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## **MEMORY IMPAIRMENTS IN CHRONIC FATIGUE SYNDROME PATIENTS**

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#### ABSTRACT

**Background:** Chronic Fatigue Syndrome (CFS) patients often report memory problems. Prior research has produced conflicting results on this topic. Episodic memory impairments appear to be robust, but tasks assessing other aspects of memory (e.g., working and semantic memory) show slower speed but no decrease in accuracy. This study examined whether the memory problems of CFS patients reflect slower responses. **Methods:** CFS patients were recruited from a specialist clinic. Sixty-seven patients carried out tasks measuring immediate recall, delayed recognition memory, logical reasoning and semantic processing. The control group were 126 healthy volunteers recruited from the general population. **Results:** The CFS patients recalled fewer words and had poorer delayed recognition. The other tasks showed slower speed but no effect on accuracy. **Conclusions:** CFS patients have poorer immediate recall and delayed recognition memory. The delayed recognition memory probably reflected the poorer immediate recall. Slower responding was present in three of the tasks, and it is possible that this also accounted for the reduced immediate recall.

**KEYWORDS:** CFS, Chronic Fatigue Syndrome, Memory, Free Recall, Recognition Memory, Working Memory, Semantic Memory, Speed and Accuracy.

#### INTRODUCTION

Chronic Fatigue Syndrome (CFS) is mainly characterised by persistent fatigue, but this can be accompanied by cognitive problems such as reports of impairment of memory. Some research has suggested that objective measurement of memory does not confirm the problems reported by the patients.<sup>[1,2]</sup> This lack of significant memory differences between CFS patients and controls has been confirmed in some of the research.<sup>[3-13]</sup> However, other studies found memory impairments in CFS patients.<sup>[14-30]</sup> These memory impairments have been interpreted in terms of impaired concentration, less effort and speed of processing.<sup>[14,15]</sup>

Other research has suggested that only certain types of tasks are impaired in CFS patients. For example, impairments in CFS have been shown to be restricted to more demanding memory tasks.<sup>[23]</sup> Visual memory tasks also appear to be more likely to be impaired.<sup>[27]</sup> Research has also examined the type of processing that may be involved. For example, one study suggested that impairments reflected poorer initial storage rather than retrieval.<sup>[26]</sup> Other studies have combined memory tasks with brain scanning, and findings showed that individuals with CFS are able to process challenging auditory information as accurately as controls but utilise more extensive 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.<sup>[28]</sup>

Another selective effect obtained in research on memory and CFS has been that CFS patients have slower information processing speed but show no differences in accuracy.<sup>[25]</sup> This view has been confirmed in studies of CFS and selective attention in choice reaction time tasks, with the CFS group having slower responses but not differing in aspects of selective attention.<sup>[31]</sup>

Research from our laboratory has shown that CFS patients have impairments in immediate free recall and delayed recognition memory of a list of words.<sup>[16-18]</sup> Other tasks involving working memory and semantic processing have shown that these are performed more slowly by CFS patients but that there is no difference in accuracy. The aim of the present analyses was to replicate these effects on recall and recognition and to examine whether effects on other outcomes are restricted to speed rather than accuracy.

#### MATERIALS AND METHODS

The study was carried out with the informed consent of the volunteers and the approval of the local regional ethical committee.

## **Participants**

Sixty-seven Chronic Fatigue Syndrome patients attended the Health Psychology Research Unit for testing. There were 20 males and 47 females whose ages ranged from 17 to 63 in the case of males with a mean age of 39.65, and 17 and 73 in the case of females, with a mean age of 43.49. 59.1% of the Chronic Fatigue patients were married, 33.3% were single, 6.1% were divorcees, and 1.5% were widowed. One hundred and twenty-six members of the general population were recruited to take part in the study as controls for a Chronic Fatigue sample. They were recruited from an advertisement in the local press and selected to participate on the basis of age and occupational status. Of the 126 general population participants, there were 43 males and 83 females. The males ranged in age from 21 to 66 years with a mean age of 39.14 (S.D.=13.53), and the females from 21 to 79 years with a mean age of 40.48 (S.D.=13.02). 50.8% of the general population participants were married, 32.5% were single, 15.9% were divorcees, and 0.8% were widowed. The patients and controls did not differ significantly in terms of gender, age, occupational status, or pre-morbid intelligence (measured using the National Adult Reading Test). Details of the reported symptoms and psychosocial characteristics of the sample are given in an earlier article.<sup>[31]</sup>

## Memory tasks

*Free recall task*: The participants were shown a list of 20 words presented at the rate of one every 2 seconds. At the end of the list, they had 2 minutes to write down (in any order) as many of the words as possible.

