Fibromyalgia and Cognition

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Patients with fibromyalgia frequently complain of cognitive problems or "fibrofog." The existence of these symptoms has been confirmed by studies of the incidence of cognitive problems in fibromyalgia patients and by the results of objective tests of metamemory, working memory, semantic memory, everyday attention, task switching, and selective attention. The results of these tests show that fibromyalgia patients have impairments in working, episodic, and semantic memory that mimic about 20 years of aging. These patients have particular difficulty with memory when tasks are complex and their attention is divided. Cognitive symptoms in these patients may be exacerbated by the presence of depression, anxiety, sleep problems, endocrine disturbances, and pain, but the relationship of these factors to cognitive problems in fibromyalgia patients is unclear. Standardized tests and treatment have not yet been established for cognitive problems in fibromyalgia patients.

(J Clin Psychiatry 2008;69[suppl 2]:20–24)

Clinicians who treat a substantial number of people with fibromyalgia know that these patients frequently have cognitive complaints, which patient support groups have dubbed "fibrofog." Patients with fibromyalgia have described significant decrease in memory, loss of vocabulary, and a feeling of mental slowness, and they particularly notice these symptoms in stressful work environments. Patients may even find the cognitive symptoms more disturbing than the physical symptoms of fibromyalgia. Researchers have examined the incidence of self-reported cognitive problems in fibromyalgia patients, compared cognitive function in fibromyalgia patients and controls, and investigated the validity of patient-reported cognitive problems by comparing self-reports with the results of objective tests.

SELF-REPORTED COGNITIVE PROBLEMS

Clinical observations of frequent self-reported cognitive problems in fibromyalgia patients were corroborated by a study[1] of 100 women with fibromyalgia and chronic fatigue syndrome. The incidence of concentration difficulties was 95%, and failing memory had a 93% incidence. This study and an Internet survey[2] completed by more than 2500 respondents with fibromyalgia both found forgetfulness and concentration problems to be the fifth and sixth greatest problems reported, after pain, fatigue, muscle tension or stiffness, and sleep problems.

Fibromyalgia patients have more self-reported cognitive problems than patients with other rheumatic disorders. Katz and colleagues[3] found self-reported memory decline in 70.2% of fibromyalgia patients versus 24.6% of patients with other rheumatic disorders, and 56.1% of the fibromyalgia patients had complaints of mental confusion versus 12.3% of the other rheumatology patients.

Colleagues and I[4] used the Metamemory in Adulthood (MIA)[5] questionnaire to compare beliefs and behavior related to memory in fibromyalgia patients and 2 education-matched control groups. One control group was age-matched to the fibromyalgia patients and the other control group was 20 years older than the fibromyalgia patients. We found that fibromyalgia patients reported having lower memory capacity and more deterioration in memory over time compared with either control group. Fibromyalgia patients also reported having less control over memory function (self-efficacy) and higher anxiety about memory performance than age-matched controls, although they were more motivated and reported using more strategies to boost their memory performance.

OBJECTIVE MEASURES OF COGNITIVE FUNCTION

Objective measures of cognitive function have shown differences between fibromyalgia patients and controls, particularly with memory[6] and attention.[7] Some types of

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This article is derived from the planning teleconference series "Understanding Fibromyalgia and Its Related Disorders" that was held in October and November 2007 and supported by an educational grant from Eli Lilly and Company.

Dr. Glass has received grant/research support from the National Institute on Drug Abuse, the National Institute on Alcohol Abuse and Alcoholism, and the Department of Defense and has received honoraria from Pierre Fabre.

