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Working memory deficits associated with chronic fatigue syndrome

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Abstract

Cognitive impairments are among the most frequently reported and least investigated components of the chronic fatigue syndrome (CFS). As part of a multifaceted study of the CFS, the present study investigated the cognitive functioning of chronic fatigue patients. The performance of 20 CFS patients was compared to that of controls ($N = 20$) on 4 tests of working memory (WM). Digit Span Forward was used to assess the storage capacity of WM. Multiple aspects of central executive functioning were assessed using several standard measures: Digit Span Backward, and Trails A and Trails B. More recently developed measures of WM were used to assess control of processing under temporal demands (working memory task) and resistance to interference (a sustained attention task). Deficits were restricted to more demanding tasks, requiring resistance to interference and efficient switching between processing routines. The overall results clearly implicate deficits in the control aspects of central executive function in CFS. (*JINS*, 2001, *7*, 285–293.)

Keywords: Chronic fatigue syndrome, Cognitive deficits, Working memory

INTRODUCTION

The chronic fatigue syndrome (CFS) is a debilitating illness with no known etiology and an uncertain prognosis (Evans, 1991; Greenberg, 1990). As the name of the syndrome suggests, the primary symptom is severe, incapacitating fatigue. The original case definition (Holmes et al., 1988) was modified in 1992 (Schluederberg et al., 1992), with a revised case definition published by the Centers for Disease Control/National Institutes of Health in 1994 (Fukuda et al. 1994). The revised case definition for CFS requires the presence of unexplained or relapsing fatigue that is of new or definite onset, not substantially alleviated by rest, and results in substantial reduction in previous level of functioning. In addition, four or more of seven specified symptoms must be present, concurrent with the fatigue, for 6 months or more (Fukuda et al., 1994). Self-reported impairments in short-term memory or concentration, severe enough to cause a substantial reduction in occupational, educational, or social functioning are included as one of the criterial symptoms noted above.

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Cognitive complaints from CFS patients are common (Euba et al., 1996; Hickie et al., 1990; Klonoff, 1992; Komaroff & Buchwald, 1991, Straus, 1988), ranking next to fatigue in frequency of reported symptoms (Klonoff, 1992). According to Straus (1988), concentration difficulties are among the most frequently cited, with up to 90% of CFS patients reporting this impairment. Other estimates of the prevalence of self-reported cognitive impairments in CFS range from 50 to 90% (Buchwald et al., 1992; Euba et al., 1996; Klonoff, 1992; Komaroff & Buchwald, 1991; Straus, 1988). These impairments are not only a cause of considerable morbidity but are a major reason for leaving the workplace (Grafman et al., 1993).

Despite the high frequency of patient reports about changes in cognitive functioning, cognitive impairments are among the least studied features of CFS (Grafman et al., 1993; Johnson et al., 1996). Moreover, the evidence that is available is mixed, with some studies showing deficits, whereas others do not (Altay et al., 1990; Blackwood et al., 1998; Brickman & Fins, 1993; Daugherty et al., 1991; DeLuca et al., 1993, 1995, 1997; Gaudino et al., 1997; Grafman et al., 1993; Johnson et al., 1996; Joyce et al., 1996; Krupp et al., 1994; Marcel et al., 1996; Marshall et al., 1996, 1997; McDonald et al., 1993; Michiels et al., 1996; Millon et al., 1989; Ray et al., 1993; Riccio et al., 1992;

Sandman et al., 1993; Vercoulen et al. 1998; Vollmer-Conna et al., 1997). This might be expected when the entire range of cognitive skills is considered because there is no reason to suspect that all cognitive abilities would be affected equally. However, apparent inconsistencies exist even when only a limited range of cognitive processes, such as those involved in working memory, is considered.