*Logical reasoning task*: Participants were shown statements about the order of the letters A and B followed by the letters AB or BA (e.g. A follows B BA). They had to read the statement and decide whether it was a true description of the order of the letters. If it was, the volunteer pressed the T key on the keyboard, if it wasn't, they pressed the F key. The sentences ranged in syntactic complexity from simple active to passive negative (e.g. A is not followed by B). The volunteers completed as many as possible in 3 minutes.

*Semantic processing task:* This task measures the speed of retrieval of information from general knowledge. Participants were shown a sentence and had to decide whether it was true (e.g., canaries have wings) or false (e.g. dogs have wings). The number completed in 3 minutes was recorded.

**Delayed recognition memory task:** At the end of the test session, the participants were shown 40 words which consisted of the 20 words shown at the start plus 20 distractors. The participant had to decide whether each word had been shown in the original list or not.

## RESULTS

#### Free recall task

Table 1 shows the results from the free recall task. **Table 1: Results from the free recall task.** 

Number recalled

	m	sd
Controls	7.47	1.99
Patients	6.75	2.13
	Number	correct
	m	sd
Controls	6.89	2.06
Patients	6.27	2.02
	Number	incorrect
	m	sd
Controls	0.59	0.81
Patients	0.48	0.17

Three Wilcoxon tests were performed to test differences between the Control and Chronic Fatigue Syndrome groups for number recalled, number correct, and number incorrect. The results showed that for number recalled, there were significant differences between groups (X2=4.84; df=1; p<0.05), for number correct, there were also significant differences between groups (X2=3.87; df=1; p<0.05), but for number incorrect there were no significant differences between groups (X2=0.49; df=1; p>0.05). The results indicate that Patients recalled fewer words than the Controls and that they recalled fewer words correctly but recalled similar numbers of incorrect words.

## Logical reasoning test

Table 2 shows the results from the logical reasoning task. Table 2: Results from the logical reasoning task.

Table 2. Results from the logical reasoning task					
	Number completed		% co	% correct	
	m	sd	m	sd	
Controls	36.35	12.6	78.11	19.46	
Patients	32.37	11.31	74.58	20.2	

A Wilcoxon test examining differences between the Control and the Chronic Fatigue Syndrome groups for the number of trials completed showed a significant difference between the groups (X2=4.28; df=1; p<0.05). A Wilcoxon test between Control and Chronic Fatigue groups for per cent correct showed no significant differences between the groups (X2=1.66; df=1; p>0.05). These results indicate that the Chronic Fatigue group completed fewer trials but had similar accuracy rates to the Control group.

## Semantic processing test

Table 3 shows the results from the semantic processing task.

## Table 3: Results from the semantic processing task.Number done% correct

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	m	sd	m	sd
Controls	99.1	24.71	95.06	2.81
Patients	84.8	24.46	95.68	3.19

A Wilcoxon test which examined differences between Patients and Controls for the number done showed significant differences between groups (X2=13.13; df=1; p<0.01). A Wilcoxon test for per cent correct did not show differences between groups, however (X2=2.35; df=1; p>0.05), illustrating that Patients completed fewer trials than controls but obtained similar accuracy rates.

