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Virtual reality tasks disclose spatial memory alterations in fibromyalgia

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Objective. The objective is to assess performance on virtual reality spatial memory tasks as well as classical neuropsychological tests in patients with fibromyalgia (FM).
Methods. Fifteen FM patients and fifteen healthy age- and education-matched controls performed the virtual versions of the Morris water maze and the hole board (a virtual version called Boxes room). All participants also completed a comprehensive neuropsychological evaluation that included measures of general intelligence, attention/working memory and visuospatial memory.
Results. Both virtual reality tasks were demonstrated to be sensitive to spatial memory alterations. FM patients performed significantly worse than controls in the spatial navigation tasks, showing significantly more errors than their matched controls, while no significant differences were found between patients and controls regarding standard neuropsychological testing. In addition, those FM patients with longer chronicity had lower auditory memory span, visuospatial memory and general intelligence within their group.
Conclusion. These results are the first to demonstrate that there is a spatial learning deficit in people with FM, which suggest that the hippocampal system can be disturbed in this syndrome.

Key words: Neuropsychological assessment, Brain, Cognitive dysfunction, Pain, Women's health, Fibromyalgia, Virtual reality, Navigation.

Introduction

Fibromyalgia (FM) is a chronic pain syndrome with unknown aetiology, characterized by diffuse musculoskeletal pain, fatigue and sleep disturbance [1]. Stiffness and mood changes are also common symptoms [2]. In addition, patients with FM frequently report problems with their cognitive function, which are severe enough to impair their functioning at work [3]. Existing literature has identified a variety of neuropsychological deficits in FM patients, including alterations in short- and long-term declarative memory [4–7], working memory and attention [6, 8–11], as well as in verbal fluency [5, 6].

A previous study has focused specifically on visuospatial memory in FM, demonstrating that these patients displayed worse performance than controls [11]; however, to our knowledge, there are no studies that have specifically attempted to disclose how FM affects spatial learning and memory.

The hippocampus is critically involved not only in memory and spatial orientation but also in pain perception and modulation of the central stress responses, all of which are altered in FM [12, 13]. Accordingly, a growing body of research considers that the hippocampus could play a central role in the diverse phenomena associated with FM [14]. Patients with FM have been demonstrated to have abnormalities in their hypothalamus–pituitary–adrenal (HPA) axis function in response to stressful conditions [15, 16]. Chronic glucocorticoid excess or deficiency is associated with hippocampal dysfunction and neuronal death, because of the anatomical connections between HPA and hippocampus [17]. Moreover, two recent studies have demonstrated metabolic abnormalities within the hippocampal complex in patients with FM [18, 19].

Given the evidences of disruption in the function and integrity of the hippocampus in the FM patients together with the well-established role of the hippocampus in spatial memory for both rodents [20–22] and humans [23–25], the purpose of this study was to use virtual reality tasks to examine spatial learning and memory in FM. Specifically, we examined possible differences between FM patients and healthy age-matched controls using the virtual reality Morris water maze (MWM) and the Boxes room (BR). The MWM is the most popular adaptation of a rodent's spatial memory maze to humans and it has been applied to both normal development and different pathologies [26, 27]. The BR is a virtual reality (VR) version of the hole board test used in rodent's research [28]. Additionally, spatial memory performance was correlated with classical neuropsychological tests.

Materials and methods

Subjects

Fifteen women with FM and 15 healthy age-matched female controls participated in this study. The FM patient group consisted of volunteers, who met the ACR classification criteria for FM, recruited by means of an advertisement at the Almeria Fibromyalgia Association (AFIAL) in which they were invited to participate in the study. Patients who were recruited into the study but who reported any other rheumatic disease or other neurological condition that might impact cognition were excluded from the study. The control group consisted of volunteers recruited from the community and individually matched to each FM patient for age (±3 years) and education. According to self-report, all controls subjects had normal or corrected-to-normal vision, were in good health and free of any medications that could potentially affect cognitive performance. Psychiatric and neurological histories were negative.