A close examination of the differences in the control groups and tasks of previous studies helps to resolve the apparent inconsistencies. In this regard, there have been two approaches to determining baseline normal performance. One approach has been to use normative data for appropriate age groups. The other approach has been to select a sample of healthy, same-aged control participants with attention to matching those subjects with CFS patients on other characteristics such as education level, IQ, and socioeconomic status, variables known to be associated with performance on a wide variety of cognitive tasks (Lezak, 1983; Poon et al., 1984). This latter approach may be especially important with an illness such as CFS in which patients (for whatever reason) tend to be more highly educated, have higher IQs, and higher socioeconomic status (Altay et al., 1990; Grafman et al., 1991; Klonoff, 1992). In addition, the tasks from previous studies also vary in their sensitivity to detecting impairments. That is, very simple tasks such as Digit Span and Trails A are not very sensitive tasks, whereas tasks which are more cognitively complex (e.g., Paced Auditory Serial Addition Task, PASAT; Stroop) are more sensitive to a wider array of memory, attention, and other cognitive deficits (Lezak, 1995).

Given these methodological differences, one would expect that studies using the simple tasks would be less likely to show deficits in CFS patients than studies using the more demanding tasks. In addition, studies employing appropriately matched control groups should be more sensitive to deficits than those comparing CFS patient performance to age appropriate normative data, without attention to relevant dimensions such as education and IQ. As Table 1 shows, the previous findings are consistent with these expectations. The tasks in the table are arranged, generally, from the simplest to the most complex. The cognitively simple tasks fail to reveal deficits, regardless of the type of control group, with the exception of two studies (Michiels et al., 1996; Vercoulen et al., 1998). Vercoulen et al. did report a significant difference between CFS and control individuals on Trails A, a simple sequencing task. Somewhat surprisingly, the difference disappeared when the scores were corrected for attention span "effects," even though the attention span difference was not significant. Michiels et al. (1996) reported a significant difference between CFS patients and matched controls on Trails A, with CFS patients slower (30.34 s) than controls (25.52 s).

A number of studies have investigated working memory by administering the digit span tasks (forward and backward) but reporting only the combined score (Brickman & Fins, 1993; DeLuca et al., 1993, 1995; Gaudino et al., 1997; Grafman et al., 1993; Krupp et al., 1994; Millon et al., 1989). However, because the two tasks involve very different mental activities which can be affected differently by pathology (Banken, 1985; Kaplan et al., 1991), interpretation of these findings is less clear. As conceptualized in Baddeley's model, digits forward provides a measure of storage capacity whereas digits backward also involves central executive control of mental manipulation of the stored information. Because CFS may be anticipated to affect only the task involving mental control, summing performance on this task with that on the digit forward task would dilute effects, as is reflected by the variability of findings using the combined measure. The most discrepant finding on combined digit span was reported by Millon et al. (1989), wherein better performance was found for the CFS individuals compared to age based norms. However, the reported scores (CFS = 12.08; norm aged 20–29 = 8.78; norm aged 40–49 = 7.13) are difficult to resolve in terms of their methodology or traditional scoring.

Michiels et al. (1996) reported poorer performance between individuals with CFS and controls on digit span forward, a simple attentional task. However, rather than reporting data intended to measure span, they administered all sets of digit strings and reported total number of digits correct. Number of digits correct for supraspan series reflects learning and perhaps organization and recall strategies that are not intended to be measured by the digit span test, and are the types of processes one might expect to be impaired in CFS.

As noted above, the digit span backward task is a more difficult task in that it requires a reordering of the information for recall. However, this reordering can be accomplished without time constraints. Most studies (Blackwood et al., 1998; Johnson et al., 1996; McDonald et al., 1993; Vercoulen et al., 1998) do not report CFS deficits as compared to normal controls or norms on digit span backward. Two studies (DeLuca et al., 1997; Michiels et al., 1996) do report CFS deficits. Whether there are sample differences (e.g., more severely affected CFS individuals) that might account for when CFS deficits are and are not found with this task is not known. Nevertheless, the general finding is for there not to be a deficit reported when CFS and normal control groups are compared on the digit span backward task.

The intermediate tasks, in general, show deficits but only when more careful attention is paid to the nature of the control sample. With few exceptions, studies using the most demanding tasks, for which deficits would show the most pronounced effects, report deficits in CFS patients, regardless of whether the control measure came from normative data or the inclusion of a healthy control group.

Although considerations of task difficulty are helpful in resolving the apparent inconsistencies of previous findings, these considerations are of limited value for elucidating the cognitive deficits associated with CFS. We have found that using a conceptual framework such as the working memory model proposed by Baddeley (1986) provides a more coherent basis for understanding at least some of the memory (processing) dysfunction associated with CFS.

