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People with Long COVID and ME/CFS Exhibit Similarly Impaired Dexterity and Bimanual Coordination: A Case-Case-Control Study

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ABSTRACT

PURPOSE: Dexterity and bimanual coordination had not previously been compared between people with long COVID and people with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). Therefore, this study determined dexterity and bimanual coordination in people with long COVID (~16-month illness duration; n = 21) and ME/CFS (~16-year illness duration; n = 20), vs age-matched healthy controls (n = 20).

METHODS: Dexterity and bimanual coordination was determined using the Purdue pegboard test.

RESULTS: The main findings of the present investigation were that people with ME/CFS and people with long COVID were generally comparable for Purdue pegboard tests ($P > .556$ and $d < 0.36$ for pairwise comparisons). It is worth noting however, that both these patient groups performed poorer in the Perdue pegboard test than healthy controls ($P < .169$ and $d > 0.40$ for pairwise comparisons).

CONCLUSIONS: These data suggest that both people with long COVID and people with ME/CFS have similarly impaired dexterity and bimanual coordination. Therefore, there is an urgent need for interventions to target dexterity and bimanual coordination in people with ME/CFS, and given the current pandemic, people with long COVID.

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INTRODUCTION

Postviral illness occurs when individuals experience an extended period of feeling unwell and fatigued after a viral infection.[1,2] Over the past 4 years, the term long COVID has gained prominence, defined by the NICE guidelines as symptoms persisting from 4 weeks to over 12 weeks after acute infection, shedding more light on postviral fatigue.[3] Long COVID encompasses a range of symptoms that endure beyond the acute phase of COVID-19.[4-8] Various symptoms manifest in postviral illnesses,[9-11] and a recent systematic review revealed a prevalence of up to 56% for mobility problems, up to 64% for decreased functional status, and up to 100% for sensory impairments in individuals recovering from acute COVID-19 infection.[4] While long COVID is a relatively recent condition, myalgic encephalomyelitis (ME) chronic fatigue syndrome (CFS) and/or ME/CFS have been documented in the medical literature for decades,[12] showing multiple overlaps with long COVID.[13,14] ME/CFS is a debilitating condition characterized by severe fatigue, cognitive impairment, and various other symptoms, lacking a known cure or definitive treatment.[15-17] Both long COVID and ME/CFS exhibit neurologic effects commonly described in medical literature.[13,16,18,19] Several mechanisms theorize how ME/CFS affects the nervous system, including autonomic nervous system dysfunction,[20] neuroendocrine disorder (especially the hypothalamic-pituitary-adrenal axis),[21] and immune system abnormalities[22] (resulting in increased production of pro-inflammatory cytokines, ultimately causing neuroinflammation).[23] Interestingly, research on long COVID has also identified autonomic nervous system dysfunction,[24] neuroendocrine abnormalities (particularly in the hypothalamic-pituitary-adrenal axis),[25] and immune system abnormalities,[26] leading to neuroinflammation.[27]

The nervous system is responsible for coordinating appropriate postural control, through sensory input, integration, motor output, feedback control, or reflexes.[28-32] As a result, both conditions (ME/CFS and long COVID) lead to impaired balance and postural control (ie, gross motor control).[33-37] Indeed, our recent article reported impaired postural control in both people with long COVID and ME/CFS.[38] The execution of basic fine motor movements relies on the collaboration of various brain regions, including the premotor and motor cortex, cerebellum, basal ganglia, corticospinal tracts, and peripheral nerves. This process also involves visuospatial, sensory, and executive function processing.[39] Unsurprisingly, given the multiple brain regions involved, manual dexterity has been associated with executive functions,[40,41] working memory,[40] and gait speed.[41] Although the nervous system is partly responsible for both postural control and dexterity, and these 2 attributes are associated in a number of conditions,[42,43] it is unknown whether manual dexterity and bimanual coordination would be affected in people with long COVID and ME/CFS.

CLINICAL SIGNIFICANCE

- Long COVID and ME/CFS cause impaired dexterity, putting these groups at greater risk of employment and activities of daily living challenges.
- People with Long COVID and ME/CFS have lower dexterity than controls, which likely cause greater fatigue in their daily lives.
- 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.

