Author(s): Attree, Elizabeth A.; Dancey, Christine P.; Pope, Alison L.
Title: An Assessment of Prospective Memory Retrieval in Women with Chronic Fatigue Syndrome Using a Virtual-Reality Environment: An Initial Study.
Year of publication: 2009
Citation: Attree, E.A.; Dancey, C.P.; Pope, A.L. (2009) 'An Assessment of Prospective Memory Retrieval in Women with Chronic Fatigue Syndrome Using a Virtual-Reality Environment: An Initial Study.' CyberPsychology & Behavior 12 (4) pp.379-385
Link to published version: http://dx.doi.org/10.1089/cpb.2009.0002
DOI: 10.1089/cpb.2009.0002

CyberPsychology & Behavior
Volume 12, Number 4, 2009

DOI: 10.1089/cpb.2009.0002

An Assessment of Prospective Memory Retrieval in Women with Chronic Fatigue Syndrome Using a Virtual-Reality Environment: An Initial Study

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Abstract

People with chronic fatigue syndrome (CFS) have increased rates of depression, anxiety, and illness intrusiveness; they may also suffer from cognitive problems such as retrospective memory (RM) deficits and concentration difficulties that can stem from diminished information-processing capability. We predicted that this diminished capacity may also lead to deficits in other cognitive functions, such as prospective memory (ProM). Event-, time-, and activity-based ProM was assessed in 11 women with CFS and 12 healthy women using a computer-generated virtual environment (VE). RM was assessed using a free-recall test, and subjective assessment of both ProM and RM was assessed by questionnaire. Groups were equivalent in age and measures of IQ. People with CFS performed slightly worse than healthy controls on both the event- and time-based ProM measures, although these were not statistically significant. However, the CFS group performed significantly worse than the healthy controls on both the free recall-task and on subjective assessment of both RM and ProM. Women with CFS do have some subtle decrements in memory, particularly RM. However, it is possible that the decrements found in the present sample would be greater in real life. Further studies utilizing both healthy controls and illness controls are now needed to ascertain how sensitive the VE measure is and to inform the development of tasks in the VE that place progressively increasing demands on working memory capacity.

Introduction

Chronic fatigue syndrome (CFS) is a debilitating and often disabling condition, the etiology of which is now thought to be multifactorial. A viral infection, combined with lifestyle factors such as taking inadequate rest at the initial stages and high stress may all contribute to CFS[1] The predominant characteristic of CFS is severe fatigue, especially following physical or mental exertion. Muscle pains, unrefreshing sleep, swollen glands, sore throats, and headaches are also features of this condition, which is estimated to affect 0.5% of the population. Moreover, women are three times more likely than men to be diagnosed with CFS.[2] For a formal diagnose CFS, the symptoms must be present for at least 6 months. In addition to physical complaints, one of the diagnostic symptoms is loss of memory and difficulties in concentration.[3] The proportion of CFS patients who complain of cognitive impairments is high, with assessments ranging from around 75%[4] to 95%.[5]

A review of work-related impairments in CFS found rates of job loss associated with the condition ranged from 26% to 89%[6]; these impairments include cognitive limitations, such as difficulty learning and remembering new material, keeping appointments, and sustaining concentration. Whether CFS patients show cognitive deficits compared to healthy controls or other illness groups depends, of course, on the task set. The evidence for objectively observable deficits in cognitive measures is inconsistent.[7] However, a number of studies have found that CFS participants perform more slowly on timed tasks,[(eg,8)] indicating that slowed information processing may account for cognitive deficits in CFS. DeLuca et al.[5] found that participants with CFS took longer to learn word lists and retrieved fewer items in a delayed recall test. They proposed that memory deficits in CFS may be due to diminished information-processing capability, which impairs CFS participants' initial learning and subsequent ability to retrieve information. One type of memory that does not appear to have been tested in people with CFS is prospective memory (ProM), which is thought to place heavy demands on working memory capacity.

