

## **Title**

Allostatic overload in patients with fibromyalgia: preliminary findings.

## **Short title**

Allostatic overload in fibromyalgia

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Fibromyalgia (FM) is a chronic syndrome characterized by not only widespread musculoskeletal pain, but also many psychological symptoms, including disrupted or non-restorative sleep, fatigue, stiffness, mood disorders and cognitive impairment [1].

The DSM-5 criteria for somatic symptom disorder could be applied to FM [2], even though there is a risk of assigning a diagnosis of mental illness to a large proportion of patients with a physical chronic illness [3]. Furthermore, the DSM approach to somatisation does not consider important features concerning psychological factors that affect physical conditions and abnormal illness behaviours, which might be relevant for diagnostic and therapeutic processes [3]. Among psychological factors it has also to be noted that some authors consider FM a stress-related syndrome [4] and there are several studies on the role of trauma and stressful events in FM aetiology [5-7].

The concept of allostasis emphasizes that healthy functioning requires continual adjustments to the internal physiological milieu [8]. Allostatic load reflects the cumulative effects of stressful experiences on daily life. When the cost of chronic exposure to fluctuating or heightened neural or neuroendocrine responses exceeds the coping resources of an individual, allostatic overload ensues [8]. Clinical criteria for the determination of allostatic overload have been developed [9]. They are based on: (a) the presence of an identifiable source of distress in the form of life events and/or chronic stress exceeding individual coping skills; (b) clinical manifestations of distress and/or impairment in well-being. Such criteria, which are part of the revised version of the Diagnostic Criteria for Psychosomatic Research (DCPR-R), have been used in a number of investigations: they have been found to entail clinical and prognostic implications and to be associated with alterations of biological markers [9].

The aim of this preliminary study is to evaluate the prevalence of allostatic overload in a sample of FM outpatients using DCPR-Revised criteria.

Participants in this study were diagnosed with FM by a rheumatologist and were regularly visited by a psychiatrist, which is the standard clinical practice in our hospital outpatient unit. The study was approved by the Institutional Ethics Committee, and only subjects who provided informed consent were included. Socio-demographic and clinical data (pain, depression, anxiety, asthenia, sleep disturbances, cognitive impairment, duration of FM and medication) were systematically recorded, and the DCPR-R was used to assess the psychosomatic syndromes.

The study population consisted 104 female FM patients. Their socio-demographic and clinical characteristics are reported in Table 1. The presence of at least one DCPR-R psychosomatic syndrome was found in 78% (n=81) of the patients, whereas two or more syndromes were found in 31% (n=32). Allostatic overload occurred in a quarter of patients (table 1); other common DCPR diagnoses were persistent somatization, functional somatic symptoms secondary to a psychiatric disorder and alexithymia (see Table 1). Nearly all the patients received pharmacological treatment, as shown in detail in Table 1. The most commonly prescribed drugs were antidepressants (especially SNRIs, as recommended in current practice), often combined with benzodiazepines, antiepileptic drugs (prescribed by the psychiatrist) or opioids (prescribed by the rheumatologist). The use of supplements was also common.

In FM patients in our study, the revised version of DCPR seemed to be rapid and simple to use, guiding the clinicians through the diagnostic process, confirming previous findings obtained with the previous version of DCPR [10]. The presence of a DCPR-R syndrome in approximately 80% of the patients interviewed seems to confirm the importance of investigating psychosomatic factors and to suggest the appropriateness of considering coexisting psychosocial issues in these patients to fully capture the complexity of the aetiology and progression of FM. A better understanding of allostatic overload could therefore influence on the therapeutic process; for example psychotherapy could focus on the patient's perception of the environment as exceeding his/her resources or on lifestyle modification.

Finally, considering that medications are commonly used in FM, and can reduce pain but are often not fully satisfactory, a better understanding of the coexisting psychosomatic factors can also help increase responsiveness to drugs and avoid excessive side effects. This integration of psychological care into the treatment of physical symptoms can increase adherence to drug regimens and improve the outcome and overall quality of life.

There were several limitations of this study, such as the lack of information about the psychosocial functioning of the patients, the lack of a standardized psychiatric assessment, the lack of biological markers related to DCPR syndromes and the limited size of the study population considered. For this reason, additional studies with larger sample sizes are needed to support the proposal of using the DCPR-R as a complementary tool in the diagnostic work-up and treatment decision-making for FM patients.

Nevertheless, these results point to the potential for allostatic overload to expand the clinician's understanding of FM patient vulnerability by providing information on additional elements that do not fit into the traditional classifications. Further, it may unravel pathophysiological links between environmental circumstances, inflammation and sensitivity to pain [8]. Of interest is also the fact that persistent somatization (patients in whom somatic symptoms have clustered, probably due to an enhanced general sensitivity to pain and discomfort) occurred in half of the patients (table 1) and mood and anxiety disorders had a primary role only about a quarter of cases (Table 1). Therefore, the use of the DCPR-R [9] may help improve the recognition and characterization of these patients, and it may allow the identification of subgroups with unique features.

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*Table 1. Characteristics of FM patients, DCPR-R syndromes distribution and medications and supplements prescribed.*

**Socio-demographic and clinical characteristics of patients**

Age	54.5±10.9 years
Education	12±4.1 mean years
Stable partner	71.9%
Stable employment	56.3%
Duration of FM	4.5±3.5 years
Pain	95.3%
Fatigue	78.1%
Sleep disturbances	46.9%
Depression	57.8%
Anxiety	62.5%
Fibrofog	70.3%
Asthenia	78.1%

**DCPR-R syndromes** **Frequency n (%)**

Persistent somatization	54 (51.6)
Allostatic overload	26 (25)
Functional somatic symptoms secondary to a psychiatric disorder	24 (23.3)
Alexithymia	23 (21.9)
Demoralization	11 (10.9)
Conversion symptoms	10 (9.4)
Type A behavior	8 (7.8)
Health anxiety	5 (4.7)
Irritable mood	3 (3.1)
Other diagnosis	4 (3.6)

**Medication(s)** **Frequency n (%)**

AD + BDZ	24 (23.1)
AD	13 (12.5)
AD + AED	10 (9.6)
AD + AED + OP	10 (9.6)
AD + AED + BDZ	10 (9.6)
AD + BDZ + OP	9 (8.7)
Other polytherapy	23 (22.1)
None	5 (4.8)
Supplements	46 (44.3)

*Notes:* AD, antidepressants; BDZ, benzodiazepines; AED, anti-epileptic drugs; OP, opioids.