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The Affective-Motivational Domain of the McGill Pain Questionnaire Discriminates Between Two Distinct Fibromyalgia Patient Subgroups – A Preliminary Study Based on Self-Organizing Maps

Monika Salgueiro and Jon Jatsu Azkue
*University of the Basque Country,
Spain*

1. Introduction

For two decades, FMS was diagnosed based on the criteria established on 1990 by the American College of Rheumatology, i.e. by the identification of widespread pain of at least 3 months duration, and pain and tenderness evoked by palpation in at least 11 of 18 specific bodily sites (Wolfe et al., 1990). Recently, the ACR preliminary diagnostic recommendations for fibromyalgia abandoned the tender point examination criterion, and were established as the following 3 conditions: (i) Widespread Pain Index (WPI) equal to or greater than 7 and Symptom Severity Score (SS) equal to or greater than 5, or WPI ranging between 3 and 6 and the SS equal to or greater than 9; (ii) steady presence of symptoms for at least 3 months; and (iii) the absence of a disorder that would otherwise explain the pain.

Despite being highly prevalent, the etiology and pathophysiology of FMS remains obscure. Diverse factors contributing to this condition have so far been identified, however none has been proven unequivocally responsible. Due to limited understanding of the etiology and pathophysiology of FMS, a diversity of pharmacological and nonpharmacological interventions alone and in combination have been attempted to treat the symptoms, largely on a trial-and-error basis. However, this condition remains largely refractory to treatment.

1.1 Overcoming clinical heterogeneity by subgrouping patients

Clinical variability within individuals whose disease manifestations meet the ACR criteria is enormous. While chronic pain represents a clinical manifestation that all FMS patients share in common, pain may be largely the only symptom experienced by some individuals with FMS while others present with a myriad of psychological manifestations, and even other disease entities such as chronic fatigue syndrome, irritable bowel syndrome or temporomandibular dysfunction also are frequently found in patients with FMS (Aaron & Buchwald, 2001).

Because of this heterogeneity of symptoms, authors have suggested that there is a need for empirically derived subgroups. These subgroups should not only be based on easily

measurable variables but also clinically relevant in assisting to target more specific therapeutic interventions to individuals (Bennett et al., 1991; Masi & Yunus, 1991; Turk et al., 1996). Indeed, there is a growing awareness regarding the need to identify subgroups of chronic pain patients on the basis of biological and psychosocial characteristics, as a strategy to overcome some of the problems derived from patient heterogeneity. On the one hand, if one assumes patient homogeneity and relies on measuring group means to assess treatment outcome, false negative outcomes may be magnified. Specificity should thus be optimized by interventions in patient subgroups characterized by operating pathogenic vectors, and intervention outcome may be more specifically assessed if targeted at homogeneous patient subpopulations even when underlying mechanisms are not well understood. On the other hand, assuming patient homogeneity when prescribing treatment will not provide relief or amelioration of symptoms for a significant proportion of patients, and subsets of patients may be receiving treatment for symptoms without necessity.

In chronic pain patients, numerous studies have attempted to respond to this need for patient subgrouping by empirically identifying patient subsets based on psychological characteristics and psychopathology. Turk and collaborators (1996) were among the first to identify chronic pain patients subgroups by using cluster analysis techniques, based on the Multidimensional Pain Inventory. Importantly, FMS patients classified into different subgroups according to those criteria may respond differently to treatment (Turk et al., 1998). FMS patients have also been classified empirically on the basis of psychopathological profiles by using the 90 Symptoms Checklist (SCL-90) (Williams et al., 1995). Indeed, a growing literature has suggested that psychological mechanisms may be important correlates in the establishment and maintenance of FMS (Boissevain & McCain 1991), and previous observations have shown that certain psychological variables, in combination with pain sensitivity indices, may best distinguish FMS patient subsets (Giesecke et al., 2003).

There have been several other attempts or proposals. Müller and collaborators (2007) proposed that FMS may be categorized as primary or secondary. According to the authors, primary fibromyalgia may be much more common than the secondary type and is characterized by the absence of any definitive organic factor triggering the syndrome, whereas in secondary fibromyalgia the underlying disease, such as inflammatory rheumatic processes or collagenosis can be easily diagnosed. Based on clinical manifestations, they defined four subtypes of patients with primary fibromyalgia that may reportedly benefit from different treatment strategies. Patients with fibromyalgia with extreme sensitivity to pain but with no associated psychiatric conditions would be best treated by administration of the 5-HT₃ receptor-antagonist tropisetron, whereas patients with fibromyalgia and comorbid, pain-related depression, or patients with depression with concomitant fibromyalgia syndrome would both ideally benefit from treatment with antidepressants. Finally, the focus of treatment should be on psychotherapy in the fourth group, which was composed of patients with fibromyalgia due to somatization (Müller et al., 2007). In secondary fibromyalgia, the initial focus should be on influencing the underlying disease, and for example a regimen of daily administration of 5 mg tropisetron for 5 days was found by these authors to be as effective in fibromyalgia patients whose pain was not relieved by non-steroidal analgesics, as in patients suffering from associated progressive scleroderma or other collagen-related diseases (Müller et al., 2007).