Mechanistically, it would seem logical that people with ME/CFS (and to an extent long COVID, given the overlap in symptomology) would exhibit lower dexterity as a result of central fatigue demonstrated by several twitch interpolation studies which identified unaltered peripheral fatiguability.[44,45] Indeed, Sacco et al[46] reported reduced amplitude of motor potentials evoked by transcranial magnetic stimulation of the motor cortex in the biceps brachii muscle, concluding diminution in central motor drive in people with ME/CFS. Similarly, brain areas associated with bimanual coordination include primary sensorimotor areas,[47,48] supplementary motor area,[49,50] premotor cortex,[49,50] prefrontal cortex,[48] motor cingulate,[48] basal ganglia,[48,51] and the cerebellum.[50,52] Unsurprisingly, given the brain regions involved in bimanual coordination, complex bimanual skills form the basis for study of higher cognitive functions in perception and action, including executive functions such as task switching, multitasking, and inhibition, and these types of tasks are helpful in revealing motor developmental trajectories and deficits due to brain disorders.[53] Schrijvers et al[54] revealed that individuals with CFS performed slower than controls in a line-copying task that required motor effort and demonstrated an overall fine motor slowing.

Dynamic upper extremity function in general, and of the fingertips in particular, is vital for activities of daily living and quality of life.[55,56] Conversely, fine motor disability is an inability or impairment when performing tasks requiring manual dexterity[57] and bimanual coordination,[58] and is generally considered a symptom of underlying pathology rather than a disease in its own right.[57] To date, however, there have not been any studies that directly compare manual dexterity and bimanual coordination in people with ME/CFS and people with long COVID in the same article. Given the considerable overlap with long COVID and ME/CFS, the objective of this case-case-control study was to investigate the effects of long COVID and ME/CFS on fingertip dexterity and gross movement of the hand, fingers, arm, and bimanual coordination. This experiment compared the Purdue pegboard test performance between individuals with long COVID, individuals

with ME/CFS, and age-matched healthy controls. We hypothesized that people with long COVID and ME/CFS would exhibit poorer performance on all parameters of the Purdue pegboard test.

METHODS

Participants

Sixty-one participants (long COVID, n = 21; ME/CFS, n = 20; and healthy controls, n = 20, Table) were recruited for this study via social media advertisement using Facebook/Meta and Twitter/X platforms. Participants attended a one-off visit to the Cardiovascular Imaging laboratory at the University of the West of Scotland, Lanarkshire, between March 2022 and January 2023. This study was carried out in accordance with the Declaration of Helsinki and approved by the Institutional Ethics Committee. Written informed consent was obtained from all participants prior to study commencement. Descriptive statistics for participants are in Table.

Table Descriptive Data of Participants at Enrolment

Variable	Group	Mean ± SD
Age (years)	Long COVID (n = 21)	47 ± 10
	ME/CFS (n=20)	50 ± 10
	Control (n = 20)	49 ± 10
Duration of illness	Long COVID (n = 21)	16 ± 6 months
	ME/CFS (n = 20)	16 ± 11 years
	Control (n = 20)	N/A
Height (cm)	Long COVID (n = 21)	168 ± 10
	ME/CFS (n = 20)	169 ± 9
	Control (n = 20)	171 ± 9
Body mass (kg)	Long COVID (n = 21)	97 ± 23
	ME/CFS (n = 20)	87 ± 24
	Control (n = 20)	71 ± 15
BMI ($kg \cdot m^2$)	Long COVID (n = 21)	34 ± 6
	ME/CFS (n = 20)	31 ± 9
	Control (n = 20)	24 ± 4
Systolic blood pressure (mmHg)	Long COVID (n = 21)	140 ± 19
	ME/CFS (n = 20)	102 ± 33
	Control (n = 20)	94 ± 40
Diastolic blood pressure (mmHg)	Long COVID (n = 21)	95 ± 15
	ME/CFS (n = 20)	87 ± 12
	Control (n = 20)	77 ± 8
Resting heart rate (bpm)	Long COVID (n = 21)	80 ± 14
	ME/CFS (n = 20)	82 ± 19
	Control (n = 20)	65 ± 10

Purdue Pegboard Test

Five separate values are obtained from the complete test battery, resulting from the 4 tasks below, plus the sum of dominant hand (task 1), nondominant hand (task 2), and both hands (task 3). Measurements were performed in following order:

1. Dominant hand (30 seconds)
2. Nondominant hand (30 seconds)
3. Both hands (30 seconds)
4. Assembly (60 seconds)

Participants completed 3 test trials of each of the 4 tasks. A general instruction manual was used and read to participants. Participants were comfortably seated at the testing table directly in front of the Purdue pegboard, placed on the table with the row of cups at the top of the board. The far right and far left cups had 25 pins in (50 pins in total). For right-handed people, the cup to the right of center had 20 collars and the cup to the left of the center had 40 washers. For left-handed people, the collar and washer locations were on the reverse side of center. Each trial consisted of a practice, and then 3 test trials.