The participants were informed in advance about the aims and procedures of the experiment. All participants gave verbal informed consent and were fully free to leave the experiment at any time. Participants did not receive financial reward, but they were offered information about their own results after the study was completed. The study was conducted in accordance with the European Communities Council Directive 2001/20/EC and Helsinki Declaration for biomedical research involving humans and received the approval from the Ethics Review Committee (University of Almeria).

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Procedure

The test session began with the completion of a questionnaire. Specifically, participants marked on a 4-point Likert-type scale the frequency with which they played 3D computer games (0: never; 1: rarely; 2: occasionally; and 3: frequently). They were also asked about their experience in joystick handling [Have you ever used a joystick? (1:Yes/2:No)]. The cultural level was established depending on the educational level (1: Illiterate; 2: Literate; 3: elementary education; 4: Junior High or Vocational Training I (VT); 5: High School or VT II; 6: Junior college or VT III; and 7: Degree). In addition, FM patients were also asked a brief questionnaire about their illness, in which medical and psychiatric diagnoses, aetiology and chronicity were recorded along with a detailed list of participants' current medication. The Fibromyalgia Impact Questionnaire (FIQ) was also administered to measure the impact of the FM disease symptoms severity on patients' lives [29].

Later, the subjects received both written and verbal instructions on how each virtual task would proceed. Half the participants started with the virtual MWM task followed by the BR task, and vice versa for the other participants.

All participants also completed a comprehensive neuropsychological evaluation that included measures of general intellect (vocabulary test) [30], attention/working memory (digit span backward and Corsi block tapping test backward) [30, 31] and visuospatial memory [digit span forward, Corsi block tapping test forward and 10/36 Spatial Recall Test (SRT)] [30–32]. The duration of the entire experiment was ~2 h.

Virtual reality tasks

An Acer 533-MHz portable computer equipped with 1000 MB of RAM and a 15 XGA TFT colour monitor (1024 × 768) was used for the two virtual tasks. Participants navigated through the mazes by manipulating a Logitech joystick. The virtual mazes gave a first-person view so that if the joystick was pushed to the right, the view of the screen would pan to the right, and similarly with other joystick movements. Backward navigation was not possible. The computer speaker was used to provide auditory feedback to the participants. Each of the virtual rooms contained various salient landmarks that disambiguated spatial locations, such as pictures on the wall and shelves present around the room (Fig. 1). Dependent variables measured from both mazes included latency, distance covered and number of errors committed. In addition, the programs provided all the paths for each participant as well.

BR task. Participants were placed in a square virtual room with 16 boxes homogeneously distributed on the floor (four rows of four boxes each). Their goal consisted in discovering the position of the rewarded boxes, which was constant during the experiment. Subjects were asked to open the lowest number of boxes necessary to achieve the goal and to do it as quickly as possible using the cues within the room to localize the rewards. Procedurally, participants started from four semi-random locations (North, South, East and West). When participants opened a rewarded box it turned green and a melody sounded; when they opened a wrong box it turned red and an aversive, discordant tone sounded. The already opened boxes remained green or red to help the participants remember their position, whereas non-opened boxes remained brown. As soon as all rewarded boxes were located a sound feedback was provided, and a visual message appeared on the display congratulating the participant and indicating that the next trial would proceed. When a new trial began all the boxes turned back to their original brown colour. Each trial had a maximum duration of 150 s, after which the screen faded and a new trial began. The inter-trial interval was 5 s. A session consisted of 10 trials.

Virtual MWM. Participants were placed in a virtual pool within a virtual room, and they were instructed that their goal would be to swim to a hidden platform located under one of four identical big yellow balls floating on the surface of the pool water. Procedurally, participants started from four different locations (North, South, East and West) for a total of 16 trials. When participants swam to the ball where the platform was located, a tone sounded and a visual message appeared on the display congratulating the participant, whereas responses to incorrect balls were followed by a discordant tone. As soon as the correct ball was located, the participants were allowed free swimming movements for 3 s after which the trial terminated. The trial had a maximum duration of 60 s, after which the platform became visible and a discordant tone was sounded. The inter-trial interval was 5 s.