ProM has been defined as "remembering to carry out intended actions at an appropriate point in the future."[9]

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Kvavilashvili and Ellis[10] distinguished three types of ProM task based on differences in their contextual retrieval demands: event-, time-, and activity-based tasks. Event-based ProM tasks are cued by an external situation, such as remembering to pass on a message when seeing a friend. Activity-based intentions are associated with carrying out a specific task before or after another activity, such as remembering to turn off the oven after cooking. In contrast, time-based ProM tasks are dependent on self-initiated monitoring, as they involve doing something at a predesignated time.

The suggestion that retrieving an intended action from memory is a controlled process[eg,5] implies that ProM tasks place demands on finite attentional resources at the point of memory retrieval. Smith[11] found empirical evidence to support the view that intentions to carry out event-based ProM tasks absorb attentional resources, which are assumed to be employed in monitoring the environment and maintaining a "state of readiness to perform the task." ProM is notoriously difficult to measure experimentally, which may explain why there appears to be no published research to date on memory for future intentions in CFS. Studies of cognitive functioning in CFS have used standardized clinical tests, which have been criticized for failing to reflect the complex interaction of cognitive functions required in everyday life.[12–14] This pilot study aimed to address such limitations by partially replicating research[15] that used a computer-generated virtual environment (VE) to assess ProM functioning in other participant groups. VE assessment provides an opportunity to study complex cognitive functioning in a more ecologically valid way than standardized clinical tests while maintaining experimental levels of control.[22–23] Based on the existing literature on cognitive function in people with CFS, we hypothesized that CFS participants would have less available attentional resources than healthy controls and would consequently have more difficulty remembering to carry out future intentions while engaged in an ongoing task. Based on the finding that people with CFS show slower information processing,[5] we predicted that CFS participants would have more difficulty encoding information and would consequently perform below the level of healthy controls on the retrospective free-recall measure. We also expected that CFS participants would rate their memory functioning as worse than controls.

Materials and Methods

Design

The study employed a quasi-experimental design by comparing CFS participants' performance on RM and ProM measures with that of healthy control participants.

Participants

Twenty-three women took part in the study. The inclusion criteria for CFS participants were that they must have been diagnosed with the condition by a medical practitioner at least 1 year ago and that they were presently still suffering from CFS. Prospective participants were excluded from the study if they had a comorbid illness. The 11 CFS participants were recruited from a recent (2006–2008) database of people who met the criteria and had expressed an interest in taking part in research. The participants were drawn from the Myalgic Encephalomyelitis (ME) Association and Action for ME, two national British charities catering for the needs of people with CFS/ME (chronic fatigue syndrome/myalgic encephalomyelitis). The participants ranged in age from 29 to 62 years ($M = 47.09$). Illness duration ranged from 3 years to 15 years ($M = 6.77$). The healthy control and CFS participants were matched for age and educational status. The control group comprised a convenience sample of 12 women aged 29 to 60 years ($M = 41.5$). Control participants were recruited via word of mouth and posters displayed in the university. No remuneration was offered to participants for participating in the study, although four of the control group took part to meet university course requirements.

Materials and procedure

Testing sessions took place at the university or in participants' homes (depending on their preference) and lasted approximately 1 hour and 45 minutes. The apparatus, including the laptop, and materials were taken to the participants' homes if this was their preferred location. Each participant completed four types of cognitive function assessment and two self-report questionnaires, described below. The procedural order of tasks follows that of Brooks et al.[15]: it was "rotated." Therefore, the first participant completed the ProM assessment (real and virtual), followed by the RM task, Wechsler Test of Adult Reading (WTAR),[16] Wechsler Abbreviated Scale of Intelligence (WASI),[17] Prospective and Retrospective Memory Questionnaire (PRMQ),[18] and Hospital Anxiety and Depression Scale (HADS).[19] The second participant completed the RM task, WTAR, WASI, PRMQ, HADS, and ProM assessment (real and virtual), and so on.