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Table 1. Summary of previous studies

Task	Investigators	Control Group	Findings
Trails A	Altay et al. (1990)	Norms	NS[a]
	Riccio et al. (1993)	Age/Educ/IQ/Sex	NS
	Sandman et al. (1993)	Norms	NS
	Brickman & Fins (1993)	Age/Educ	NS
	Krupp et al. (1994)	Age/Educ	NS
	DeLuca et al. (1995)	Age/Educ/Sex	NS
	Michiels et al. (1996)	Age/Educ/IQ/Sex	CFS worse
	Vercoulen et al. (1998)	Age/Educ/Sex	CFS worse
Digit Span (Combined)	Millon et al. (1989)	Norms	CFS better
	Brickman & Fins (1993)	Age/Educ	CFS worse[e]
	Grafman et al. (1993)	Age/Educ	NS
	DeLuca et al. (1993)	Age/Educ/IQ	CFS worse
	Krupp et al. (1994)	Age/Educ	NS
	DeLuca et al. (1995)	Age/Educ/Sex	NS
	Gaudino et al. (1997)	Age/Educ/IQ	NS
Digit Span (Forward)	Smith, 1991	Age/Educ	NS
	McDonald et al. (1993)	Norms	NS
	Michiels et al. (1996)	Age/Educ/IQ/Sex	CFS worse[c]
	Blackwood et al. (1998)	Age/Sex/IQ	NS
	Johnson et al. (1996)	Age/Educ	NS
	Marcel et al. (1996)	Age/Educ/IQ	NS
	DeLuca et al. (1997)	Age/Educ/Sex	NS
	Vercoulen et al. (1998)	Age/Educ/IQ	NS
Digit Span (Backward)	McDonald et al. (1993)	Norms	NS
	Michiels et al. (1996)	Age/Educ/IQ/Sex	CFS worse[c]
	Blackwood et al. (1998)	Age/Sex/IQ	NS
	Johnson et al. (1996)	Age/Educ	NS
	DeLuca et al. (1997)	Age/Educ/Sex	CFS worse[d]
	Vercoulen et al. (1998)	Age/Educ/IQ	NS
Trails B	Altay et al. (1990)	Norms	CFS better
	Riccio et al. (1992)	Age/Educ/IQ/Sex	NS
	Sandman et al. (1993)	Norms	NS
	Brickman & Fins (1993)	Age/Educ	CFS worse
	Krupp et al. (1994)	Age/Educ	NS
	DeLuca et al. (1995)	Age/Educ/Sex	NS
	Michiels et al. (1996)	Age/Educ/IQ/Sex	CFS worse
	Gaudino et al. (1997)	Age/Educ/IQ	NS
	Vercoulen et al. (1998)	Age/Educ/IQ	NS
Digit Symbol	Altay et al. (1990)	Norms	CFS better
	Brickman & Fins (1993)	Age/Educ	CFS worse
	Krupp et al. (1994)	Age/Educ	CFS worse
	Michiels et al. (1996)	Age/Educ/IQ/Sex	CFS worse
	Gaudino et al. (1997)	Age/Educ/IQ	CFS worse
	Blackwood et al. (1998)	Age/Educ/IQ	NS
	Vercoulen et al. (1998)	Age/Educ/IQ	CFS worse
Attention and Sequencing Tasks[f]	Daugherty et al. (1991)	Norms	CFS worse
Star Cancel	McDonald et al. (1993)	Norms	CFS worse
Serial 7s	McDonald et al. (1993)	Norms	CFS worse
Sternberg task	Vollmer-Conna et al. (1993)	Age/Educ/IQ	CFS worse
Stroop (Interference)	Brickman & Fins (1993)	Age/Educ	CFS worse[g]
	Ray et al. (1993)	Age/Educ/Sex	NS
	Smith et al. (1993)	Age/Educ	CFS worse
	Marcel et al. (1996)	Age/Educ/IQ	CFS worse
	Marshall et al. (1997)	Age/Educ/IQ/Sex	NS
PASAT[h]	DeLuca et al. (1993)	Age/Educ/IQ	CFS worse
	DeLuca et al. (1995)	Age/Educ/Sex	CFS worse
	Johnson et al. (1996)	Age/Educ	CFS worse
	DeLuca et al. (1997)	Age/Educ/Sex	CFS worse
	Kane et al. (1997)	Age/Educ/Sex	No difference
	Marshall et al. (1997)	Age/Educ/IQ/Sex	CFS worse

[a]NS = not significantly different.
[b]Wechsler Memory Scale.
[c]Nonstandard administration.
[d]CFS–no psychiatric impairment group.
[e]Males only.
[f]Wisconsin Neuropsychological Test Battery.
[g]Females only.
[h]Paced Auditory Serial Addition Test.