Following the 16 training trials, a probe trial was given. For the probe trial, a new verbal message was displayed indicating that in the next trial the balls and the platform would be removed and that their goal would be to navigate through the area where the platform was located during training. The message also indicated that after this trial, there would be another trial block (four trials) where the platform would be raised slightly out of the water so that it was visible to the participant and they had to swim to it as quickly as possible. This condition is referred to as visible platform condition. All events and consequences were identical to those in the hidden condition. During all phases the platform location was fixed in region 2. Two controls did not complete the MWM.

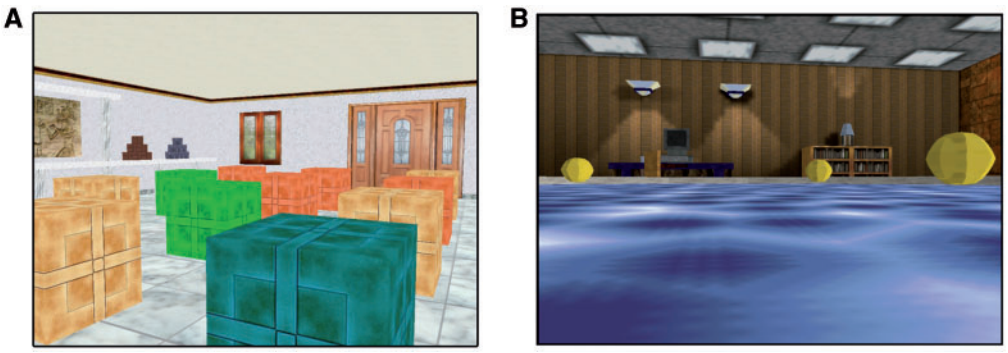

FIG. 1. Representative views of the environments from a participant's perspective. (**A**) BR task. All boxes were brown at the start of the trial. However, they changed colour after being opened. Hence, a green box indicated that the box was rewarded; a red colour was assigned to non-rewarded boxes and blue showed that the box could be opened by pressing the joystick button. (**B**) Virtual MWM. A hidden platform was located followed by a tone sound and a verbal message on the display congratulating the participant. Approaching an incorrect ball was followed by a discordant tone sound.

TABLE 1. Demographic and clinical characteristics of study participants

	FM patients, $n=15$	Controls, $n=15$
Age, mean ± S.D.	53.33 ± 6.29	53.67 ± 6.71
Educational level, mean ± S.D.	4.27 ± 1.53	3.73 ± 1.16
Vocabulary, mean ± S.D.	10.87 ± 1.59	11.80 ± 2.04
Videogame experience, mean ± S.D.	1.2 ± 0.41	1.33 ± 0.48
Joystick experience, mean ± S.D.	1.86 ± 0.35	2 ± 0.00
Chronicity, mean ± S.D., months	85.20 ± 63.5	
FIQ, mean ± S.D.	67.42 ± 12.68	
Pharmacological treatments, %		
Pregabaline	13.33	
Analgesic	53.33	
Anxiolytics	46.66	
Anti-depressant	40.00	
Sleeping pills	33.33	

Results

Comparisons across groups

Characteristics of the study participants are detailed in Table 1. The two groups were not statistically different in terms of age, education level and videogame playing experience. Clinical characteristics for FM patients are also included in Table 1.

BR. Latency and distance to discover all the rewarded boxes as well as the number of errors (visiting a non-rewarded box) in each trial were statistically analysed using an analysis of variance (ANOVA), with Group as the between-subjects factor and Trial as the repeated measure factor, followed by *post hoc* Newman–Keuls tests. Significant differences were reported for $P < 0.05$.

Analysis of the latency to find all the rewarded boxes showed that there were no significant differences between Groups [$F(1,28) = 1.01$, $P > 0.05$], but there was a significant effect of Trial [$F(9,252) = 11.15$, $P < 0.001$]. Specifically, participants reduced latencies with more trials. However, there was also a significant interaction [$F(9,252 = 2.37$, $P < 0.01$]. *Post hoc* Newman–Keuls test indicated that there is a decrease in searching time in the last four trials with respect to the four initial ones ($P < 0.05$) (Fig. 2A).

