
Editorial

Fibro-fog

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Fibromyalgia (FM) is a chronic pain syndrome characterised by widespread musculoskeletal pain associated with a heterogeneous series of other symptoms, including disrupted or non-restorative sleep, fatigue, stiffness, mood disorder and cognitive impairment (1-3). Patients with FM often complain about a wide range of cognitive difficulties such as forgetfulness, memory lapses, mental confusion, reduced verbal fluency and diminished ability to concentrate. These subjectively experienced cognitive dysfunctions are commonly called “fibro-fog” (4). Dyscognition is, instead, the term used to include both the subjective and objectively determined cognitive symptoms (5). The cognitive dysfunction is very common in FM patients: it has been reported in 50% to 80% of FM patients (6) and it is 2.5 times more prevalent in FM patients than in patients with other rheumatologic disorders (4). Furthermore, cognitive dysfunction largely influences the impact of the FM syndrome on patients’ daily life. In fact, whereas widespread musculoskeletal pain, tenderness and fatigue are the hallmark symptoms of FM, patients rank cognitive dysfunction as the fifth most severe symptom (7). According to FM patients, fibro-fog can be more disturbing than the pain, in terms of disease impact, and can impair job performance and daily activity (8). On the contrary, expert clinicians ranked the relevance of cognitive symptoms only tenth in importance (7). One possible explanation for these divergent perceptions is the uncertainty that remains over whether these patients’ complaints reflect truly impaired function or biased perception of the patient. Some data suggested, in fact, that FM patients tend to overestimate the magnitude of their concentration and memory deficits (9,10). Moreover it is well known that physicians usually underevaluate the symp-

toms of their patients particularly when such symptoms (such as pain, fatigue and cognitive performance) have both a physical and emotional component (11). What is more, patients’ cognitive complaints are not always reflected in poor test-based performance and literature often reports inconsistent results, due to subtle differences in the neuropsychological test.

According to recent reviews of the literature, the most consistent cognitive deficits in FM have been found in working memory, attention and executive function, particularly in the presence of distractors or competing stimuli (4-6). Working memory (WM) is a basic cognitive mechanism that underlies successful performance on many other cognitive tasks and is crucial to accurately perform in cognitive situations highly demanding. It is usually measured by determining how well people can simultaneously store and process information. As reported in the most recent reviews on the topics, several studies had shown a quite robust WM impairment in FM subjects, compared with controls, using a variety of different tests (4-6, 12, 13). Consistently with patients’ perspective of difficulty dealing with complex, rapidly changing environments, studies on attention and distraction suggest that WM deficits in patients with FM are mainly due to difficulties in the management of the contents, rather than to the loss of storage capacity (6). Attention is, in fact, a cognitive function strictly linked to WM and allows the brain to select and control the relevant inputs for storage and processing into WM. Patients with FM, in fact, show to be mostly impaired in tasks in which distraction from a competing source of information is prominent and attention is divided between two tasks, such as the Paced Auditory Serial Attention test (PASAT), the auditory consonant

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trigram (ACT) test, the reading span task or the Test of Everyday Attention (TEA), a standardised test with a high ecological validity (4-6). The ability to dealing with distraction is part of executive function (EF), a broad term that includes different processes, including planning of long-term goals, decision-making, suppression of inappropriate responses, and the ability to resisting distracting information. Taken together, results strongly suggest that FM patients appear to have selective deficits on this latter EF process (4-6).

Other two domains in which FM patients seem to present cognitive dysfunction are semantic and episodic memory (4-6, 12, 13). Semantic memory is the knowledge of words and facts. It is usually measured with verbal fluency tasks, that evaluates how quickly and efficiently patient could access to the stored knowledge about words. Several studies reported impairments in patients with FM in semantic memory, not only on verbal fluency tests, but also in naming speed and vocabulary tests, in line with the patients' reported difficulties to think quickly and to come up with the right word for a given situation. However, other studies did not find any difference between subjects who have FM and controls on fluency tests, suggesting the need of further research to fully understand semantic memory problems in FM (4-6, 12-14). Inconsistent results have also been reported for episodic memory, the ability to remember specific events or episodes (4-6, 12, 13). In fact, even if several studies have found mild episodic memory deficits in patients with FM, it does not seem to be as consistent and robust as the WM results. The findings concerning episodic and semantic memory could suggest that memory in FM may be strong enough to perform well under the ideal conditions of the neuropsychological evaluation, but performance could decrement in the presence of distraction, situation that more closely represents patients' daily life (15). Finally, reduced mental processing speed has been reported in some studies in patients with FM, even if other studies failed to demonstrate it (4, 6, 12).