ProM Assessment (real life and virtual reality). ProM was tested by using both real-life and virtual-environment assessments. Before commencing the VE assessment, participants were asked if they could lend the researcher a small personal item (e.g., a watch) and were told to observe where it had been hidden. They were then instructed to request the return of the personal item from where it had been hidden and to ask for a participant information sheet immediately after completing the VE assessment task. This real-life assessment measure was based on item 3 of the Rivermead Behavioural Memory Test.[20] Immediately after these instructions had been given, participants were given a brief "tour" of the VE bungalow with an accompanying voice recording that explained the furniture-removal task.

The VE assessment was run on a laptop computer (Toshiba Satellite Pro P100 with an Intel Core Duo T2400 1.83GHz processor on a 100-GB SATA [5400 RPM] hard drive and a 667-MHz FSB) with a 17″ color screen. The program was written using Superscape VRT software to create a virtual bungalow with five rooms. The computer-generated 3D bungalow consisted of an entrance hall (Figure 1) with different colored doors leading to four rooms. Figure 2 shows an example of one of the rooms, the kitchen.

The bungalow contained 54 items of furniture and household objects with "to go" labels on them, four of which were made of glass. Participants were told that the owner of the bungalow was moving to a larger house with eight rooms. Their task was to identify which of the items in the bungalow should be moved to each of the rooms in the new house.

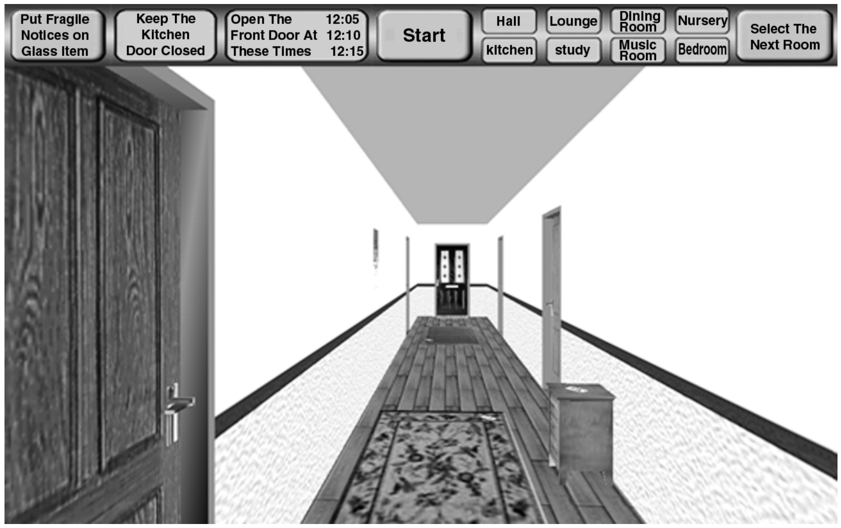

FIG. 1. Virtual bungalow (hall).

These rooms were shown on the toolbar at the top of the screen (see Figures 1 and 2). Participants were informed that the owner of the bungalow had left three additional instructions to be carried out while engaged in the furniture-removal task. These instructions were to remind the tester to place "fragile" labels on any glass items (event-based task), to shut the door each time they left the kitchen to prevent the owner's cat from escaping (activity-based task), and to open the front door for the removal men at exactly 5-minute intervals (at 12.05, 12.10, and 12.15) using the clock at the top of the screen (time-based task). Participants were *not* told that there was a time limit in which to complete the task.