Regarding distance covered, there was a trend for an effect of Trial [$F(9,252) = 1.\ 82$, $P = 0.06$], but there were no significant differences between Groups [$F(1,28) = 1.40$, $P > 0.05$] or interaction [$F(9,252) = 0.76$, $P > 0.05$] (Fig. 2B).

Analysis of the number of errors disclosed a significant main effect of Group [$F(1,28) = 6.31$, $P < 0.05$] and Trial [$F(9,252 = 21.97$, $P < 0.001$] with no interaction [$F(9,252) = 0.16$, $P \geqslant 0.05$]. Specifically, participants reduced the number of errors with more trials. Moreover, FM patients made significantly more errors than controls (Fig. 2C).

MWM. Mean latency, distance and number of errors to locate the platform were grouped according to blocks (four trials per block) in order to apply statistical tests. The resulting means were then statistically analysed using an ANOVA, with Group as between-subjects factor and Trial blocks as the repeated measure, followed by *post hoc* Newman–Keuls tests, when necessary. Significant differences were reported for $P < 0.05$.

Analysis of latencies to find the platform showed that there was no significant effect of Group [$F(1,26) = 2.21$, $P > 0.05$], but there was a significant effect of Trial [$F(3,78) = 12.27$, $P < 0.001$]. Specifically, participants reduced latencies in the last trials. There was no significant interaction, $F(3,78) = 0.83$, $P > 0.05$ (Fig. 3A).

Regarding the distance covered to reach the platform, there was no significant effect of Group [$F(1,26) = 0.43$, $P > 0.05$], but there was a significant effect of Trial [$F(3,78) = 6.27$, $P < 0.001$]. Specifically, participants found the platform faster with more trials. There was no significant interaction [$F(3,78) = 1.45$, $P > 0.05$] (Fig. 3B).

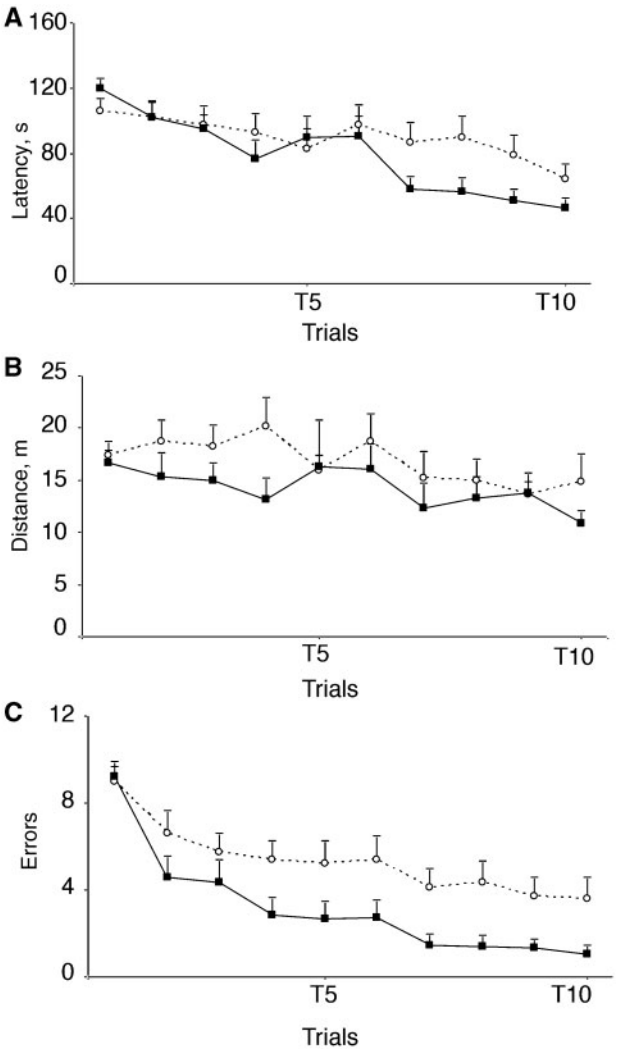

FIG. 2. (**A**) Latency (**B**) distance and (**C**) errors to locate the rewards at the BR test. FM group is represented by dotted lines. Note that FM patients made significantly more errors than controls, while no differences appeared in latency and distance covered. Mean + S.E.M.

