wjpmr, 2022,8(7), 50-59

SJIF Impact Factor: 5.922

WORLD JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.wjpmr.com

Review Article

ISSN 2455-3301

WJPMR

CHRONIC FATIGUE SYNDROME, DEPRESSION, SLEEP, AGE, INTELLIGENCE AND MEMORY

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Article Received on 15/05/2022 **Article Revised on 05/06/2022** **Article Accepted on 26/06/2022**

ABSTRACT

Background: Memory problems are frequently reported by Chronic Fatigue Syndrome (CFS) patients. These self-reports are often not confirmed using objective memory tests. Indeed, conflicting results have been obtained in previous studies examining the performance of CFS patients on a variety of memory tasks. Results have shown that CFS patients perform working and semantic memory more slowly but show no decrease in accuracy. The present study examined whether sleep disturbances, depression, age and intelligence may modify the effects of CFS on memory. **Methods:** CFS patients were recruited from a specialist clinic and compared with healthy controls. Three experiments were carried out. The first used memory tasks designed to examine the different components of working memory. The second used working memory and semantic memory tasks and also examined psychomotor speed. The third used the "Doors and People" task, which measures immediate recall and forgetting of names and visual shapes. Measures of intelligence, insomnia and depression were also recorded. **Results:** The CFS patients reported frequent memory problems and showed a trend of impaired memory performance. However, only the differences in speed scores and the recall of shapes were significant. Depression, insomnia, age and intelligence did not significantly modify the performance of the CFS patients. **Conclusions:** CFS patients reported frequent memory problems, but objective testing largely failed to confirm this. The CFS patients were slower at several tasks (Digit-Symbol Substitution; Semantic Processing; writing and simple reaction time), and this slowing may be involved in the poorer immediate recall of shapes. Depression, insomnia, age and intelligence did not change the CFS effects. Future research should use large sample sizes as the effect sizes of being in the CFS group were small.

KEYWORDS: Chronic Fatigue Syndrome; Depression; Sleep problems; Intelligence; Age; Memory; Working memory; Semantic Memory; Writing Speed; Simple reaction time; Doors and People Test.

INTRODUCTION

Persistent debilitating fatigue is the primary symptom of Chronic Fatigue Syndrome (CFS). Cognitive problems such as reports of impairment of memory and loss of concentration may be reported by a large percentage (66-75%) of patients. This has led to a number of studies using objective tasks to measure possible memory impairments in CFS.[1-30] Initial findings showed that the memory problems reported by the patients are not replicated with objective measurement.[4,21] Indeed, a number of studies have failed to find significant memory differences between CFS patients and healthy controls.[2,3,5,7,13,14,20,22,24,29] In contrast, some research has demonstrated memory impairments in CFS patients.[9,10,11,12,18,19,23, 25,26,27,28,30] Research has also found that only certain types of memory tasks are impaired in CFS patients. For example, more demanding memory tasks are more likely to be impaired in CFS patients.[17] Visual memory tasks are also more sensitive.[1]

Research has also examined the type of processing that may be involved. These memory impairments have been interpreted in terms of changes in the amount of effort applied or slower information processing.[12, 23] One study suggested that impairments reflected poorer initial storage rather than retrieval.[19] Results from a recent study[31] suggest that slower responding may account for impairments in episodic, semantic and working memory tasks. This explanation can also account for slower responses by CFS patients in focused attention and categoric search tasks.[32]

Other research has combined memory tasks with brain scanning, and the results showed that CFS patients process challenging auditory information as accurately as controls but have to use more regions of the network associated with the verbal WM system. Individuals with CFS appear to have to exert greater effort to process

auditory information as effectively as demographically similar healthy adults.[28]

It has been suggested that CFS may have many similarities to depression. This has led to studies comparing CFS and depressed patients with healthy controls.[6,8,15,30] An alternative way of examining the role of depression in memory problems in CFS is to compare CFS patients with and without depression. Effects of CFS may be restricted to those with or without depression. Alternatively, depression may influence memory, and the removal of this influence from the error term makes it more likely that you can detect an effect of CFS.