Instructions for dominant and nondominant hand:

> "Pick up one pin at a time with your right hand/left hand (depending on dominant hand) from the right-handed/left-handed cup (if right-handed then right cup). Starting with the top hole, place each pin in the right hand/left hand row (if right-handed then right-hand row). Now you may insert a few pins for practice. If during the testing time you drop a pin, do not stop to pick it up. Simply continue by picking another pin out of the cup."

After practice session, instructions were as follows:

> "When I say 'Begin', place as many pins as possible in the right-hand/left hand row, starting with the top hole. Work as rapidly as you can until I say 'Stop.' Are you ready? Begin." (Allow participants 30 seconds for dominant hand test trial).

Instructions for the nondominant hand, and the test trial duration were identical to dominant hand.

Instructions for both hands:

> "For this part of the test, you will use both hands at the same time. Pick up a pin from the right-hand cup with your right hand, and at the same time pick up a pin from the left-hand cup with your left hand. Then place the pins down the rows. Begin with the top hole of both rows."

Practice and test trial instructions were identical to dominant and nondominant hand instructions, but information about the task differed: When I say "Begin," place as many pins as possible with both hands, starting with the top hole of both rows. Work as rapidly as you can until I say "Stop."

Instructions for assembly for right-handed people:

"Pick up one pin from the right-hand cup with your right hand. While you are placing it in the top hole in the right-hand row, pick up a washer with your left hand. As soon as the pin has been placed, drop the washer over the pin. While the washer is being placed over the pin with your left hand, pick up a collar with your right hand. While the collar is being dropped over the pin, pick up another washer with your left hand and drop it over the collar. This completes the first 'assembly,' consisting of a pin, a washer, a collar, and a washer. While the final washer for the first assembly is being placed with your left hand, start the second assembly immediately by picking up another pin with your right hand. Place it in the next hole, drop a washer over it with your left hand, and so on, completing another assembly. Now, take a moment to try a few practice assemblies."

If the participant was left-handed, the washer and collar locations in the cups were switched. The participant began by picking up the pin with left hand, the washer with right hand, the collar with left hand, another washer with right hand and so on through all assemblies.

After participant had practiced the assemblies, the researcher said:

"Stop. Now return the pins, collars, and washers to their proper cups. When I say 'Begin,' make as many assemblies as possible, beginning with the top hole. Work quickly until I say 'Stop.'"

After exactly 1 minute (60 seconds), the researcher said "stop."

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 (ANOVA) were performed with Games-Howell post hoc tests performed where necessary. Data were analyzed using Jamovi (Version 2.3.21). Data are presented without subjective terminology and alpha levels are reported as exact P values, without dichotomous interpretation of "significant" or "nonsignificant" as advised by the American Statistical Association.[59] 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, and 0.8 for small, moderate, and large effects were used for Cohen's d.[60] Figures were generated in GraphPad Prism (GraphPad Prism 8.4.3, GraphPad Software Inc., San Diego, CA) and display grouped dot plots with mean and 95% confidence intervals (CIs) as recommended by Drummond and Vowler.[61,62] 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

Purdue pegboard performance data are displayed in Figure. The ANOVA main effect of group was $P = .008$ for the left-hand pegboard task, $P = .003$ for the right-hand pegboard task, $P = .033$ for the both hands pegboard task, $P = .005$ for the left, then right, then both hands pegboard task, and $P = .198$ for the assembly task. Pairwise comparisons suggest the differences between long COVID and ME/CFS ranges from trivial (right hand task) to small (left hand task, both hands task, left, then right, then both hands task, assembly task). Differences between the long COVID group and controls ranges from small (assembly task) to large (right hand task, left, then right, then both hands task). Differences between ME/CFS group and controls ranges from medium (assembly task) to large (left hand task, right hand task, both hands task, and the left, then right, then both hands task).

DISCUSSION

The purpose of this study was to compare fingertip dexterity and gross movement of the hand, fingers, arm, and bimanual coordination in people with long COVID, people with ME/CFS, and age-matched healthy controls. The main findings of the present investigation were that people with ME/CFS and people with long COVID were generally comparable for Purdue pegboard tests ($P > .556$ and $d < 0.36$ for pairwise comparisons). It is worth noting, however, that both patient groups performed these tests poorer than healthy controls ($P < .169$ and $d > 0.40$ for pairwise comparisons). Furthermore, as illustrated in the individual dot plots, not only did the mean values of both patient groups fall below those of the controls, but there was also a wider dispersion, suggesting that some participants experienced significant impairment in terms of dexterity and bimanual coordination. Therefore, our hypothesis that individuals with long COVID and ME/CFS would demonstrate inferior performance in the test compared to healthy controls is supported.

