# Immune-inflammatory pathways and clinical changes in fibromyalgia patients treated with Mindfulness-Based Stress Reduction (MBSR): A randomized, controlled clinical trial.

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### **Abstract**

Fibromyalgia (FM) is a highly prevalent and disabling syndrome characterized by chronic widespread musculoskeletal pain and a broad range of cognitive and affective symptoms. Up to now, the pathogenesis of FM is unknown although a peripheral and central sensitization involving an imbalance on immune biomarkers appears to have a relevant role in its aetiology. The aim of this study was to extend previous clinical findings of Mindfulness-Based Stress Reduction (MBSR) to both its impact on clinical symptomatology and immune biomarkers (IL-6, CXCL8, IL-10 and hs-CRP), and also to explore the role of biomarkers as predictors of efficacy.

### **METHODS:**

A total of 70 female patients with FM were randomly assigned to two treatment modalities, namely Treatment as Usual (TAU) plus MBSR (n = 35) or TAU alone (n = 35). This study is embedded within a larger RCT (n = 225) that includes three study arms (TAU; TAU plus MBSR; and TAU plus the psychoeducative intervention FibroQoL), and a 12-month follow-up (clinical trial registration: NCT02561416). Blood cytokine assays and clinical assessment were conducted at baseline and post-treatment. Treatment effects were analysed using linear mixed models with intention to treat and per protocol analyses. In order to evaluate the balance between pro- and anti-inflammatory pathways, ratios of pro-inflammatory IL-6, CXCL8 and hs-CRP with the anti-inflammatory cytokine IL-10 were calculated (i.e. IL-6/IL-10, CXCL8/IL10 and hs-CRP/IL-10).

## **RESULTS:**

The results show that MBSR is an efficacious intervention to reduce clinical severity of patients with FM. MBSR also prevents the tendency of IL-10 to decrease as observed in the TAU group. Higher levels of baseline CXCL8 levels attenuate the beneficial effect of MBSR practice on clinical symptomatology, including pain, energy, stiffness or quality of sleep. Furthermore, higher baseline IL-6/IL-10 and CXCL8/IL-10 ratios were associated with less improvement in psychological inflexibility following MBSR treatment.

# **DISCUSSION:**

Our results show that mindfulness training has clinical efficacy in patients with FM. The results suggest that MBSR has significant immune regulatory effects in FM patients, while immune-inflammatory pathways may in part predict the clinical efficacy of MBSR. These cytokines and chemokines may be adequate biomarkers to monitor responsivity to MBSR.

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