#### Delayed recognition memory test

Table 4 shows the accuracy results of the delayed recognition memory test. A Wilcoxon test examined differences between the Chronic Fatigue Syndrome patients and the Control group and for 'Hits' showed significant differences between groups (X2=5.21; df=1; p<0.05). For 'False Alarms', a Wilcoxon test showed no significant differences between groups (X2=3.11; df=1; p>0.05). These results indicate that the Chronic Fatigue patients had fewer 'Hits' (identified fewer correct words) but made similar numbers of 'False Alarms' (make false identification of incorrect words). The fewer hits plausibly reflect the smaller number of words correctly recalled immediately after the presentation.

Table 4: Results from the delayed recognitionmemory task.

	Hits	
	m	sd
Controls	15.71	2.68
Patients	14.35	3.72
	False Alarms	
	m	sd
Controls	4.91	2.83
Patients	4.09	2.72

Reaction times were also recorded in this task, and these results are shown in Table 5.

# Table 5: Reaction time (msec) results from thedelayed recognition memory task.

	Hits	
	m	sd
Controls	993	249
Patients	1422	958
	False Alarms	
	m	sd
Controls	1350	563
Patients	1857	1203

Wilcoxon tests showed significant differences between the Chronic Fatigue and Control groups for 'Hits' (X2=15.92; df=1; p<0.01) and for 'False Alarms' (X2=14.0; df=1; p<0.01). These results indicate that the Chronic Fatigue patients were slower at responding both when correctly identifying a word and when incorrectly identifying a word.

Overall, the present results support the view that the impaired memory performance of the chronic fatigue syndrome patients largely reflects slower responding rather than differences in accuracy. The slower response could even reflect the poorer free recall, where slower writing speed may lead to an impaired recall.

#### DISCUSSION

The results presented here confirm the slower performance of memory tasks by CFS patients. The slower responses were observed in the delayed recognition memory task, logical reasoning task and semantic processing task. Tasks which demonstrated significant effects for speed rarely showed significant effects for accuracy. The exceptions to this were the immediate free recall and delayed recognition memory task. The reduced recognition memory accuracy plausibly reflected the lower levels of immediate recall. The immediate free recall task involved writing down the words, and it is likely that the CFS patients took longer to do this. The longer writing time may then have had a negative impact on the subsequent recall of more words.

A recent study<sup>[31]</sup> investigated whether CFS patients had impaired selective attention in choice reaction time tasks. The results showed no difference in selective attention between CFS patients and controls, although the speed of response of the CFS patients was slower than that of controls. It should be pointed out that the varying results in studies of memory in CFS patients could reflect variation in correlated attributes of CFS. The most likely factors are depression and sleep problems, and these have been shown to be important in the cognitive problems of CFS patients.<sup>[21,32]</sup> Further research is needed to address this issue, and it will also be important to use other memory tasks and measures of both speed and accuracy to determine whether explanations based on slower responses will generalise to other aspects of memory.

## CONCLUSIONS

The results of the present study confirm that CFS patients have impaired performance on recall and recognition memory tasks, logical reasoning and semantic processing. The slower speed of performing the tasks was apparent, and it is suggested that this may lead to impaired recall due to the longer time taken to write down the words.

## REFERENCES

- Ray C, Phillips L, Weir WR. Quality of attention in chronic fatigue syndrome: Subjective reports of everyday attention and cognitive difficulty, and performance on tasks of focused attention. Br. J. Clin. Psychol, 1993; 32 Pt 3: 357–364. doi: 10.1111/j.2044-8260.1993.tb01068.x.
- Cockshell SJ, Mathias JL. Cognitive functioning in people with chronic fatigue syndrome: a comparison between subjective and objective measures. Neuropsychology, 2014 May; 28(3): 394-405. doi: 10.1037/neu0000025.
- 3. Cockshell SJ, Mathias JL. Cognitive deficits in chronic fatigue syndrome and their relationship to

psychological status, symptomatology, and everyday functioning. Neuropsychology, 2013 Mar; 27(2): 230-42. doi: 10.1037/a0032084.