Before the VE task began, a list of six instructions appeared on the screen. These six instructions included the three listed previously that the participants had to ask the tester to perform. The participants were asked to correctly identify the three tasks from the six listed. If they failed to identify the correct tasks, the program automatically reminded them and prompted them to select the correct tasks from the list. In order to control for the potentially confounding factor of the participants' varying levels of expertise in navigating the VE and consequent varying levels of cognitive demand, participants did not have to concern themselves with operating the laptop. The researcher, under the direction of the participant, used the arrow keys to move around the bungalow and controlled the mouse. Each chosen item for removal to the designated room was selected using the mouse, and in response to a click, the item disappeared from the visual display. When participants had chosen the items (labeled fragile as appropriate) for a specified room, they then instructed the tester to select the next room from the toolbar. At any point during the furniture removal task, participants could ask the tester to check the time on the clock at the top of the screen. The program timed out after 18 minutes, and participants were again asked to recall from a list the three ProM tasks that they had been asked to perform.

Participants were provided with feedback on their performance (in written form) and an explanation of the purpose

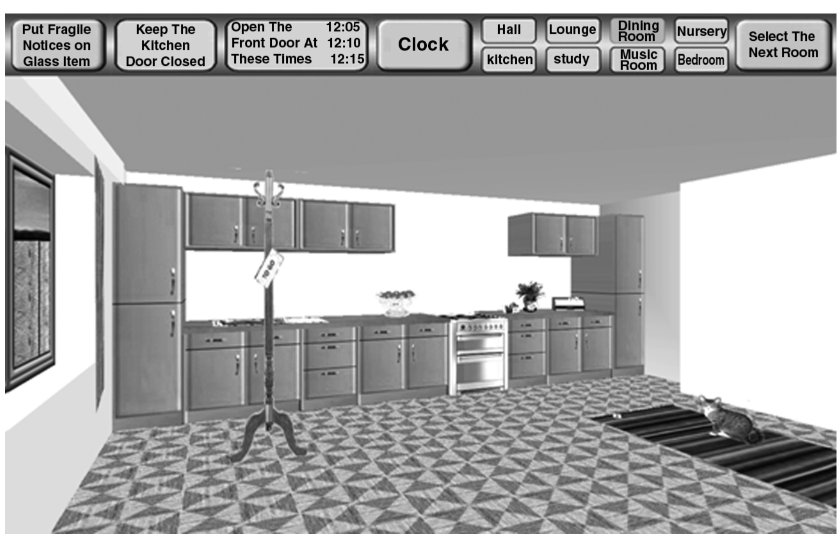

FIG. 2. Virtual bungalow (kitchen).

of the test. They were then informed that they had finished the test, which was the trigger for them to recall the two real-life ProM tasks described previously. If participants did not remember to request their personal items, these were returned to them at the end of the assessment session. These two real-life ProM tasks were measured using categorical data ("remembered" versus "failed to remember"). At the end of each participant's trial, the VE program automatically calculated the percentage scores for each of the three ProM levels: event-, time-, and activity-based tasks. Event-based ProM was measured as the percentage of fragile items labeled as fragile. Time-based ProM was measured as the percentage of times the front door was opened for the removal men (within ± 30 seconds time limit). Activity-based Prom was measured as a percentage of times the kitchen door was shut after it had been opened.

RM free-recall task[21]. A series of 20 images of common objects (selected from Snodgrass & Vanderwart's[21] object pictorial set) were presented on the laptop screen for 3 seconds followed by a 1-second interval before the next image appeared. Immediately after the last image had been presented, participants were asked to recall aloud as many objects as possible in any order (no time limit). Correct responses were noted on a pre-prepared record sheet.

Wechsler Test of Adult Reading[16]. To measure premorbid level of intellectual functioning, participants were asked to read out loud a list of 50 words with atypical grapheme to phoneme translations. Responses were recorded on the standard Wechsler scoring sheet. The WTAR was scored according to the published instructions, and these scores provided the means to calculate the premorbid performance intelligence quotient (PIQ), premorbid verbal intelligence quotient (VIQ), and premorbid full-scale intelligence quotient (FSIQ) measures using the standard Wechsler conversion charts.