Another factor influencing the performance of CFS patients may be sleep disturbance. This is common in this group and is also known to have an effect on their cognitive functioning.[33] Again, it may be the CFS group with disrupted sleep that shows the greater performance decrement. Alternatively, removing the influence of sleep disturbance from the error term may make it easier to detect effects due to CFS. There are also other background factors that need to be controlled in research on memory. Memory performance will change with age and intelligence. It has not been suggested that sub-groups of CFS patients based on age or intelligence show the greatest impairments. However, both age and intelligence have direct effects on memory, and these effects should be removed in order to obtain a clearer profile of the effects of CFS on memory.

The aim of the present study was to continue the research on memory in CFS patients. The first aim was to confirm that these patients report real-life memory problems. Secondly, a range of different memory tasks was used in order to identify sensitive outcomes. It was predicted that the speed measures would be more sensitive than the accuracy variables. Memory for shapes was also examined, and it was predicted that this visual memory might be impaired in CFS. Finally, the analyses included measures of sleep disruption, depression, age and intelligence. Both the direct effects of these factors and their interactions with CFS/control groups were examined.

MATERIALS AND METHODS

Three separate studies were carried out. These studies were carried out with the informed consent of the volunteers and the approval of the local regional ethical committee. The present article presents studies that examined CFS and memory, then looked at depression, sleep, age and intelligence. Depression was measured using the Beck Depression Index,[34] insomnia from the symptom checklist, and intelligence was based on National Adult Reading scores (NART).[35]

The CFS patients were recruited from a specialist clinic. The healthy controls were recruited from a participant panel.

Study 1: Working memory

Participants

CFS patients: 8 males (mean age: 48.7 years, range 36-59 years), 13 females (mean age: 39.3 years, range 18-56). 61.9% married, 14.3% single, 23.8% divorced or separated.

Controls: 8 males (mean age: 39.9, range 18-57), 12 females (mean age 45.5 years, range 34-61 years). 35% married, 35% single, 30% divorced or separated.

The CFS and control groups did not differ in terms of age or socio-economic status.

The symptoms reported by the CFS patients are shown in Table 1. The CFS patients had a mean illness duration of 110.3 months (range 24-360 months). 57.1% were in the high depression (based on a median split) and high insomnia groups.

Table 1: Chronic Fatigue Syndrome Sample: Symptom checklist.

Physical weakness (50% more than before you were ill)	85.0%
Excessive fatigue (50% more than before you were ill)	81.0%
Legs feeling heavy	81.0%
Muscle pain	76.2%
Painful joints	61.9%
Pain in chest	42.9%
Nausea	52.4%
Indigestion	38.1%
Bloated stomach	57.1%
Wind	52.4%
Sore Throat	52.4%
Headache	57.1%
Earache	23.8%
Sore eyes	33.3%
Sensitive to noise	52.5%
Sensitive to light	66.7%
Feeling hot/cold	61.7%
Sweating	57.1%
Shivering	41.7%
Swollen glands	38.1%
Racing heart	42.9%
Insomnia	57.1%
Depression	57.1%
Anxiety/Panic	57.1%
Loss of concentration	81.0%
Loss of memory	76.2%
Allergies	28.6%

Working Memory Tests

These tasks were designed to investigate components of working memory (the central executive, articulatory loop and the visuospatial scratchpad).[39]

a) Serial Recall Test
This task is designed to investigate the articulatory loop of Baddeley's working memory model. A sequence of eight single-digit numbers was displayed on the computer screen. The numbers were presented consecutively at a rate of one per second. After observing the sequence, participants were required to write down the numbers in the order in which they had been shown. If they were unsure of a number, they were encouraged to guess. This process was repeated five times, and their responses were recorded on a response sheet.

b) Running Memory Task
Similar to the serial recall task, this was designed to examine the central executive of Baddeley's working memory model. A sequence of consecutive single-digit numbers was presented at a rate of one per second. However, the length of the sequence is unknown, and thus they did not know when it would end. Participants were required to write down the last five digits of the sequence in the order in which they had been presented. If unsure of a number, they were again encouraged to guess. This process was repeated three times, the sequence length varying each time.

c) Spatial Memory Task
This task is designed to investigate the visuo-spatial scratch pad described in Baddeley's working memory model. Participants were asked to concentrate on five red buttons displayed on a response box. The red buttons lit up in a randomised sequence consisting of eight flashes. After observing the light sequence, they were required to reproduce the sequence by pressing the buttons in the same order as previously presented. This process was repeated five times, and their responses were recorded on the computer.