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Table 1. Performance on Cognitive Tasks by Fibromyalgia Patients, Age-Matched Controls, and Older Controls[a,b]

Task	Fibromyalgia Patients (N = 23)	Age-Matched Controls (N = 23)	Older Controls (N = 22)	p Value[c]
Information-processing speed	139.45 ± 29.55	139.23 ± 29.55	118.50 ± 19.15	.975
Working memory	22.22 ± 7.85	26.30 ± 1.67	22.09 ± 6.27	.042
Free recall	23.56 ± 7.80	27.83 ± 6.43	23.91 ± 6.77	.005
Recognition memory	2.53 ± 1.19	2.95 ± 1.07	2.80 ± 1.19	.035
Verbal fluency	49.78 ± 11.63	56.08 ± 15.65	49.43 ± 13.74	.055
Verbal knowledge	43.17 ± 7.62	51.26 ± 6.01	50.56 ± 7.93	< .001

[a]Adapted with permission from Park et al.[9]
[b]Values shown as mean ± SD.
[c]p Values are for fibromyalgia patients compared with age-matched controls.

memory that are troublesome for fibromyalgia patients are working (short-term) memory, episodic long-term memory, and semantic memory access. Short-term memory refers to memory of less than about 30 seconds, and working memory combines short-term memory with other mental processes. Mental arithmetic is an example of a task that makes heavy use of the working memory system. Episodic long-term memory is the ability to remember particular episodes, such as items on a grocery list or personal experiences. Semantic memory involves facts and knowledge about the world. Also problematic for fibromyalgia patients is the ability to pay attention to things that are important while ignoring distracting items.

Objective Tests of Memory

Working memory. One objective test of working memory is the Reading Span Test,[8] which colleagues and I used in a study of patients with fibromyalgia.[9] In this test, the experimenter reads a sentence aloud, for example, "The fans at the football game wore hats and scarves." On a computer screen, the participant sees a question—in this case, "Where were the fans?" Then the participant selects one of the multiple choice answers. Next, the experimenter reads another sentence, for example, "The Grants told their guests from France about the city." Again, the participant selects a multiple choice answer to a question about the sentence. At the end of the trial, the subject is prompted to recall the last word of each sentence in the order in which the words appeared, so in this case, the participant would need to remember *scarves* and *city*. This task is challenging because it includes a lot of competing information that requires storage and manipulation. This test starts with 2 sentences per trial and moves up to 3 sentences and more until the participant can no longer successfully recall all the words. When the patients with fibromyalgia were compared with education-matched controls who were either age-matched or 20 years older, the fibromyalgia patients performed like the older controls, less well (p = .042) than the age-matched controls (Table 1).

A standardized test of working memory is the Paced Auditory Serial-Addition Test (PASAT).[10] This test measures memory competence when a source of distraction is introduced. A tape recorder is normally used to present digits one at a time and the subject's task is to add the most recent digit to the one that preceded it and state the answer aloud. Participants have to continually update the digit they are holding in working memory, which is very challenging. Although Suhr[11] found no between-group differences on PASAT scores in a study of patients with fibromyalgia or chronic pain versus healthy controls, Leavitt and Katz[12] found that fibromyalgia patients performed at a level below normal on this task. Furthermore, using the Auditory Consonant Trigram,[13] Leavitt and Katz[12] found impairment in 82.6% of fibromyalgia patients.

Episodic long-term memory (free recall). Colleagues and I also investigated episodic long-term memory in patients with fibromyalgia compared with age-matched controls and controls who were 20 years older.[9] A word-list, free recall test[14] was used, in which subjects are presented with a list of words to learn and then about 5 minutes later are asked to recall the words. Participants are allowed to recall the words in any order. As shown in Table 1, the fibromyalgia patients performed like older controls, at a significantly (p = .005) lower level than age-matched controls.

Semantic memory (verbal fluency). A standard verbal fluency test can be used to test semantic memory. In the study of patients with fibromyalgia compared with older controls and age-matched controls,[9] colleagues and I used a standard verbal fluency test[15] in which participants are given paper with the letters *f*, *a*, and *s* at the top and in 90 seconds must write as many words as possible that start with each letter. Again, as shown in Table 1, the fibromyalgia patients performed like the older controls, at a lower level than the age-matched controls.

These results show impairment in working memory, episodic memory, and semantic memory access in fibromyalgia patients that mimics about 20 years of aging.

Objective Tests of Attention

Results of attention tests in patients with fibromyalgia are consistent with the working memory results already discussed because the attention tests require people to store some information for a short period of time and also process distracting information.