Wechsler Abbreviated Scale of Intelligence[17]. The WASI assessed participants' verbal, nonverbal, and general cognitive functioning. The test was administered, according to the published instructions, using the 4-subtest format. Participants completed the Matrix Reasoning assessment (nonverbal fluid abilities) and the Block Design assessment (visuomotor/coordination skills); these two subtests provided a measure of PIQ. Participants also completed the Vocabulary and Similarities subtests (VIQ). Responses were recorded on the standard Wechsler scoring sheets. The WASI was scored according to the published instructions, and the scores on the four sub-tests provided PIQ, VIQ, and FSIQ measures using the standard Wechsler conversion charts.

Prospective and Retrospective Memory Questionnaire. This 16-item self-report instrument[18] required participants to rate the frequency with which they made particular types of memory error using a 5-point scale ranging from *very often* to *never*. The questions reflected different aspects of both ProM and RM, including short-term and long-term memory functioning and internally and externally cued memory retrieval.

Hospital Anxiety and Depression Scale[19]. Participants responded to 14 statements about mental well-being (e.g., "I feel tense or 'wound up'"). These statements were designed to measure depression and anxiety. Participants responded by indicating how they felt in "the past week" using a 4-point scale. This provided separate measures of anxiety and depression out of a maximum score of 21 for each measure.

Results

The following data were obtained for each participant: age; HADS score (depression and anxiety); premorbid IQ (WATR); and verbal, performance, and full-scale IQ scores (WASI). These results are shown in Table 1.

It can be seen that groups are similar on all the above variables.

In relation to memory, the following test data were obtained for each participant: percentage correct scores for each of the three VE ProM tasks (event-, time-, and activity-based); categorical data (remembered versus failed to remember); categorical data (yes/no) for the two real-life ProM measures; and number of items correctly recalled (out of 20) on the retrospective memory task. The PRMQ yielded separate scores for prospective and retrospective memory: the higher the score on each of these subscales (out of a maximum of 40), the worse participants rated their memories to be. These test data are shown in Table 2.

Although there were no significant relationships between anxiety and cognitive measures or between depression and cognitive measures, (all $p > 0.09$) we carried out analyses of covariance (ANCOVA) on the measures above using anxiety,

Table 1. Means, Standard Deviations, and Results on Independent t-Tests for Age, Depression, Anxiety, and IQ Measures

	CFS (n = 11)		*HC (n = 12)*					
Measure	*Mean*	*SD*	*Mean*	*SD*	*t*	*p*	*95% CI*	
Age	47.09	12.22	41.50	8.02	1.31	0.21	−3.29	14.48
Depression	12.36	2.73	11.50	2.15	0.85	0.41	−1.26	2.99
Anxiety	10.09	2.91	12.58	4.66	−1.52	0.14	−5.90	0.92
Premorbid IQ	115.73	5.26	114.83	7.46	0.33	0.75	−4.8	0.65
Full-scale IQ	111.18	11.39	113.92	10.70	−0.59	0.56	−12.31	6.84
Performance IQ	111.09	11.94	112.83	8.22	−0.41	0.69	−10.56	7.08
Verbal IQ	108.73	12.23	112.17	13.22	−0.65	0.53	−14.51	7.64

CFS, chronic fatigue syndrome; HC, healthy controls.

Table 2. Means, Standard Deviations, and Results for Independent t-Tests on Memory Measures

	CFS (n = 11)		HC (n = 12)					
Memory	*Mean*	*SD*	*Mean*	*SD*	*t*	*p*	*d*	*95% CI*
Event-based ProM %	36.36	37.69	43.75	38.62	0.46	0.65	0.19	−40.53–25.76
Time-based ProM %	26.09	22.24	37.08	24.66	−1.12	0.28	0.47	−31.43–9.44
Activity-based ProM %	85.00	31.23	82.50	29.50	0.20	0.85	0.08	−23.83–28.83
Self-report ProM*	30.91	6.64	23.08	6.53	2.85	0.01	1.19	2.11–13.54
Recall RM*	13.09	2.34	15.75	2.56	2.59	0.02	1.09	0.523–4.80
Self-report RM*	24.55	6.28	18.08	6.36	2.45	0.02	1.02	0.973–11.951

CFS, chronic fatigue syndrome; HC, healthy controls; ProM, prospective memory; RM, retrospective memory.
*High ratings relate to high forgetfulness.

depression, and IQ measures as covariates. As these did not alter the pattern of results, and in the interests of brevity, the ANCOVAs are not reported here.