Psychosocial Questionnaires
Psychosocial questionnaires showed that patients had a lower positive mood[36], higher negative mood[36], higher anxiety[37] and depression[33], greater fatigue[38], more somatic symptoms[38] and more cognitive difficulties[38] (see Table 2).

Table 2: Mental and physical symptoms of CFS patients and controls (means, SDS in parentheses).

Measure	CFS Patients	Controls
Positive mood	28.3 (11.8)	36.6 (11.1)
Negative mood	24.1(10.5)	14.2 (11.1)
CESD depression	43.3 {9.6)	30.7 (6.8)
Somatic symptoms	59.5 (17.1)	25.4 (11.5)
Fatigue	64.2 (12.0)	29.9 {20.1)
Cognitive difficulties	50.6 (14.7)	26.9 (13.8)
Beck depression inventory	15.1(6.5)	7:8 (9.8)
Trait anxiety	49.5 (10.4)	36.3 {10.0)
Cohen-Hobermann index of physical symptoms	25.9 (8.0)	6.4 (7.9)
Cognitive failures questionnaire	61.2 (17.8)	45.0 (13.1}
Perceived stress	27.4 (10.2)	22.7 (7.4)

Intelligence
National Adult Reading Test (NART)
A test of reading ability, well-preserved in those with cognitive impairment, involves reading out loud 50 words differing in pronounceability. Scores give an estimate of premorbid IQ.

RESULTS

The performance of the CFS patients was generally worse than the controls:

- Serial recall: CFS mean: 60.8% correct; Controls: 69.9% correct.
- Running memory: CFS mean 51.0% Controls: 61.2%
- Visual memory: Patients: 42.2% Controls: 45.4%

Analyses of variance were carried out on the performance data. The first compared the patients and the controls, whilst the second subdivided the patients and controls and also included age as a factor (groups being divided by a median split). Degrees of freedom vary because of missing data. There was no statistically significant difference in mean scores of the CFS and control groups on the serial memory task ($F=2.55$, $df=1,40$, $p < 0.1$). The analysis of variance for running memory demonstrated no significant effect on the group, indicating that there were no significant differences in mean performance ($F=2.75$, $df=1,40$, $p <0.1$). The analysis of variance for the visual memory sequence also revealed no significant difference in the performance of CFS patients and healthy controls ($F=1.14$, $df=1,34$, $P<0.29$).

The addition of age as a factor did not modify the differences between CFS and control groups. A third analysis included intelligence as a factor. Again division was based on a median split. This revealed an effect of intelligence on serial and visual memory sequence tasks ($F==5.46$, $df-=1,35$, $P<.05$; $F=7.68$, $df-=:1,29$, $P<.01$), although no effect was found for running memory. Again, these analyses showed no significant differences between the CFS/control groups.

Further sets of analyses were carried out, splitting the groups into those with high and low levels of depression (on the basis of a BDI median split; CFS depressed: 47.2%, CFS not depressed: 65.0%; Control depressed: 42.5% Control not depressed: 66.6%). The analyses demonstrated a significant effect of depression on running memory ($F=9.22$, $df=l,36$, $p<0.01$), but it was not found to be related to performance on either serial recall or visual memory sequence. In addition, CFS participants were also sub-divided into those with and

without insomnia. Analyses showed no statistical significance of sleep on performance for any task:

- Running memory F=2.54, df=2,36, p=0.09,
- Serial recall F=2.42, df=2,37, p=0.10,
- Visual memory F= 0.78, df=2,31, p=0.47.

Summary of results from study 1

Over 75% of the CFS patients reported memory problems. Performance of objective tests measuring the components of working memory showed that the CFS patients were worse than the controls but that the effects were not statistically significant. This suggests that larger sample sizes are needed to detect such objective memory impairments. Inclusion of age, intelligence, depression and insomnia did not alter the significance of the difference between patients and controls.

Study 2: Working memory, semantic processing and motor speed.

The next study examined both working memory and semantic memory tasks and included measures of both speed and accuracy. Motor speed was also measured using writing and simple reaction time tasks.

Participants

24 CFS patients aged 21 to 65 years took part in the study. The mean and standard deviation of their ages were 43.8 and 10.6 years. Fifteen (62.5%) were female, and nine (32.5%) were male. The average length of the patients' illness was 97.2 months, with a range of 1.5 - 30 years.

