depression in COVID-19 survivors: role of inflammatory and clinical predictors. *Brain Behav Immun* 2020;89:594–600.
11. Pfefferbaum B, North CS. Mental health and the Covid-19 pandemic. *N Engl J Med* 2020;383(6):510–2.
12. Craparo G, La Rosa VL, Marino G, et al. Risk of post-traumatic stress symptoms in hospitalized and non-hospitalized COVID-19 recovered patients. A cross-sectional study. *Psychiatry Res* 2022;308:114353.
13. Matalon N, Dorman-Ilan S, Hasson-Ohayon I, et al. Trajectories of post-traumatic stress symptoms, anxiety, and depression in hospitalized COVID-19 patients: A one-month follow-up. *J Psychosom Res* 2021;143:110399.
14. Tu Y, Zhang Y, Li Y, et al. Post-traumatic stress symptoms in COVID-19 survivors: a self-report and brain imaging follow-up study. *Mol Psychiatry* 2021;26(12):7475–80.
15. Shin LM, Rauch SL, Pitman RK. Amygdala, medial prefrontal cortex, and hippocampal function in PTSD. *Ann N Y Acad Sci* 2006;1071 (1):67–79.
16. Cao Y, Siu JY, Shek DTL, Shum DHK. COVID-19 one year on: identification of at-risk groups for psychological trauma and poor health-protective behaviour using a telephone survey. *BMC Psychiatry* 2022;22(1):252.
17. Office for National Statistics. Prevalence of ongoing symptoms following coronavirus (COVID-19) infection in the UK. Available at: https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/prevalenceofongoingsymptomsfollowingcoronaviruscovid19infectionintheuk/3march2022. Accessed April 1, 2022.
18. Hayes LD, Sanal-Hayes NEM, Mclaughlin M, Berry ECJ, Sculthorpe NF. People with long Covid and ME/CFS exhibit similarly impaired balance and physical capacity: a case-case-control study [online ahead of print]. *Am J Med* 2023. https://doi.org/10.1016/j.amjmed.2023.06.028 [Jul 23:S0002-9343(23)00465-5.
19. Mclaughlin M, Sanal-Hayes NEM, Hayes LD, Berry EC, Sculthorpe NF. People with long COVID and myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) exhibit similarly impaired vascular function [online ahead of print]. *Am J Med* 2023. https://doi.org/10.1016/j.amjmed.2023.09.013 [Oct 12:S0002-9343(23)00609-5.
20. Saltzman LY, Longo M, Hansel TC. Long-COVID stress symptoms: mental health, anxiety, depression, or posttraumatic stress [online ahead of print]. *Psychol Trauma* 2023. https://doi.org/10.1037/tra0001567 [Aug 10.
21. Van Den Hurk AWV, Ujvari C, Greenspan N, Malaspina D, Jimenez XF, Walsh-Messinger J. Childhood trauma exposure increases long COVID risk. *[Preprint]* 2022. https://doi.org/10.1101/2022.02.18.22271191.
22. Nishimi K, Tan J, Scoglio A, et al. Psychological resilience to trauma and risk of COVID-19 infection and somatic symptoms across 2 years. *Psychosom Med* 2023;85(6):488–97.
23. Simani L, Ramezani M, Darazam IA, et al. Prevalence and correlates of chronic fatigue syndrome and post-traumatic stress disorder after the outbreak of the COVID-19. *J Neurovirol* 2021;27(1):154–9.
24. Bangash MN, Owen A, Alderman JE, Chotalia M, Patel JM, Parekh D. COVID-19 recovery: potential treatments for post-intensive care syndrome. *Lancet Respir Med* 2020;8(11):1071–3.

25. Hurlbert SH, Levine RA, Utts J. Coup de grâce for a tough old bull: "statistically significant" expires. *Am Stat* 2019;73(suppl):352–7.
26. Lakens D. Calculating and reporting effect sizes to facilitate cumulative science: a practical primer for t-tests and ANOVAs. *Front Psychol* 2013;4:863.
27. Drummond GB, Vowler SL. Do as you would be done by: write as you would wish to read. *J Physiol* 2012;590(24):6251–4.
28. Drummond G, Vowler S. Show the data, don't conceal them. *Br J Pharmacol* 2011;163(2):208–10.