- Krupp LB, Sliwinski M, Masur DM, Friedberg F, Coyle PK. Cognitive functioning and depression in patients with chronic fatigue syndrome and multiple sclerosis. Arch Neurol, 1994 Jul; 51(7): 705-10. doi: 10.1001/archneur.1994.00540190089021.
- Cope H, Pernet A, Kendall B, David, A. Cognitive functioning and magnetic resonance imaging in chronic fatigue. British Journal of Psychiatry, 1995; 167: 593–597.
- Riccio M, Thompson C, Wilson B, Morgan DJ, Lant AF. Neuropsychological and psychiatric abnormalities in myalgic encephalomyelitis: a preliminary report. Br J Clin Psychol, 1992 Feb; 31(1): 111-20. doi: 10.1111/j.2044-8260.1992.tb00975.x.
- Joyce E, Blumenthal S, Wessely S. Memory, attention, and executive function in chronic fatigue syndrome. J Neurol Neurosurg Psychiatry, 1996 May; 60(5): 495-503. doi: 10.1136/jnnp.60.5.495.
- Vercoulen JH, Bazelmans E, Swanink CM, Galama JM, Fennis JF, van der Meer JW, Bleijenberg G. Evaluating neuropsychological impairment in chronic fatigue syndrome. J Clin Exp Neuropsychol, 1998 Apr; 20(2): 144-56. doi: 10.1076/jcen.20.2.144.1160.
- Kane RL, Gantz NM, DiPino RK. Neuropsychological and psychological functioning in chronic fatigue syndrome. Neuropsychiatry Neuropsychol Behav Neurol, 1997 Jan; 10(1): 25-31.
- Scheffers MK, Johnson R Jr, Grafman J, Dale JK, Straus SE. Attention and short-term memory in chronic fatigue syndrome patients: an event-related potential analysis. Neurology, 1992 Sep; 42(9): 1667-75. doi: 10.1212/wnl.42.9.1667. PMID: 1513453.
- Caseras, X., Mataix-Cols, D., Giampietro, V., Rimes, K. A., Brammer, M., Zelaya, F., Chalder, T., & Godfrey, E. L. (2006). Probing the working memory system in chronic fatigue syndrome: A functional magnetic resonance imaging study using the n-back task. Psychosomatic Medicine, 68(6): 947-955.

https://doi.org/10.1097/01.psy.0000242770.50979.5f

- Busichio K, Tiersky LA, Deluca J, Natelson BH. Neuropsychological deficits in patients with chronic fatigue syndrome. J Int Neuropsychol Soc., 2004 Mar; 10(2): 278-85. doi: 10.1017/S1355617704102178.
- Moss-Morris R, Petrie KJ, Large RG, Kydd RR. Neuropsychological deficits in chronic fatigue syndrome: artifact or reality? J Neurol Neurosurg Psychiatry, 1996 May; 60(5): 474-7. doi: 10.1136/jnnp.60.5.474.
- 14. Grafman J, Schwartz V, Dale JK, Scheffers M, Houser C, Straus SE. Analysis of neuropsychological functioning in patients with

chronic fatigue syndrome. J Neurol Neurosurg Psychiatry, 1993 Jun; 56(6): 684-9. doi: 10.1136/jnnp.56.6.684.