The 19 healthy controls were matched for age, gender, and educational level of the CFS patients. The mean and SD of their ages were 44.7 and 13.7 years. There were 11 females and eight males.

The reported symptoms and psychosocial scores are shown in Tables 3 and 4.

Table 3: Chronic Fatigue Syndrome Sample: Symptom checklist.

Physical weakness (50% more than before you were ill)	87.5%
Excessive fatigue (50% more than before you were ill)	83.3%
Legs feeling heavy	75%
Muscle pain	83.3%
Painful joints	79.2%
Pain in chest	45.8%
Nausea	29.2%
Indigestion	41.7%
Bloated stomach	58.3%
Wind	45.8%
Sore Throat	58.3%
Headache	66.7%
Earache	33.3%
Sore eyes	58.3%
Sensitive to noise	54.2%
Sensitive to light	66.7%
Feeling hot/cold	70.8%
Sweating	58.3%
Shivering	50.0%
Swollen glands	54.2%
Racing heart	54.2%
Insomnia	41.7%
Depression	29.2%
Anxiety/Panic	50.0%
Loss of concentration	79.2%
Loss of memory	75.0%
Allergies	37.5%

Table 4: Mental and physical symptoms of CFS patients and controls (means, SDS in parentheses).

Measure	CFS Patients	Controls
Positive mood	27.7 (10.2)	35.8 (11.9)
Negative mood	22.5 (12.0)	14.5 (11.0)
Somatic symptoms	54.4 (18.2)	25.4 (15.0)
Fatigue	59.4 (13.7)	24.2 (20.1)
Cognitive difficulties	46.5 (14.7)	22.8 (11.7)
Beck depression inventory	14.7 (7.3)	8.1 (8.1)
Trait anxiety	48.3 (11.5)	33.4 (11.1)
Cohen-Hobermann index of physical symptoms	23.5 (7.8)	5.7 (6.1)
Cognitive failures questionnaire	58.7 (14.0)	41.4 (16.9)
Perceived stress	25.2 (8.9)	23.6 (10.1)

DESCRIPTION OF THE TESTS

Semantic Processing Test

This was a timed test of semantic memory and involved answering true (e.g. canaries have wings) or false (e.g. dogs have wings) to fifty simple sentences indicating their general knowledge. Speed and accuracy were recorded.

Recall of Category Instances

The participant wrote down as many instances from a given category (e.g. animals or colours) as they could in a minute.

Digit-Symbol Substitution Test

This is a test of search and memory, measuring working memory. Participants drew symbols correctly matching digits which had been paired in a table at the top of the sheet. They carried out this task for 3 minutes, and speed and accuracy were recorded.

PSYCHOMOTOR TESTS

Word writing

This writing test measured the speed with which the participants copied a list of 25 5-letter words.

Simple reaction time test

This test of psychomotor speed measured the mean reaction time for responses to the appearance of a solid

square in a box on the screen. This test was completed in three minutes.

RESULTS

The CFS patients showed a general trend for worse performance, but the majority of the effects were not significant (see Table 5). The writing speed of patients with CFS was significantly slower $F=5.37$, $df=1,41$, $p<.05$.

Age and intelligence as covariates:

The age and NART scores were employed as covariates, CFS/controls group was the independent variables, and the performance scores (number of instances recalled, the speed and accuracy of semantic processing, and number of symbols drawn and accuracy on DSST) were used as dependent variables. The results showed effects of age on tests of recall of instances, semantic processing speed, speed on DSST (number of symbols drawn), writing speed, and simple reaction time. This shows that the tests are sensitive measures of changes in the state due to ageing. The NART scores only significantly affected semantic processing speed only ($p<.01$). After age and intelligence were adjusted, a significant difference between patients with CFS and matched controls was still only found for writing speed.

Table 5: Performance of CFS and control groups on the memory and psychomotor tasks (scores are the means, SDS in parentheses).