CFS participants rated themselves as more forgetful than healthy controls on both ProM and RM. Although women with CFS performed less well on the time- and activity-based ProM tasks, these differences were slight and not statistically significant.

Women with CFS performed significantly worse than healthy controls on the free-recall RM.

Seven of the CFS participants (64%) and 10 healthy controls (83%) remembered to ask for their property back at the end of the VE assessment. A 1-variable chi-square showed these results were not statistically significant ($\chi^2 = 0.53$, $df = 1$, $p = 0.63$). Everyone who remembered to request the return of their property also remembered where the researcher had hidden it. Six of the CFS group (56%) and 10 of the healthy controls (83%) remembered to ask for a participant information sheet. This was not statistically significant ($\chi^2 = 1.00$, $df = 1$, $p = 0.45$).

Discussion

This pilot study aimed to compare both RM and ProM performance between women with CFS and healthy women, using, for ProM, a VE assessment. Results showed slight differences in the expected direction between groups on two of the three ProM tasks and the real life ProM measures. These differences were not statistically significant. Due to the constraints of an initial study, participant numbers were small, and therefore the power to find statistically significant results is naturally reduced in such studies. Brooks et al.[15] were successful in using the VE assessment tool to detect differences in ProM functioning between 25 stroke patients and 25 control participants, but their patient sample was recruited from a hospital stroke rehabilitation unit. In contrast, the CFS participants in this study were recruited from the community; therefore their reported memory impairments are likely to be more subtle than those experienced by patients recovering from a stroke.

Nevertheless, there were clear decrements in the measures of RM, both self-reported and actual. These findings offer some support for the deficient acquisition hypothesis,[5] which proposes that RM deficits found in patients with CFS are attributable to difficulties encoding information due to slower information processing. In particular, these difficulties may be task dependent—for example, whether cues are present or absent.

The VE program controls for potential problems in encoding information, as participants have to identify the ProM tasks that they are required to perform from a list of examples before the assessment begins. If they select the wrong tasks, they are reminded of the correct tasks and prompted to choose from the list again. This process is repeated at the end of the furniture-removal task to ensure that participants are still able to recall the three ProM tasks. ProM is thought to comprise a retrospective component,[25] as it is assumed that future intentions must be stored and accessed in a similar way to past experiences. Interestingly, 17 of the 42 stroke patients in the Brooks et al study[15] were unable to recall the three ProM tasks at the end of the assessment, whereas all participants in this study correctly remembered the three tasks. Salient environmental cues (e.g., the cat in the kitchen) may have facilitated CFS participants' recall of the ProM tasks in the VE, as DeLuca et al.[5] found that CFS participants had intact recognition memory. In contrast, the free-recall task depends on self-generated retrieval of information, which is consistent with DeLuca et al.'s[5] finding of impaired delayed recall in CFS. It is therefore possible that CFS patients may be impaired on everyday ProM tasks when no environmental cues are readily available. The fact that CFS participants performed within the control range on the real-life ProM measures despite the absence of external cues is not surprising, as Brooks et al.[15] found that stroke patients who were impaired on the VE measure did generally remember to ask for their personal property back. They attributed the difference between performance on the VE and real-life measures to motivational factors, which are thought to influence the salience of ProM tasks.[25] In the present study, remembering to ask for their personal property back may have prompted CFS participants to recall the second real-life task.