Many pathogenetic factors contribute to the cognitive cluster of FM symptoms. First of all, pain interferes with cognitive functioning, and it has been provided an association between the level of pain and the amount of the impairment (5). It has been suggested that dyscognition may derive from the brain resources competition between pain processing and cognitive performances, since many brain areas involved in cognitive tasks contribute also to the perception and control of the cognitive aspects of pain (16). The disruptive effect of pain on cognitive functioning could be partially mediated by deviant cerebral blood flow regulation during cognitive task (17). In fact, cognitive impairment in FM has been associated with alterations in cerebral blood flow responses during the cognitive task, with pain severity correlating with both cognitive performance and cerebral blood flow responses (17).

Some studies have associated anxiety and depression with cognitive dysfunction, but these results are controversial (16) and the effects of mood seem to be primary related to pain (12). Moreover depression and cognitive impairment are two disorders that share a closely linked inflammatory aetiology. Therefore an important link between mood and cognitive disorders can be related to a common background of a low grade inflammation that is one of the pathogenetic hypotheses of FM (16). In this way, positive reflexes on cognition can be achieved with regular physical exercise, possibly through the reduction of pro-inflammatory cytokines and increasing of BDNF peripheral levels, as confirmed in patients with cognitive mild impairment (18).

Furthermore, FM patients often present sleep disorders, which are known to have a negative impact on cognitive performances, but also these data are discussed because cognitive deficits remain after controlling for sleep problems (19).

Also medications have an important influence on cognition: FM patients are often treated for long periods with antidepressants, antiepileptics or strong analgesics. Literature presents controversial data: while it is expect-

able that medication may decrease cognitive performances, some studies have shown no differences between pharmacologically treated and non-treated patients, and, actually, there is evidence for a beneficial effect of analgesics, probably due to the reduction of pain intensity (19). Finally, even though there is no evidence confirming this perception, FM patients identify fatigue as another element contributing to cognitive impairment (12).

In order to develop management strategies to lessen dyscognition severity, pain, depressive symptoms, sleep disorders, fatigue and medication have, therefore, to be considered in the diagnostic process, as they may contribute to the cognitive impairment and be a target for the treatment. Even though a full neuropsychological test battery is the best tool to evaluate FM patients' cognitive status, in clinical practice self-reported questionnaires would provide a first and easy screen for the presence of cognitive impairment. Recent studies, in fact, revealed correlations between subjective cognitive complaints and neuropsychological test, focusing on self-reported memory and attentional function in a specific daily life context (20-22). Using the Metamemory in Adulthood (MIA) questionnaire, Glass and colleagues found that patients' self-report about memory function appears accurate (20). Using the Everyday Memory Questionnaire (EMQ), Landrø and colleagues not only confirmed the association between objective tests and subjective complaints of cognitive impairments, but also showed that basic aspects of attentional control were still significantly associated with subjective complaints when controlling for the degree of depressive symptoms (21). The fact that cognitive impairments are reflected in patient self-reports independently of depressive symptoms has further been confirmed in a more recent study, using the Functional Assessment of Cancer Therapy cognition scale, version 2 (FACT-Cog 2) (22). Taken together, these data suggest that subjective complaints might reflect genuine cognitive deficits to a larger extent than previously thought.

Currently, there is no a defined and ideal treatment for dyscognition, but several symptom-based strategies have been suggested to decrease its severity. The complexity of FM cognitive dysfunction requires a treatment addressed to neurobiological, psychological, and behavioural factors. First of all, a better control of pain, depression, fatigue and other fibromyalgia symptoms has been associated to improvement in cognitive performance, even though not in all cognitive domains (10). Pharmacological strategies have to be considered to manage these FM symptoms. Also non-pharmacological treatments have potential benefits: rehearsal techniques and exercise programs, included recovery of peripheral muscle function, have a promising role, but further researches are needed (4, 23).

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