Test	CFS	Controls
NART	35.0 (7.2)	38.8 (5.1)
Recall of category instances	14.0 (4.5)	15.6 (4.2)
Semantic processing speed - completion time secs.	122.1 (33.1)	104.2 (33.7)
Semantic processing acc %	96.8 (2.5)	97.5 (2.3)
Digit symbol – speed – number completed	72.8 (19.8)	81.1 (23.3)
Writing speed - secs	54.3 (7.5)	43.7 (9.7)
Simple Reaction Time msecs	388 (120)	332 (110)

Effects of depression

The CFS patients and controls were sub-divided into two groups based on their median BDI scores to assess the effects of depression in CFS. The results showed that high depression was associated with slower motor responses, but it had no effect on the memory tasks and did not change the difference between the CFS patients and controls:

Writing speed (secs; mean (sd))

- CFS/high depression: 55.1 (19.2)
- CFS/low depression: 53.3 (15.7)
- Controls/high depression: 46.3 (11.6)
- Controls/low depression: 43.8 (9.7)

Simple Reation time (msecs; mean (sd))

- CFS/high depression: 404 (94)
- CFS/low depression: 367 (149)
- Controls/high depression: 388 (178)
- Controls/low depression: 321 (88)

When the CFS group were subdivided into those with and without insomnia, the main effects of groups were also observed in the psychomotor tasks and semantic processing speed. These significant effects reflected the CFS/insomnia group being slower than the CFS/no insomnia group and controls.

Semantic processing speed (secs; mean (sd))

- CFS/insomnia 140 (24)
- CFS/no insomnia 109 (34)
- Controls 104 (34)

Writing speed (secs; mean (sd))

- CFS/insomnia 55.6 (17)
- CFS/no insomnia 53.4 (19)
- Controls 43.7 (10)

Simple reaction time (msecs)

- CFS/insomnia 457 (160)
- CFS/no insomnia 348 (68)
- Controls 332 (110)

Summary of Study 2

This study confirmed that CFS patients report problems with memory. It also confirmed the slower motor performance of CFS patients, both in terms of simple reaction time and writing speed. The semantic memory and working memory tasks were also performed more slowly by the CFS group, but their accuracy was similar to the controls. Effects of age, intelligence and depression were found, but the addition of these factors did not change the CFS effects. The motor tasks were performed more slowly by the CFS patients with insomnia, and those without insomnia showed little difference from the control group. The memory tasks were not influenced by insomnia.

The next study used a task which involved real-life memory tasks, including a task often reported as problematic by CFS patients, namely recall of people's names.

Study 3: Doors and people task

This study used the Doors and people task[40], which measures immediate and delayed recall of verbal and visual material.

Participants

The demographic characteristics of the participants are summarised below:

- Mean age of female CFS patients (N=16): 45.3 years, range 22-65 years
- Mean age of male CFS patients (N=8): 41.8 years, range 24-59 years
- Mean age of female controls (N=11): 401. Years range 22-65 years
- Mean age of male controls (N=7): 49.1 years, range 28-67 years.
- Mean illness duration CFS patients: 95.2 months

The results from the symptom checklist are shown in Table 6.

Table 6: Chronic Fatigue Syndrome Sample: Symptom checklist.

Physical weakness (50% more than before you were ill)	87.5%
Excessive fatigue (50% more than before you were ill)	87.5%
Legs feeling heavy	79.2%
Muscle pain	83.3%
Painful joints	79.2%
Pain in chest	20.8%
Nausea	50.3%
Indigestion	20.8%
Bloated stomach	50.0%
Wind	33.3%
Sore Throat	50.0%
Headache	79.2%
Earache	29.2%
Sore eyes	58.3%
Sensitive to noise	70.8%
Sensitive to light	58.3%
Feeling hot/cold	75.0%
Sweating	58.3%
Shivering	41.7%
Swollen glands	41.7%
Racing heart	25.0%
Insomnia	41.7%
Depression	41.7%
Anxiety/Panic	45.8%
Loss of concentration	95.8%
Loss of memory	87.5%
Allergies	37.5%

The patients and controls also completed psychosocial questionnaires, and the usual differences between the groups were found (a more negative mood; greater fatigue; more cognitive difficulties; more somatic symptoms; higher anxiety and depression). These are shown in Table 7.

Table 7: Mental and physical symptoms of CFS patients and controls (means, SDS in parentheses).