ME/CFS and long COVID represent incapacitating conditions marked by severe fatigue, cognitive impairment, and diverse symptoms, lacking a known cure or definitive treatment.[15-17] Our findings are substantiated by several twitch interpolation studies,[44,45] establishing a relationship between dexterity and fatigue. This suggests that diminished dexterity may stem from central fatigue, a hallmark of both ME/CFS and long COVID. Considering those individuals with ME/CFS and long COVID experience fatigue, diminished performance (in comparison to controls) in assessments of dexterity and bimanual coordination among individuals with ME/CFS and long COVID is logical. Several mechanisms postulate the impact of ME/CFS and long COVID on the nervous system, encompassing autonomic nervous system dysfunction,[20-24] neuroendocrine disorder,[21-25] and immune system abnormalities.[22-26] Sacco et al[46] reported reduced amplitude of motor potentials induced by transcranial magnetic stimulation of the motor cortex in

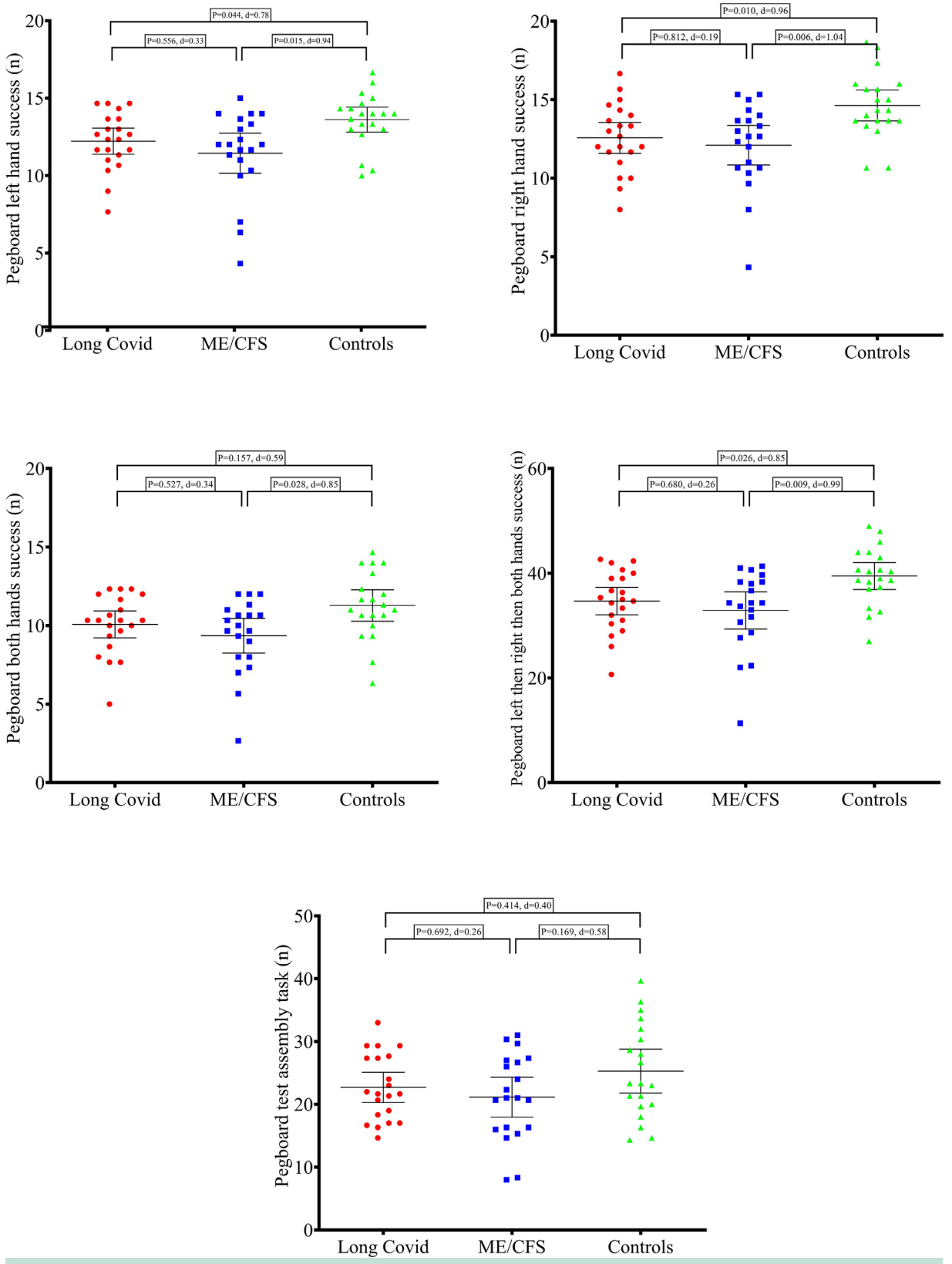

Figure Purdue pegboard parameters from people with long-COVID (n = 21), ME/CFS (n = 17), and controls (n = 19) during a timed up and go test. Data are presented as individual dot plots and means and 95% confidence intervals.

the biceps brachii muscle, indicating a diminution in central motor drive in people with ME/CFS. Schrijvers et al[54] revealed that individuals with CFS exhibited slower performance than controls in a line-copying task necessitating motor effort, demonstrating a reduced fine motor speed.

Fine motor disability, defined as an incapacity or hindrance when executing tasks demanding manual dexterity,[57] and bimanual coordination,[58] are generally regarded as symptoms of underlying pathology rather than independent diseases.[57] Therefore, data presented herein suggest fine motor disability may be a symptom of the underlying pathology of ME/CFS and long COVID. This is pertinent because upper extremity function, particularly in the fingertips, is imperative for daily activities and quality of life.[55,56] Consequently, rehabilitation programs directed at enhancing fine motor skills could be of interest to these patient groups, with the aim of enhancing quality of life. However, individuals with ME/CFS and long COVID experience severe fatigue, so rehabilitation should be approached cautiously and probably confined to a subset of individuals. Deciphering these data is intricate given the limited understanding of long COVID and the scarcity of comparative data on the duration of ME/CFS and fine motor performance. With regards to disease time course, people with long COVID in the present study had a disease duration of ~16 months, whereas the ME/CFS group had a disease duration of ~16 years. Therefore, the long COVID group data presented here might signify baseline effects, and prolonged durations of long COVID could witness restricted further deterioration. Nonetheless, it is also plausible that, in a relatively brief period, participants with long COVID have declined to a similar extent as those with ME/CFS over several years. Further research will be required to determine the time course of dexterity effects in people with long COVID.