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According to Baddeley (1986), working memory is an active system with two types of components: slave systems for the temporary storage of information and a central executive, which controls processing. Baddeley and others have provided evidence consistent with the existence of components concerned with storage of verbal and spatial information (Baddeley, 1984, 1986; Frick, 1988). The central executive is assumed to be a limited capacity system responsible for coordinating the processing demands of storage and other processing (e.g., retrieval, search) and, as such, is postulated to play a role in many cognitive tasks (Babcock & Salthouse, 1990; Baddeley, 1986; Dobbs & Rule, 1989; Morris & Jones, 1990). Deficits in central executive functioning are associated with an impairment in attention, selection, activation, inhibition, and/or coordination of information processing (Baddeley, 1986). Interestingly, these working memory deficits are strongly reminiscent of the types of difficulties most frequently reported by CFS patients.

In an attempt to identify more specifically the underlying cognitive deficits, the present study, part of a larger multidisciplinary investigation of the CFS, investigated cognitive performance of CFS patients and matched controls on tasks measuring different aspects of working memory function. Storage capacity was assessed using the forward Digit Span Test. Multiple aspects of central executive functioning were assessed using several standard measures: (1) Digit Span Test Backward, a measure of manipulation of information in working memory without temporal constraints; (2) Trails A, a simple sequencing task; and (3) Trails B, a sequencing task that requires multiple shifts between sequences. Several more recent measures designed to tap central executive functioning also were used: (4) the Dobbs and Rule working memory task (Dobbs & Rule, 1989), a task that emphasizes more intensive manipulation of information with temporal demands; and 5) a sustained selective attention task, the resources task (Dobbs & Li, 1990), which was used as an index of the ability to resist interference from background noise during processing. Taken together, these tasks provide an assessment of the storage capacity of working memory and multiple aspects of mental control. The mental control tasks range from those in which strong prior learning must be inhibited (e.g., Trails B), to ones involving constant shifting of mental processes with temporal constraints (e.g., Dobbs and Rule Working Memory Task), and continuous selective attention (e.g., Resources Task).

METHODS

Research Participants

Patients were diagnosed by an infectious disease specialist at the University of Alberta Hospitals using the CFS criteria (Holmes et al., 1988; Schluederberg et al., 1992). Individuals were excluded from the study if (1) they were diagnosed with CFS for longer than 5 years, (2) were on steroid or nonsteroidal antiinflammatory therapy, and/or (3) carried a diagnosis of fibromyalgia, diabetes, hypertension, or osteomalacia/rickets. Twenty healthy volunteers were *individually* matched to the 20 CFS participants with respect to age, sex, education, and estimated verbal, performance, and full scale IQ (Wilson Barona Index Formula; Barona et al., 1984: Wilson et al., 1978). The means and ranges/standard deviations for these matching variables are shown in Table 2. All participants underwent complete medical examinations that included medical and surgical histories and recent and current medications. None of the control participants had any past or present condition(s) that would exclude them from inclusion in a normal control group. Participants entered the protocol only after informed consent was obtained.

Procedure

The tests were administered in the morning in a constant order: Digit Span, Dobbs and Rule Working Memory Task, Trails A and B, and the Resources Task. In addition to the cognitive tests, the Beck Depression Inventory (Beck et al., 1961) was administered to all research participants to provide a measure of depression.

Forward and backward Digit Span Tests were administered and scored using standard procedures (Wechsler, 1945). Performance measurements included number correct and number of errors for each of the tests. The Trail Making Test (Trails A and B) performance measures were task completion time and number of errors (Halstead, 1947; Reitan & Davison, 1974).