Measure	CFS Patients	Controls
Positive mood	28.6 (10.5)	34.8 (10.8)
Negative mood	21.3 (10.5)	15.8 (10.5)
Somatic symptoms	54.3 (19.8)	23.6 (11.7)
Fatigue	64.6 (19.6)	27.7 (15.3)
Cognitive difficulties	45.0 (16.5)	25.6 (13.0)
Beck depression inventory	14.7 (7.3)	10.0 (7.0.1)
Trait anxiety	45.5 (10.7)	40.5 (11.8)
Cohen-Hobermann index of physical symptoms	25.0 (8.0)	7.5 (6.1)
Cognitive failures questionnaire	56.0 (19.4)	38.8 (16.4)
Perceived stress	23.6 (8.9)	22.6 (11.5)

Performance Tasks

Two tasks were used, the Doors and People test and a simple reaction time task. Immediate recall was examined, followed by the simple reaction time task, and then delayed recall.

The Doors and People Test

Immediate and delayed visual and verbal recall tasks were taken from the 'Doors and People' memory test. This test was thought to provide better ecological validity for investigating the more subtle memory impairments noted by CFS patients in their everyday lives. Both the People and Shapes tests used in the study were contained in a single flip chart presented to participants. For the Shapes test, participants were provided with a pencil and paper. Scoring details and conversion tables were taken from the Doors and People testing manual.

Immediate verbal recall

The 'People' test was comprised of four photographs presented via a flip chart. A name and occupation accompanied each photograph. Participants were asked to learn the 'names' of the four people and their occupations. Each photograph was presented for three seconds. After all, had been presented, the recall was prompted by the researcher with the occupation of each person, e.g. "What was the doctor's name?" Participants' performance was then scored. If the names were recalled correctly on trial one, then participants proceeded with the Shapes test; if not, the procedure was repeated for trials two and three.

Immediate visual recall

The 'Shapes' test contained four simple drawings based on a 'cross' design. Participants were asked to look at each drawing for five seconds and then copy it onto the paper provided. When all four had been copied, the researcher removed the copy and asked participants to draw them again from memory. If the drawings were not completely recalled correctly, then participants were shown the drawings again. This time they were not allowed to copy them, and the presentation time was reduced to three seconds. This procedure was followed for trials two and three.

Delayed verbal and visual recall elements of both tasks

For the People test, participants were asked to recall the names they had learned earlier. Their recall was recorded as the number correct. Participants were then asked to reproduce the drawings from the Shapes task. For analysis, participants' raw scores were converted into age-scaled scores using age-group norm tables listed in the Doors and People test.

Simple Reaction Time task:

This was the same task as described in study 2.

RESULTS

Simple reaction time task

As has been found in previous research, the patient group were significantly slower at the SRT task compared with the control group performance ($F = 4.97$; $df=1,40$, $p<0.05$). The mean reaction time for patients was 363.5 (ms) compared with a mean of 297.1 (ms) for the control group.

The results for the two groups on the different memory tasks are shown in Table 8.

Table 8: Performance of CFS patients and controls on the memory tasks (scores are the means and SDS and are age-adjusted).

	CFS (N=24)	Controls (N=18)
Age-scaled People	10.4 (3.5)	11.5 (2.7)
Age-scaled shapes	10.25 (3.2)	12.61 (2.85)
Combined age-scaled recall	10.6 (3.5)	11.5 (3.0)
Verbal forgetting	9.2 (3.4)	9.7 (3.2)
Visual forgetting	10.5 (2.4)	10.1 (2.6)
Combined forgetting	9.8 (3.55)	9.8 (3.0)

Comparison of patient and control· group performance of immediate verbal and visual recall and forgetting, taken from the difference between immediate and delayed recall found only age-scaled 'shapes' performance to be significantly different between the two groups ($p < 0.1$). No significant differences were found for age-scaled 'people' ($F = 1.28$, $df=1,40$, $p>0.1$), combined age-scaled recall, visual and verbal tests ($F = 0.72$, $df=1,40$, $p>0.1$), age-scaled 'verbal forgetting', people scores ($F = 0.20$, $df=1,40$, $p>0.1$), age- scaled 'visual forgetting', shapes scores ($F = 0.20$, $df=1,40$, $p>0.1$) and 'overall forgetting' combined verbal and visual age-scaled forgetting ($F = 0.00$, $df=1,40$, $p>0.1$).

The effect of age and intelligence on the performance of memory and SRT tasks

After controlling for the possible effects of age and intelligence, the difference between patient and control group SRT was only significant at the one-tailed level ($F = 3.80$, $df=1,37$, $p<0.1$ and $p>0.05$).