- Sandman CA, Barron JL, Nackoul K, Goldstein J, Fidler F. Memory deficits associated with chronic fatigue immune dysfunction syndrome. Biol Psychiatry, 1993 Apr 15-May 1; 33(8-9): 618-23. doi: 10.1016/0006-3223(93)90100-r.
- Smith AP. Cognitive changes in Myalgic Encepalomyelitis. In: A.Jenkins and J. Mowbray (eds), Postviral Fatigue Syndrome. Wiley: London, 1991; 179-1994.
- Smith AP. Chronic fatigue syndrome and performance. In: Handbook of Human Performance, Vol.2: Health and performance. (eds) A.P.Smith & D.M. Jones. London: Academic Press, 1992; 261-278.
- Smith AP, Behan PO, Bell W, Millar K, Bakheit M. Behavioural problems associated with the chronic fatigue syndrome. British Journal of Psychology, 1993; 84: 411-423.
- Thomas MA, Smith AP. An investigation into the cognitive deficits associated with chronic fatigue syndrome. The Open Neurology Journal, 2009; 3: 13-23. Doi: 10.2174/1874205X009030010013
- Fukuda K, Straus SE, Hickie I, Sharpe MC, Dobbins JG, Komaroff A. The chronic fatigue syndrome: a comprehensive approach to its definition and study. International Chronic Fatigue Syndrome Study Group. Ann Intern Med., 1994 Dec 15; 121(12): 953-9. doi: 10.7326/0003-4819-121-12-199412150-00009.
- DeLuca J, Johnson SK, Beldowicz D, Natelson BH. Neuropsychological impairments in chronic fatigue syndrome, multiple sclerosis, and depression. J Neurol Neurosurg Psychiatry, 1995 Jan; 58(1): 38-43. doi: 10.1136/jnnp.58.1.38.
- Vollmer-Conna U, Wakefield D, Lloyd A, Hickie I, Lemon J, Bird KD, Westbrook RF. Cognitive deficits in patients suffering from chronic fatigue syndrome, acute infective illness or depression. Br J Psychiatry, 1997 Oct; 171: 377-81. doi: 10.1192/bjp.171.4.377.
- Marshall PS, Forstot M, Callies A, Peterson PK, Schenck CH. Cognitive slowing and working memory difficulties in chronic fatigue syndrome. Psychosom Med., 1997 Jan-Feb; 59(1): 58-66. doi: 10.1097/00006842-199701000-00008.
- Dobbs BM, Dobbs AR, Kiss I. Working memory deficits associated with chronic fatigue syndrome. J Int Neuropsychol Soc., 2001 Mar; 7(3): 285-93. doi: 10.1017/s1355617701733024.
- 25. Deluca J, Christodoulou C, Diamond BJ, Rosenstein ED, Kramer N, Natelson BH. Working memory deficits in chronic fatigue syndrome: differentiating between speed and accuracy of information processing. J Int Neuropsychol Soc., 2004 Jan; 10(1): 101-9. doi: 10.1017/S1355617704101124.
- 26. Michiels V, Cluydts R, Fischler B, Hoffmann G, Le Bon O, De Meirleir K. Cognitive functioning in

patients with chronic fatigue syndrome. J Clin Exp Neuropsychol, 1996 Oct; 18(5): 666-77. doi: 10.1080/01688639608408290.

- 27. Aoun Sebaiti M, Hainselin M, Gounden Y, Sirbu CA, Sekulic S, Lorusso L, Nacul L, Authier FJ. Systematic review and meta-analysis of cognitive impairment in myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). Sci Rep., 2022 Feb 9; 12(1): 2157. doi: 10.1038/s41598-021-04764-w.
- Lange G, Steffener J, Cook DB, Bly BM, Christodoulou C, Liu WC, Deluca J, Natelson BH. Objective evidence of cognitive complaints in Chronic Fatigue Syndrome: a BOLD fMRI study of verbal working memory. Neuroimage, 2005 Jun; 26(2): 513-24. doi: 10.1016/j.neuroimage.2005.02.011.
- Marcel B, Komaroff AL, Fagioli LR, Kornish RJ 2nd, Albert MS. Cognitive deficits in patients with chronic fatigue syndrome. Biol Psychiatry, 1996 Sep 15; 40(6): 535-41. doi: 10.1016/0006-3223(95)00422-x.
- 30. Constant EL, Adam S, Gillain B, Lambert M, Masquelier E, Seron X. Cognitive deficits in patients with chronic fatigue syndrome compared to those with major depressive disorder and healthy controls. Clin Neurol Neurosurg, 2011 May; 113(4): 295-302. doi: 10.1016/j.clineuro.2010.12.002.
- 31. Smith AP. Cognitive impairments in Chronic Fatigue Syndrome Patients: Choice reaction time, encoding of new information, response organisation and selective attention. World Journal of Pharmaceutical and Medical Research, 2022; 8(4): 27-36.
- 32. Smith AP, Pollock J, Thomas M, Llewelyn M, Borysiewicz LK. 1996. The relationship between subjective ratings of sleep and mental functioning in healthy subjects and patients with Chronic Fatigue Syndrome. Human Psychopharmacology, 1996; 11: 161-167.