For the Dobbs and Rule working memory task (Dobbs & Rule, 1989), randomly ordered digit sets were presented auditorily (1 digit/1.8 s). Four response conditions were ordered as follows: Report the digit just presented (*lag zero*), report the digit one prior to the digit just presented (*lag 1*),

Table 2. Demographics of CFS patients and controls: means, ranges/standard deviations

Group	Age	Sex	Educ	VIQ[a]	PIQ[b]	FIQ[c]
CFS	37.7; (18–48)	12 (F); 8 (M)	14 (11–19)	110.1 (7.13)	107.6 (5.19)	109.6 (6.93)
Controls	37.9; (25–51)	12 (F); 8 (M)	15 (11–18)	110.2 (6.97)	107.5 (5.52)	109.6 (6.79)

[a]Verbal IQ as estimated by Wilson-Barona Index Formula.
[b]Performance IQ as estimated by Wilson-Barona Index Formula.
[c]Full Scale IQ as estimated by Wilson-Barona Index Formula.

report the digit two before the one just presented (*lag 2*), and report the digit three before the one just presented (*lag 3*). A total of 10 correct responses was possible in all conditions. Performance was scored in terms of total number correct to first error.

For the resources task (Dobbs & Li, 1990), the participants listened to taped messages that differed in familiarity and linguistic complexity. The messages consisted of an easy and familiar rhyme (*Mary Had A Little Lamb*) and a difficult rhyme that was less familiar and more syntactically complex (*Cock Robin*). Each participant was presented with two trials of each rhyme. Half of each group received the easier rhyme followed by the more difficult rhyme with the remainder in each group receiving the more difficult rhyme followed by the easier rhyme. Background noise consisted of four unrelated passages, each read simultaneously by five people, with each person starting at a different point in the passage. This resulted in unintelligible, but distinctively verbal, "crowd noise." During testing, the background noise was adjusted to a threshold, wherein threshold was the highest decibel level of the noise at which the person could just comprehend the target rhyme. Each individual controlled the adjustment of the background noise level by signalling the tester through defined hand movements whether the adjustment was to be of higher or lower intensity. This continued until the person signalled that the background noise was at the level which just allowed comprehension. Approximately 3 s after this signal, the tape was stopped without warning and the participant was asked to repeat the last two words presented to ensure the person could comprehend the message at the chosen level of background noise. Threshold was further checked by having the loudness of the background noise preset approximately 4 dB above the threshold determined by the participant. If the participant correctly identified the last two words of the rhyme at the predetermined level, the decibel level was progressively increased until the participant failed to correctly identify the last two words using this procedure. The dependent measure was the final decibel level of the background noise for each of the rhymes.

Statistical Analyses

Scores from each of the tasks were first analyzed by multivariate analysis of variance using diagnosis (CFS, controls) as the between-subject factor. The task conditions formed the within-subject factors. A second analysis was carried out treating the task conditions as between-subject factors as if no matching of participants had been accomplished. This provides a check on the robustness of the findings because a between-subjects analysis is an overly conservative test when there is close matching of participants. The findings from the first analysis are reported here.

RESULTS

The group means for the tasks are shown in Table 3. Performance for Digit Span Forward and Backward are presented in the first two rows. There was a main effect for test in that performance was better on Digit Span Forward than on Digit Span Backward [$F(1,19) = 57.67$, $p < .001$]. However, the trend for CFS patients to perform less well than the control group on the span tasks was not statistically reliable.

Table 3. Performance of the CFS and control groups

Task	CFS *M* (*SD*)	Controls *M* (*SD*)
Digit Span Forward	6.35 (1.06)	6.90 (.83)
Digit Span Backward	4.50 (1.02)	5.05 (1.72)
Trails A Time	28.02 (10.85)	25.40 (9.10)
Trails A Errors	0.20 (0.4)	0.25 (0.64)
Trails B Time	61.25 (13.42)	53.65 (17.01)
Trails B Errors	0.45 (0.60)	0.25 (0.44)
Resources Task*	68.13 (3.09)	70.04 (2.30)

*CFS significantly different from controls, $p < .037$.

CFS group performance did not differ significantly [$F(1,19) = .30$, $p > .59$] from controls on total number of errors for Trails A or Trails B (Table 3), nor were there significant differences [$F(1,19) = 2.63$, $p > .12$] between the CFS patients and the controls on time to completion. As expected, time to completion was faster for Trails A than for Trails B [$F(1,19) = 157.49$, $p < .001$].