The analysis of the number of errors indicated that there was a significant main effect of Group [$F(1,26) = 8.56$, $P < 0.05$] and trial [$F(3,78) = 10.55$, $P < 0.05$] with no significant interaction [$F(3,78) = 0.42$, $P > 0.05$]. Specifically, healthy controls made significantly fewer errors than FM patients, and both groups made fewer errors with more trials ($P < 0.05$) (Fig. 3C).

During the no-platform probe trial, a *t*-test for independent samples showed no differences between both groups in the time spent in the platform quadrant [$t(26) = -1.50$, $P > 0.05$; all performance analyses two-tailed, equal variances not assumed].

To assess whether differences between motivational, sensory or motor factors interacting with the computer program could explain these results, analysis of the latency, distance and number of errors to reach a visible platform was conducted. There was no significant difference between the Groups in latency, distance or number of errors to find the visible platform [$F(1,26) = 2.10$, $P > 0.05$; $F(1,26) = 1.52$, $P > 0.05$; $F(1,26) = 2.15$, $P > 0.05$]. Hence, this performance difference cannot be explained by motivation, sensory or motor factors.

Neuropsychological measures. Results of one-way ANOVAs did not show group differences in any of the considered measures (Table 2)

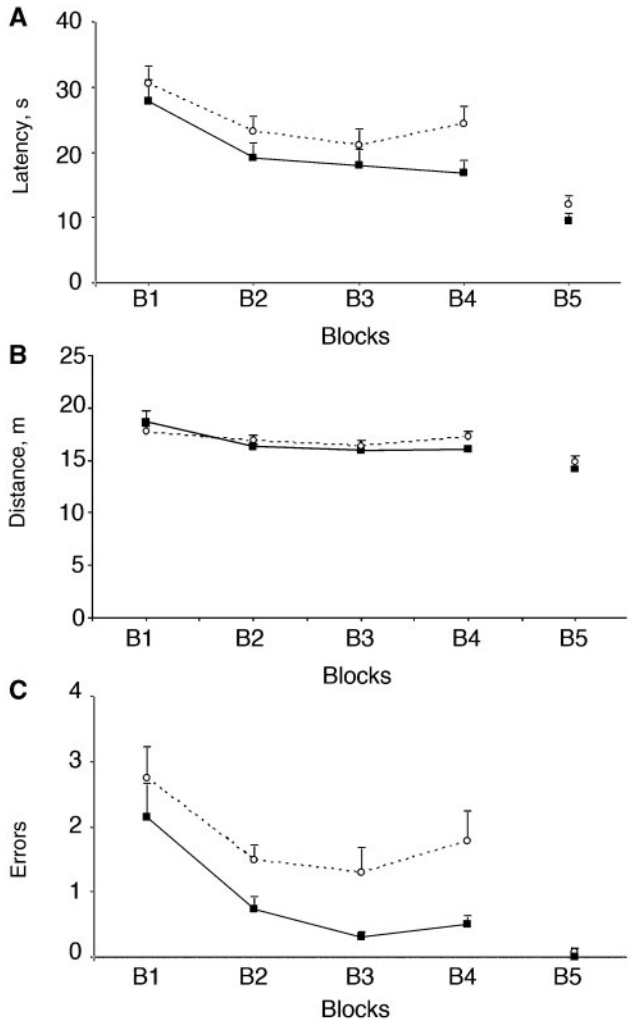

FIG. 3. (**A**) Latency, (**B**) distance and (**C**) errors to reach the platform during the hidden and visible platform phases. FM group is represented by dotted lines. Note that healthy controls found the hidden platform sooner than FM patients in the last trials of the hidden platform phase (B4) (**A**). (**C**) shows that controls made fewer errors than FM group. B1–B4: hidden platform phase; B5: visible platform phase. Mean + S.E.M.