Intelligence was found to have a highly significant effect for age-scaled people ($F = 14.21$, $df=1,39$, $p<0.01$), shapes ($F = 14.13$, $df=1,39$, $p<0.01$) and combined age-scaled recall ($F= 9.52$, $df=1,39$, $p<0.01$). This did not alter the significant differences between CFS patients and controls found for shapes nor the non-significant differences found for both people and combined recall. There were no significant effects of intelligence on either verbal (people), visual (shapes) or overall (verbal and visual) forgetting scores ($p>0.1$). Thus, immediate recall was found to be sensitive to variations in premorbid intelligence, whilst forgetting scores were not. Scores used in the analysis were adjusted for age-group norms, and so age was not introduced as a covariate.

The role of depression in the performance of memory and SRT tasks

After both groups were sub-divided into high (scoring above the median, 10.5) and low (below 10.5) depression, a two-way ANOVA showed a highly significant effect of depression on the combined age-scaled recall ($F =5.05$, $df=1,36$, $p<0.05$). Age-scaled people did not quite reach significance at the 5% level ($F = 4.01$, $df=1,36$, $p>0.05$). No significant effects of the depression were found for either SRT, age-scaled shapes ($p>0.1$), verbal forgetting ($p>0.05$), or visual and overall forgetting tasks ($p>0.1$).

Effects of insomnia

Patients were divided into those with and without insomnia and compared with control group performance using analysis of variance. There was a slight effect of sleep on SRT performance, showing patients with insomnia to be slower than other patients, though this did not quite reach significance at the 5% level ($F = 2.81$, $df=2,39$ $p<0.1$). The effects of sleep on memory performance were also analysed for age-scaled memory scores. No significant differences were found for age-scaled people, combined recall, verbal and visual forgetting and overall forgetting scores ($p>0.1$). The significant effect of groups on age-scaled shapes scores ($F = 48.96$, $df=2,39$ $p<0.01$), was found by post-hoc testing to reflect only a difference between patient groups and controls, as the control group was not divided by insomnia.

Summary of study 3

These results confirm the subjective reports of memory problems by CFS patients. They also confirm the slower reaction times of the CFS patients. The only memory task which showed a significant difference between the CFS and control groups was the immediate recall of shapes. These significant effects were not due to intelligence, depression or insomnia. No other significant effects of CFS were observed when other factors were included in the analyses, although these other variables

did have direct effects (e.g., intelligence was important in immediate recall but not forgetting).

DISCUSSION

The results presented here confirm subjective reports of memory problems by CFS patients. They also confirm slower reaction times and demonstrate that the writing speed of CFS patients is slower. The speed of response by CFS patients in certain semantic memory and working memory tasks was also slower, although accuracy was not impaired. All of these results confirm the view that response speed may underlie many of the reported memory impairments of CFS patients. This view was supported by the results from the Doors and People test, where the shapes test, requiring a motor response, was the only task that showed impaired performance by the CFS group.

Analyses including age, intelligence, depression and insomnia provided little evidence of the effects of CFS reflecting these factors. This does not mean that these variables have no effects on performance, but rather, they are direct effects rather than modifications of the effects of CFS. These effects of age, intelligence, depression and insomnia demonstrate the sensitivity of the tests, which shows that the limited effects of CFS do not reflect the use of insensitive measures.

One important factor to consider is the size of the effects of CFS. In all of the studies, the general trend of the results was for the CFS group to be impaired relative to controls. The lack of significance probably reflects the effect size. Future research on memory impairments in CFS should be powered to detect small effect sizes rather than the moderate sizes that much of the previous research has tried to detect.

CONCLUSIONS

The results of the present studies confirm that CFS patients report memory impairments. Objective testing of memory showed few significant differences between CFS patients and controls, although the general trend was for the CFS group to have worse performance than the controls. Significant effects were found in the speed of performance, and this was observed in reaction times, writing speed and the speed of certain memory tasks. The immediate visual recall involving drawing shapes was also significantly worse in the CFS group. Age, intelligence, depression and insomnia had some direct effects of performance but did not underlie effects of CFS. Future research should consider the effects of CFS on memory as small effects and use appropriate sample sizes to obtain statistically significant differences from controls.

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