Dick and colleagues[7] studied attentional functioning in patients with fibromyalgia using the Test of Everyday Attention,[16] a computerized battery that is meant to mimic the kinds of things that people do in everyday life. They found that fibromyalgia patients scored significantly ($p < .005$) worse than pain-free controls in selective attention and auditory-verbal working memory.

Leavitt and Katz[12] suggested that the memory difficulties seen in fibromyalgia patients may be due to attentional distraction. They found that when patients with fibromyalgia were taking standardized tests of memory function, higher levels of impairment were observed for tasks that involved distraction.

Colleagues and I conducted a study[17] in which we specifically looked at distraction during memory performance. We asked participants to memorize a list of 24 words, and sometimes while they were memorizing and/or recalling a list of words, they also had to perform a "distractor" task. The distractor task was a simple digit monitoring test in which the participant held a counter in his or her nondominant hand and listened to a tape recording of digits. Half of the participants were asked to press the counter whenever they heard an odd digit and the other half of the subjects were asked to press the counter whenever they heard an even digit.

For one list of words there was full attention at learning and at recall.[17] For another list, attention was divided while learning the list but not while recalling the words. For a third word list, attention was divided while recalling the list but not while learning it. For a final list of words, attention was divided while learning and while recalling the list. The overall results showed that healthy controls on average recalled 15.7 words, whereas the fibromyalgia patients recalled on average 13.3 words ($p = .006$). Dividing attention had costs for both controls and fibromyalgia patients, but the greatest cost incurred was among the fibromyalgia patients when attention was divided during both learning and recall.

These results may explain why fibromyalgia patients report poor memory performance in real-world environments. Distracting information competes for attention, people rarely get a chance to concentrate on one thing at a time, and memory performance is therefore highly disrupted.

Task switching/selective attention. My colleagues and I[18] studied the ability of fibromyalgia patients to switch attention between different aspects of a task. We used a computerized version of a card sorting task in which a card appears at the bottom of a screen and, above the card, 4 piles of cards appear in a row and the top card on each pile has a different shape on it. The size, shading, and number of shapes can differ. The participant has to press keys on the keyboard to indicate which pile the card at the bottom of the screen should join. The rules for sorting the cards can be simple, for example, by shape, size, shading, or number of objects on the card, or the rules can be complex so that participants have to put 2 variables together. The same rules may apply throughout the whole test, or participants may have to switch back and forth between rules. The data showed that the cost in accuracy was greatest when fibromyalgia patients had to switch between complex rules.

These results confirm patients' accounts that they are most aware of cognitive problems when tasks are difficult, multiple tasks are required, and there is a lot of distraction. Overall, the results of these objective tests of memory and attention suggest that fibromyalgia patients have lower memory performance and are more susceptible to distraction than those without fibromyalgia.

FACTORS THAT CONTRIBUTE TO FIBROFOG

Several factors may contribute to cognitive problems in patients with fibromyalgia. These potential causes include comorbid depression and anxiety, sleep problems, neuroendocrine abnormalities, pain, and central augmentation of sensory input.

Psychiatric Comorbidity

Symptoms of depression and anxiety frequently occur in fibromyalgia patients.[11] Depression and anxiety have been associated with lowered memory performance.[19,20] Colleagues and I[9] did not find a correlation between depression and anxiety symptoms and results on cognitive tests, but other researchers[11,21,22] have reported a correlation between psychiatric symptoms and cognitive function in patients with fibromyalgia. Depression or anxiety could be related to cognitive function in some fibromyalgia patients, but these symptoms do not explain all of their memory and attention problems.

Sleep Problems

Fibromyalgia patients usually have sleep problems.[1,23] In healthy subjects, insufficient sleep has been found to impair learning and memory.[24,25] Colleagues and I included some measures of sleep when studying patients with fibromyalgia, but we did not find any correlation with cognitive performance. As is the case with depression, poor sleep undoubtedly contributes to some of the cognitive difficulties of fibromyalgia patients but does not tell the whole story.

Neuroendocrine Abnormalities

Neuroendocrine disturbances or abnormalities and sensitivity to stress occur in fibromyalgia patients.[26] Stress-level cortisol doses have been shown to decrease memory function in healthy adults,[27] and elevated levels of cortisol were associated with lower performance on cognitive tests in those with Cushing's disease.[28] However, in a study by Sephton and colleagues,[29] higher salivary cortisol levels correlated with better visual-spatial memory, the opposite of other findings. Neuroendocrine function does seem to have some effect on memory function, but exactly how this may affect fibromyalgia patients is still unclear.