Correlations between FM symptoms and cognitive measures

In an effort to understand the relative impact of the FM disease symptoms severity and to further understand the role of the duration of the illness and hence the chronicity on neuropsychological and spatial memory measures, correlations between these variables were performed in FM patients. For the correlation matrix, there were two FM measures: FM chronicity (months) and FIQ. The neuropsychological measures were: vocabulary, digit span forward, digit span backward, Corsi test forward, Corsi test backward, 10/36 SRT average immediate recall, 10/36 SRT delayed recall, and three spatial measures: probe trial performance (percent time in the training quadrant in the MWM), total number of errors in the MWM, total number of errors in the BR (Table 3).

FM symptoms and neuropsychological measures

FM chronicity had a strong negative correlation with forward digit span ($r=-0.67$, $P<0.01$), delayed recall of 10/36 SRT ($r=-0.59$, $P<0.05$), as well as vocabulary subtest ($r=-0.65$, $P<0.01$). Specifically, those FM patients with longer chronicity had lower auditory memory span, visuospatial memory and general intelligence. There were no significant correlations with any of the other neuropsychological measures or with the spatial memory measures. The FIQ had no correlations with any of the neuropsychological or spatial memory measures.

TABLE 2. Descriptive values, contrast and statistical significance for each one of the neuropsychological tests employed

Test	Mean ± S.D.	*F* *F*(1,28)	*P*
Vocabulary			
FM	10.86 ± 1.6	1.94	0.17
Controls	11.80 ± 2.04		
Digit span forward			
FM	5.20 ± 1.14	0.29	0.59
Controls	5.00 ± 0.84		
Digit span backward			
FM	3.93 ± 1.16	1.04	0.32
Controls	4.33 ± 0.97		
Corsi test forward			
FM	4.86 ± 1.12	1.62	0.21
Controls	5.26 ± 0.46		
Corsi test backward			
FM	4.80 ± 1.08	0.64	0.43
Controls	5.06 ± 0.70		
10/36 SRT average immediate recall			
FM	6.15 ± 1.60	0.24	0.63
Controls	6.40 ± 1.08		
10/36 SRT delayed recall			
FM	6.13 ± 2.20	1.86	0.18
Controls	7.20 ± 2.07		

When we considered the FIQ domains separately, we found that the rested subscale had a moderately strong positive correlation with the digit span (backward) ($r=0.56$, $P<0.05$) and a strong positive correlation with the total number of errors committed in the BR ($r=0.75$, $P<0.001$). No other correlations were statistically significant.

Spatial memory and neuropsychological measures

The total latency in the correct quadrant during the pool probe trial had a strong positive correlation with forward Corsi test ($r=0.72$, $P<0.01$) and 10/36 SRT delayed recall ($r=0.76$, $P<0.01$) and also had a moderately strong positive correlation with the vocabulary subtest ($r=0.64$, $P<0.05$), backward digit span ($r=0.58$, $P<0.05$) and immediate recall of 10/36 SRT ($r=0.59$, $P<0.05$). Specifically, for all of these measures, the better the performance of the FM patients on the probe trial (as evidenced by more amount of time swum in the training quadrant), the better the performance on the tasks. The total number of errors in the MWM had no correlation with any of the neuropsychological measures.

The total number of errors in the BR had a moderately strong negative correlation with forward ($r=-0.62$, $P<0.05$) and backward digit span ($r=-0.52$, $P<0.05$, respectively). Specifically, those patients who committed fewer errors in the BR also performed better in these tests, as exhibited by longer sequences of digits recorded. There were no correlations with any other measures.