For the Dobbs and Rule (1989) working memory task, error-free performance was obtained for both groups in the lag zero condition. This indicates that all participants could perceive the digits and respond within the allotted time and that any performance decrements with lag 1 to 3 must be due to the additional requirements for mental manipulations of information required by those tasks. The mean performance for lags 1 to 3 are shown in Figure 1. For these conditions, there was a main effect for group [$F(1,19) = 11.22$, $p < .003$] indicating that the CFS group ($M = 5.13$) performed less well than the controls ($M = 6.68$). There also was a main effect of lag [$F(2,38) = 55.80$, $p < .001$], such that both groups' performance decreased from lags 1 through 3 (M lag 1 = 8.81, M lag 2 = 5.06, M lag 3 = 4.1). The Group × Lag interaction was not reliable.

On the resources task, both groups tolerated higher decibel levels of the background noise for the easy ($M = 71.11$) compared to the more difficult message [$M = 67.06$; $F(1,17) = 204.62$, $p < .001$]. This confirms the effectiveness of the background noise for reducing resources, and subsequently reducing the amount of resources needed for processing the messages. As predicted, the CFS participants required lower levels of background noise to perceive the target rhyme compared to control participants [$F(1,17) = 5.11$, $p < .037$; Table 3]. There was a significant Rhyme Type (easy, difficult) × Trial interaction [$F(1,17) = 6.00$, $p < .025$]. The difference between the easy and more difficult rhymes was slightly larger on Trial 1 (M difference = 4.67) than on Trial 2 (M difference = 3.57). The Group × Difficulty of Rhyme interaction was

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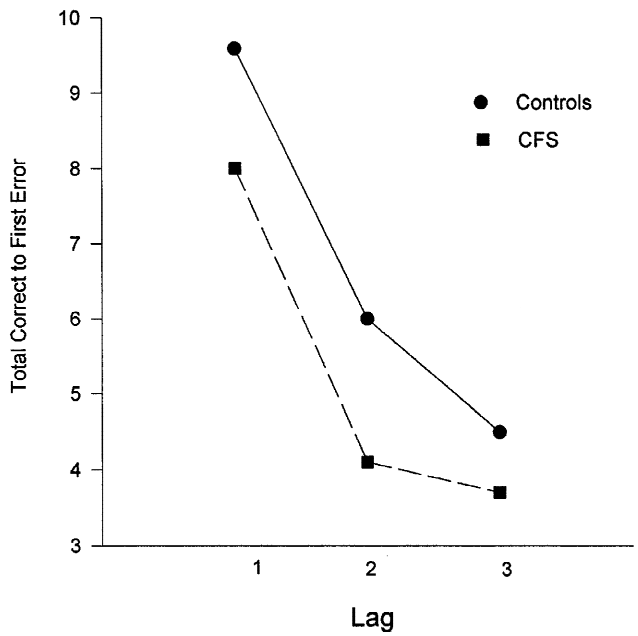

Fig. 1. CFS and control groups mean total correct to first error as a function of lag.

not statistically significant. The pattern of results from the threshold checks confirms the findings from the threshold measures as determined in the first half of the task.

There has been considerable debate about the contribution of depression to the symptoms associated with CFS. Although the present study was not intended to address this issue specifically, it is of interest to consider the extent to which depression might have contributed to the findings for the CFS group. To test this, the CFS subjects were classified in terms of their degree of depression as measured by the Beck Depression Inventory (*mild*: 5–7; *moderate*: 8–15, *severe*: > 16). A multivariate analysis of variance for the CFS group was then conducted. The analysis included level of depression and the task conditions as between-subject factors. The main effect for level of depression was nonsignificant, Wilks's Lambda $[F(2,17 = 1.56, p > .23]$, indicating that level of depression within the CFS group was not reliably related to performance on the cognitive tasks.