Pain

Fibromyalgia patients experience pain, which disrupts cognition, especially attention, and may contribute to fibrofog. Painful stimulation is attention-demanding and activates brain areas associated with cognitive attention. Studies[30] in different chronic pain patient groups have shown that pain is related to cognitive function. Colleagues and I[9] found that although scores on the McGill Pain Questionnaire[31] were not related to cognitive function, scores on the Arthritis Impact Measurement Scales[32] pain subscale were. Correlations have been shown between cognitive function and both self-reported and evoked pain in fibromyalgia,[33] so it seems likely that pain contributes to the cognitive problems experienced by fibromyalgia patients.

Central Augmentation of Sensory Input

Evidence suggests that almost all patients with fibromyalgia have central processing abnormalities[34]; central augmentation of sensory input may interfere with other activities involved in processing sensory input and the ability to ignore items that are distracting and maintain focus on what is important. Gracely and colleagues[35] used functional magnetic resonance imaging (fMRI) to examine the pattern of cerebral activation during the application of painful pressure in patients with fibromyalgia compared with controls and found central nervous system augmentation of pain. The fMRI results showed that when similar levels of moderate pressure were applied to the patients and the controls, no common regions of activation were seen and greater effect was seen in patients. When the stimulation was increased to deliver a subjective level of pain in the control group similar to that experienced by fibromyalgia patients, similar activation patterns were seen in patients and controls. Enhanced processing of sensory signals has implications for attention in fibromyalgia because it may lead to increased distractibility.

FEASIBILITY OF TESTING VERSUS PATIENT SELF-REPORT IN CLINICAL PRACTICE

Physicians often ask how cognitive function in fibromyalgia patients should be measured in clinical practice. Generally, neuropsychological and cognitive tests are extensive and time-consuming, which may not be feasible in practice. Many of the tests that are sensitive to the problems that fibromyalgia patients experience are not standardized, and some of the standard neuropsychological tests may miss the attention difficulties of fibromyalgia patients. No quick and easy test of cognitive function in fibromyalgia patients exists as yet.

In the clinic, self-report may be the best and quickest measure of cognitive problems in fibromyalgia patients. Using the MIA questionnaire,[5] colleagues and I[4] found that performance on an objective memory recall task correlated significantly with fibromyalgia patients' perceived capacity ($p < .01$), achievement motivation ($p < .05$), and self-efficacy ($p < .01$), but no significant correlations were found between the recall task performance and the perceptions about memory in either control group.

The high correlation between objective and subjective measures of cognitive function that my colleagues and I found[4] is exceptional. Typically, in all kinds of groups, including healthy young adults, self-reported cognitive function is not correlated well with actual cognitive function. Lack of specificity between the self-report measure and the specific performance measure used frequently accounts for the lack of correspondence. Lack of correspondence may also occur when people with high ability are tested because these individuals may be more sensitive to changes in cognitive function than those of lesser ability. High-ability patients may report a large memory loss when they still appear to perform well on a memory test. Additionally, self-report of cognitive problems may track effort instead of actual performance.[36] A patient may perform at normal levels, but has to put a great deal of effort into attaining that performance. Future neuroimaging studies could examine whether brain activity correlates well with self-report of task difficulty.

CONCLUSION

Research using objective tests has verified fibromyalgia patients' self-report of cognitive difficulties. As no simple and quick tests exist for cognitive problems in fibromyalgia patients, patient self-report can be used instead of complex testing in clinical practice. More research is needed to delineate the exact nature of these cognitive difficulties, including memory and attention problems. Lastly, uncovering causes of cognitive difficulties in fibromyalgia patients may lead to treatments that will improve cognitive function.

Disclosure of off-label usage: The author has determined that, to the best of her knowledge, no investigational information about pharmaceutical agents that is outside U.S. Food and Drug Administration–approved labeling has been presented in this article.

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