Neuropsychological measures

The vocabulary test had a moderately positive correlation with the digit span (forward) ($r=0.60$, $P<0.05$), Corsi test (forward) ($r=0.58$, $P<0.05$) and 10/36 SRT ($r=0.56$, $P<0.05$ and $r=0.59$, $P<0.05$, immediate and delayed recall, respectively). For all these measures, the higher the level performed on vocabulary, the better the performance on the tasks. Additionally, the digit span backward had a positive correlation with the Corsi test (forward) ($r=0.59$, $P<0.05$) and the average immediate recall of the 10/36 SRT ($r=0.57$, $P<0.05$). Specifically, those FM patients who exhibited longest sequences of digits recorded also showed better visuospatial ability. Moreover, we noted a strong positive correlation between the two visuospatial tasks

TABLE 3. Correlation chart of FM symptoms, neuropsychological measures and spatial memory

Variables	1	2	3	4	5	6	7	8	9	10	11	12
Chron	–											
FIQ	0.181	–										
Voc	−0.645**	0.132	–									
DS Fward	−0.669**	−0.033	0.601*	–								
DS Bward	−0.179	−0.089	0.418	0.332	–							
CT Fward	−0.423	0.315	0.585*	0.520*	0.593*	–						
CT Bward	−0.158	0.206	0.066	0.150	0.102	0.211	–					
SRT AIR	−0.509	0.005	0.557*	0.358	0.568*	0.633*	0.060	–				
SRT DR	−0.590*	0.163	0.595*	0.527*	0.534*	0.844**	−0.078	0.649**	–			
MWM Probe	−0.382	0.328	0.636*	0.335	0.578*	0.716**	−0.024	0.590*	0.761**	–		
MWM Errors	0.406	0.473	−0.346	−0.327	−0.370	−0.128	−0.145	0.066	−0.133	−0.132	–	
BR Errors	0.310	−0.150	−0.388	−0.618*	−0.523*	−0.439	−0.218	−0.226	−0.345	−0.424	0.578*	–

*Correlation is significant at the 0.05 level (two-tailed). **Correlation is significant at the 0.01 level (two-tailed). Chron: chronicity; Voc: vocabulary; DS: digit span; Fward: forward; Bward: backward; CT: Corsi test; AIR: average inmediate recall; DR: delayed recall.

($P < 0.01$). Specifically, those who performed best on Corsi test (forward) also remembered more positions in the 10/36 SRT. The Corsi test (backward) had no correlations with any of the other neuropsychological measures.

MWM and BR

There was a strong positive correlation between the number of errors committed on the MWM and on the BR ($r = 0.59$, $P < 0.05$). Specifically, those patients who made more errors in finding the hidden platform on the MWM also made significantly more errors in the BR. The latency in the MWM probe trial had no correlations with the total errors on the MWM or on the BR.

Discussion

To the best of our knowledge, this is the first study to report spatial memory deficits in people with FM. Patients with FM displayed spatial memory impairments as evidenced by significantly more errors in performing both the BR and the virtual MWM. The fact that there was no difference between the groups in navigating to a visible platform suggests that these spatial memory deficits are not due to differences in understanding the tasks, motivational factors, using the joystick or computer programs.

There is a large amount of data that indicates that the hippocampus is both involved and necessary for spatial navigation through virtual environments [33]. Hence, it was reported that this brain structure is involved in spatial navigation through virtual cities [34], and hippocampal cells firing responses to the behaviour of finding the way around in a virtual reality town [35]. In our study, the virtual MWM parallels well with the non-human version, specifically converging on the theme that proficient performance is critically dependent upon the hippocampus [26] as well as documentating the effects of a variety of biological factors including sex differences, ageing and lesions [26, 27, 36, 37]. Moreover, a recent research using the BR has described sexual dimorphism in performing the task, which supports its spatial component [38].

These spatial memory deficits corroborate some of the studies indicating hippocampal or temporal lobe abnormalities in people with FM [18, 39, 40]. Specifically, Emad *et al.* [18] reported a decrease in hippocampal neuronal integrity as shown by a decreased *N*-acetylaspartate level in people with FM. Additionally Kuchinad *et al.* [39] showed that grey matter volume in the left parahippocampal gyrus decreased in these patients. Combining these studies with our data suggests that there are both structural and functional hippocampal and temporal lobe abnormalities in people with FM.