DISCUSSION

Consistent with previous research (Brickman & Fins, 1993; Daugherty et al., 1991; DeLuca et al., 1993, 1995, 1997; Gaudino et al,, 1997; Johnson et al. 1996; Joyce et al. 1996; Marcel et al., 1996; McDonald et al., 1993; Michiels et al., 1996; Smith et al., 1993; Vercoulen et al., 1998; Vollmer-Conna et al., 1997), the findings indicate reliable differences in performance between the CFS participants and an appropriately matched control group for the difficult tasks, with only unreliable trends for differences on the simple tasks. Baddeley's (1986) model of working memory provides a useful framework for understanding what constitutes simple and difficult tasks. One kind of simple task requires little in the way of mental control. A second kind of simple task does require mental control, but there are relaxed or generous time limits within which the mental control can be completed, even when it is slowed by pathology. In either of these kinds of simple tasks, a decrease in the efficiency of mental control would be missed. Difficult tasks are ones requiring mental control either to (1) sustain a processing routine in the face of distractions, or (2) shift among mental processes or processing routines within a limited time frame such that slowed or otherwise inefficient mental control will impair performance. The pattern of the present findings adds to a growing body of literature indicating that tasks requiring mental control are the ones most likely to show impairments in individuals with CFS. This will be illustrated in the following discussion of the present findings.

The Digit Span Forward task places few demands on the control aspects of working memory; instead it provides a measure of the storage capacity of WM. This task did not reveal performance differences between the two groups. This indicates that the locus of CFS deficits is not in decreased storage capacity. This is not surprising in that (storage) capacity aspects of WM seem to be spared in normal aging (Dobbs & Rule, 1989) and are only marginally affected by various pathologies (Bromley, 1958; Caird, 1966; Inglis & Caird, 1963; Kriauciunas, 1968). For example, longitudinal studies have found forward digit span to be unimpaired in patients with mild-to-moderate dementia of the Alzheimer's type (Botwinick et al., 1986), unimpaired or only mildly decreased in patients with Korsakoff's syndrome (Kopelman, 1985), and normal forward digit span performance has been reported in patients with frontal lobe damage (Lezak, 1979; Teuber, 1964). Similarly, there was no impairment in CFS individuals when the task involved a simple well-learned sequence with minimal mental control requirements (Trails A).

The Backward Digit Span task has been considered by some to provide an assessment of mental control, since one must mentally manipulate the information (reverse the order of the digits) to successfully complete the task. However, the amount of time required to complete the mental manipulation is not constrained in this task. The lack of temporal constraints or a time measure may be a critical shortcoming, in that efficiency (or amount of mental manipulation that can be completed per unit of time) is a very important aspect of mental control. This becomes apparent when the patients' abilities are assessed with tasks that do involve temporal constraints. In the present study, the Dobbs and Rule working memory task exemplifies this type of task, which has demonstrated sensitivity in distinguishing minor head injury, normal aging, and early dementia (Dobbs & Rule, 1989; Schwartzberg et al., 1992, 1988). With the Dobbs and Rule working memory task, digits are presented at a fixed rate and the person must respond within that time frame. Lag zero was not impaired for the CFS group, indicating that these patients can complete the encoding and response

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requirements within the allotted time frame. However, when mental manipulation involving shifts among the processing required for storage, retrieval, and updating of memory was introduced (lags 1–3), the CFS patients showed deficits in performance. Consistent with an interpretation of impaired mental control, CFS patients show deficits on a variety of tasks placing demands on mental control including Serial sevens and star cancellation (McDonald et al., 1993), the Sternberg task (Vollmer-Conna et al., 1997), a spatial working memory task (Joyce et al., 1996), and the Stroop interference task (Brickman & Fins, 1993; Marcel et al., 1996; Smith et al., 1993). Two studies (listed in Table 1) failed to find increased interference on the Stroop task. The data from Ray et al. (1993) did show the pattern of greater interference on the Stroop for a CFS group compared to a control group (61.50 *vs.* 48.58 s), but the difference was not statistically reliable. In the Marshall et al. (1997) study, a CFS group did not demonstrate an interference effect compared to controls. It may be important to note, however, that the Marshall et al. methodology was limited to the number of items correct in 45 s. Lezak (1995) notes that even patients with substantial deficits on the Stroop tasks can be missed when the task is limited to only 1 or even 2 min.