Despite performing within the control range on both the VE and real-life ProM measures, CFS participants rated themselves to be more forgetful than control participants. This disparity between objective task performance and subjective memory appraisal supports the finding that CFS participants appear to set high performance thresholds, which may induce feelings of insufficiency.[24] Due to the limited scope of the present study, no illness control groups were used. If the scores of an appropriately matched organic disease control group and a psychiatric illness group had been obtained, further comparisons could have been made between self-report measures of memory functioning and actual performance in order to determine whether (and the extent to which) subjective memory appraisal contributes to the perception of cognitive deficits in CFS.

The CFS participants in this study were recruited from the community; therefore, their reported memory impairments are likely to be more subtle than those experienced by clinical patients (e.g., patients recovering from a stroke). All of the CFS participants had expressed an interest in participating in research, which may have biased the sample toward individuals who had developed strategies for managing their condition.

Some of the CFS participants had been diagnosed with the condition for a number of years, and others were well enough to be in full- or part-time employment; therefore, the sample may not be representative of the general CFS population. Another difficulty with examining cognitive functioning in CFS is that the severity of the condition is variable in nature. Participants chose when it was convenient to be assessed; therefore, it is possible that they may have opted for times when they knew that they would be minimally affected by fatigue. Future studies would benefit from the addition of current fatigue measures. The furniture-removal task measures ProM functioning over an 18-minute period, whereas many intentions in the real world need to be remembered over much longer time frames. Marshall et al.[12] found that CFS participants typically scored 1 standard deviation below the healthy control mean on tests where motor and cognitive processing speeds were a critical factor. In the VE assessment, participants are not under any explicit time pressure and are required only to process static visual information. Presenting information in one modality places fewer demands on attentional resources than those encountered in real-life environments, where filtering of extraneous information is frequently required. Several CFS participants commented that they experienced difficulty following conversations in groups or in the presence of background noise. Future studies should examine whether increasing the attentional demands of the VE task (e.g., by requiring participants to respond to unexpected events in the VE) would have a more detrimental effect on CFS participants' ProM performance than on that of healthy controls. Further investigation of other conditions associated with cognitive decline is also required to ascertain the VE measure's sensitivity, as it arguably offers potential for assessing patients in a more ecologically valid way than standardized clinical tests.

At present, the ProM scores generated by the VE program record only whether participants remember to carry out the three ProM tasks; therefore, it is impossible to ascertain the extent to which successful performance is influenced by "top-down," conscious processing or environmental triggers. It is possible that CFS participants may have employed different strategies for remembering the ProM tasks than did control participants in order to compensate for potential cognitive deficits. Recording the number and temporal distribution of participants' time checks would help to differentiate participants who suddenly remember to check the time or "linger" by the front door for the correct time to arrive from those who systematically check the clock. Einstein and McDaniel[26] found that time-checking strategies are correlated with successful performance on tasks measuring time-based ProM. Similarly, a system could be developed for recording and coding the strategies that participants adopt when conducting the furniture-removal task; this may provide a window on other cognitive capacities, including RM. For example, some participants repeatedly forgot which rooms they had visited when looking for items, whereas those who adopted the most efficient strategies tended to remember where items were located in the bungalow.

In conclusion, differences between the CFS group and healthy controls on measures of ProM were slight, and on two of the three ProM tasks were in the expected direction. For RM, women with CFS performed worse than healthy controls. For both types of memory, CFS participants considered themselves to have more problems than healthy controls. From this study as well as previous studies, it seems reasonable to conclude that people with CFS do have some subtle decrements in memory, particularly RM. It is possible that the decrements found in the present sample would be greater in real life, for the reasons explained above. However, the use of presence questionnaires[27] may be employed in future studies to ascertain if the participants felt present in the VE, as the level of presence may correlate with ProM functioning in a real environment. Further studies utilizing both healthy controls and illness controls are now needed to ascertain how sensitive the VE measure is and to inform the development of tasks in the VE that place progressively increasing demands on working memory capacity.

Disclosure Statement

No competing financial interests exist.

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