Interestingly, we noted that there were no significant correlations between FM symptoms and spatial memory performance. Specifically, those who reported having FM for a longer amount of time or with more severity did not show more severe impairments. It may be that the deficit manifests itself early in the course of the disease and does not increase as severity worsens. Alternatively, it may be that the chronic treatment patients with FM usually taken produced a significant cognitive protection on a higher spatial memory decline. Specifically, anti-depressants such as citalopram in populations of middle-aged women have shown an improvement in mood and cognitive efficacy in complex attention, short- and long-term recall and cognitive flexibility. Low doses of citalopram are useful for the treatment of memory deficits and alterations in conscience [41]. Within analgesics, the same effect is seen with tramadol, one of the most commonly prescribed opioid drugs for chronic pain [42]. Recently, Dick *et al.* [8] found that FM patients taking stable doses of prescribed opioids had significantly better memory than those with FM not taking opioids.

Along with the treatments mentioned above, many other medications were regularly being taken by our FM patients. Seven of our FM patients used benzodiazepines. However, these patients did not differ from the other FM patients who did not receive benzodiazepines (data not shown).

For the neuropsychological tests, there were no significant differences between the groups. This is surprising given the number of complaints and dysfunction that are apparent in people with FM. However, we did note that the duration of FM strongly predicts deficits in working memory, visuospatial memory and vocabulary (as evidenced by the digit span, delayed recall of 10/36 SRT and vocabulary subtest, respectively). It is not clear offhand why these skills were more impaired with a longer duration FM than other skills. Published literature suggests deficits in cognitive ability in people suffering from chronic pain [8, 43–45]. However, the mechanism of chronic pain interference with cognition and its relation to other concomitant disorders, such as depression, anxiety and chronic fatigue, need to be further elucidated. We predict that a more homogeneous sample would have provided more robust results, but until these experiments are performed, it remains unclear which specific factors contribute to these differences in performance.

On the other hand, there were a variety of correlations between neuropsychological tests such as vocabulary, digit span, 10/36 SRT and Corsi test in FM group. These correlations can be expected given the amount of overlap in skills between the various tasks. For example, the Corsi block and the 10/36 SRT are both tests of spatial memory span, so the significant correlations between the two tasks corroborate their spatial memory burden. However, it is unclear why these do not correlate with the virtual tests of spatial memory.

Because there have been so few studies examining cognitive deficits in people with FM, it is difficult to compare our findings with those of previous studies. Moreover, this was the first time that virtual environments were used to delimit spatial learning and memory performance in FM syndrome. One of the first studies

performed on people with FM reported alterations in measures of attention, concentration and memory, relating them to the severity of pain and aspects of anxiety in those patients [46]. In visual memory, a previous study by Roldán-Tapia *et al*. [11] found that FM patients obtained worse performance than controls on visuospatial memory tasks. This contrasts with our lack of difference between the FM and control group, although the two studies differed significantly both in patients' disease duration as well as in the specific neuropsychological tests employed. In fact, because of the difference across studies in terms of patient population, disease duration, comorbidity and cognitive testing administered, it is difficult to make comparisons across published studies.

One important question that arises is whether spatial learning and memory difficulties are a particular characteristic of only FM patients, suggesting that it may be an important screening tool for FM if it is manifested in the early stages of the disease. Alternatively, it may be that these reported deficits are common in other diseases with chronic pain. For example, it would be interesting to compare the FM group with groups suffering from RA or another chronic pain disease because they share common factors, such as pain and cognitive dysfunction.

In conclusion, this study has identified spatial navigation as a specific cognitive process that appears to be disrupted by FM. The evaluation of other chronic pain populations, as well as a more accurate control of the influence of several characteristics associated with the FM, are challenges for future studies.

Rheumatology key messages

- There is a spatial learning deficit in people with FM.
- FM is likely to involve structural and functional hippocampal and temporal lobe abnormalities.

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