The Paced Auditory Serial Addition Task (PASAT) of Gronwall (1977) is another example of a task placing heavy demands on mental manipulation with strict time constraints. Digits are presented at a fixed rate and the person is to give the sum of the last two digits presented. DeLuca et al. (1993, 1995, 1997), Johnson et al. (1996) and Marshall et al. (1997) all report CFS deficits on the PASAT (but see Kane et al., 1997). Johnson et al. compared performance of a CFS group to that of healthy controls on the PASAT and a visually presented version of this task. Results revealed the CFS group was impaired only on the auditory (PASAT) version. The results were interpreted as indicating a selective deficit in the storage aspect of working memory as it is conceptualized by Baddeley (1986). More specifically, because the task showed CFS deficits only with the auditory presentation of the task, it was suggested that this indicated a selective impairment of the phonological loop, whereas the visual–spatial scratchpad was unaffected. This interpretation positions the CFS impairment as a storage deficit rather than one affecting central executive (mental control) functioning. There is, however, a cautionary note about the Johnson et al. (1996) interpretation. Brooks (1968) has shown that, when the presentation and response modalities are the same, there is greater interference than when the presentation modality (e.g., visual) is different from the response modality (e.g., aural). Brooks' findings indicate demands on mental control may have been lessened in the visual version of the task because this change resulted in different input and output modalities.

Another way of assessing mental control is through the use of a task that involves sustained selective attention. The resources task used in this study represents that aspect of mental control in that an ongoing message was presented in the presence of continuous background noise which must be suppressed. The reduced ability of the CFS patients to perform on this task again implicates a deficit in mental control. Interestingly, this finding is consistent with CFS patient reports of particular difficulties in functioning in the presence of multiple sources of stimulation and of being easily distracted by irrelevant stimuli (Smith, 1991; Straus, 1988).

A time measure is part of Trails B, and that task does require repetitive shifting between well-learned alphabetical and numerical sequences. On the surface, then, it seems that this task should have resulted in poorer performance by CFS patients if they have deficits in mental control. Unfortunately, this task allows for speed–accuracy trade-offs, and this may account for why statistically reliable performance differences between the two groups were not obtained, results consistent with previous research (DeLuca et al., 1995; Gaudino et al., 1997; Krupp et al., 1994; Riccio et al., 1992; Sandman et al., 1993; Vercoulen et al., 1998). Recall that in absolute terms, the CFS group was less accurate and required more time on the Trails B task. This suggests that if the CFS group had responded at the same rate as the control group, their accuracy rate would have suffered, or conversely, if they had performed at the same level of accuracy, the response rate of the CFS patients would have had to be slower. Tasks such as this are less than ideal and should be avoided in future studies. In any case, the indication of speed–accuracy trade-offs, without reliable differences on either accuracy or time measures, provide neither strong support for deficits in mental control nor evidence to the contrary.

Taken together, the findings from the present research suggest that the CFS may have minimal or negligible effects on the storage capacity of working memory but pronounced effects on the efficiency of mental control. This interpretation is consistent with previous reports of substantial CFS deficits on tasks that require the manipulation of complex information (Brickman & Fins, 1993; Daugherty et al., 1991; DeLuca et al., 1993, 1995, 1997; Gaudino et al., 1997; Johnson et al., 1996; Joyce et al., 1996; Marcel et al., 1996; McDonald et al., 1993; Michiels et al., 1996; Prasher et al., 1990; Smith et al., 1993). These findings, and the interpretation, may have value not only in reconciling the current and past research, but also in predicting under what circumstances CFS patients will show deficits on both laboratory and real-world tasks. The prediction is that whenever a task places a premium on mental control with temporal constraints, or when there are requirements for sustained control, CFS patients are likely to show deficits. The importance of temporal constraints in exposing deficits suggests that processing skills *per se* may not be altered. Instead, it is more likely to be the efficiency with which those processes can be controlled (initiated, sustained, and terminated) that is altered in CFS. This impaired efficiency could result in deficits in a wide variety of work situations, driving, and even recreational pursuits. Using a conceptual framework such as that introduced by Baddeley (1986) can help to organize and interpret the existing research and suggest fruitful avenues of research. The present findings and interpretation point to important deficits in executive control associated with CFS.

Future research directed toward delineating the extent and nature of cognitive deficits associated with CFS will be important for a more complete understanding of the syndrome and for defining functional limitations.

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