Limitations

This study acknowledges certain limitations that merit recognition. First, the sample size was relatively modest. To mitigate this constraint, we employed magnitude-based inferences and presented precise α values instead of relying solely on dichotomous classifications of "significant" and "nonsignificant." This approach was considered appropriate due to the recent emergence of long COVID, which has left measures of central tendency and spread largely unknown, especially for parameters related to dexterity and bimanual coordination, making a sample size calculation unfeasible. Second, the findings may not readily apply to the broader population of individuals with long COVID (or ME/CFS), particularly those who are unable to participate in a laboratory setting, such as those severely affected. Recognizing this limitation is crucial, as per NICE guidelines, where 25% of individuals with ME/CFS are bedbound or housebound, making it impractical for them to visit a laboratory.[63] Consequently, the observed magnitude of difference in dexterity and bimanual coordination deficits in this study likely underestimates the true effect, given the inherent recruitment bias.

CONCLUSION

In summary, results of this study bear significant implications for the management of long COVID and ME/CFS. Despite experiencing the postviral illness for an average of only 16 months, individuals with long COVID demonstrate dexterity and bimanual coordination comparable to those with ME/CFS, who have had their condition for an average of 16 years. The identified deficits in dexterity and bimanual coordination among individuals with long COVID likely contribute to their disability, emphasizing the need to recognize and address these issues to improve their quality of life.

Moreover, as we navigate the early stages of the long COVID pandemic, there is a legitimate concern that declines in dexterity and bimanual coordination may worsen in the coming years, posing substantial challenges for affected individuals, their support networks, and global economies. Patient groups frequently express a conflict between their emphasis on physical symptoms and clinical services that may perceive the illness as psychosomatic, potentially harming the care and well-being of patients and leading to misdiagnosis, mistreatment, and stigmatisation.[64] The findings of this study align with the growing body of evidence affirming that both ME/CFS and long COVID involve authentic physiological symptoms impacting health and well-being, necessitating direct attention. Looking forward, future research should focus on uncovering the mechanisms underlying long COVID and ME/CFS, as well as developing interventions to improve outcomes.

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