In one-hundred fifteen patients with FMS, Thieme and co-workers (2004) assessed mental status by using the DSM-IV, as well as pain, impact of pain, anxiety and depression,

posttraumatic stress disorder-like symptoms, and sexual and physical abuse. Based on the Structured Clinical Interview for DSM-IV, axis I disorders were grouped into (i) anxiety and (ii) mood disorders, the latter including major depressive episode, major depressive disorder, and dysthymic disorder. The authors conducted a multivariate analysis of variance (MANOVA) to assess differences among the groups with no axis I disorders, anxiety disorders, and mood disorders, and one-way ANOVAs were conducted following a significant MANOVA. Their analysis yielded three psychosocial subgroups that were termed Dysfunctional, Interpersonally Distressed, and Adaptive Copers. The Dysfunctional and Interpersonally Distressed groups mainly reported anxiety and mood disorders, respectively, while the Adaptive Copers group exhibited little comorbidity. These findings were further suggestive that, rather than being a homogeneous diagnosis, varying proportions of FMS patients present with comorbid anxiety and depression dependent on psychosocial characteristics, emphasizing the importance of assessing patients with FMS for the presence of affective distress and not treating them as a homogeneous group. A recent, additional attempt to identify FMS patient subgroups was that advanced by Hasset and co-workers (2008). These authors proposed a classification based on affect balance styles, which considered four categories, including (i) healthy subjects with high levels of positive affects (PA) and low levels of negative affect (NA), (ii) low (low PA/low NA), reactive (high PA/high NA), and depressive (low PA/high NA). The authors found high prevalence of depressive and reactive affect balance styles in patients with FMS, and reported an association between affect balance style and psychiatric comorbidity.

Giesecke and co-workers (2003) proposed a classification scheme based on variables from three clinical domains, namely pain sensitivity and hyperalgesia, cognitive variables including coping strategies and catastrophizing, as well as mood and negative affective states such as depression and anxiety. They assessed pressure pain sensitivity by the use of an algometer, whereas cognitive evaluation was largely conducted by means of the Coping Strategies Questionnaire and psychological distress was assessed by using the Center for Epidemiologic Studies Depression Scale and the State-Trait Personality Inventory. By using agglomerative hierarchic cluster analysis and multiple analyses of variance to confirm that each variable used in the analysis was differentiated by the cluster solution, these authors claimed the existence of three clinical profiles that were distinctly different in terms of anxiety, depression, catastrophizing, control over pain and pressure-pain sensitivity. One subgroup of patients was distinguished by moderate mood scores, moderate levels of catastrophizing and perceived control over pain, and low levels of pain sensitivity. A second subgroup exhibited poorer mood scores, highest scores on the catastrophizing subscale, the lowest values for perceived control over pain, and high levels of tenderness. The third group displayed normal mood, very low levels of catastrophizing, high perceived control over pain, but increased pain sensitivity.

More recently, de Souza and collaborators (de Souza et al., 2009) relayed on hierarchical clustering analysis techniques of selected items of the Fibromyalgia Impact Questionnaire (FIQ), a self-administered report that comprehensively reflects the functional capacity and the occurrence and severity of typical symptoms of the disease (Burckhardt et al., 1991). These authors proposed a two-cluster group solution based on differences in scores on specific items of the FIQ, where so termed type II subjects reported higher scores on anxiety, depression and morning tiredness items over type I subjects (de Souza et al., 2009). A major strength of this classification scheme is that it assesses the most prevalent complaints

reported by persons with FMS while being easy to administer in the clinical setting. These two subgroups scored differently on Pain Catastrophizing Scale scores, Interference and Life Control subscales of the Multidimensional Pain Inventory, or the SF-36 mental component summary. This classification scheme highlighted the contribution of emotional status to clinical variability in FMS patients and provided an avenue for refining treatment by addressing psychological comorbidities in discrete subpopulations. Observations by de Souza's group have been replicated in a larger sample, and differences in depressive and anxiety symptoms have been corroborated by using the Beck Depression Inventory and the Hospital Anxiety and Depression Scale, respectively (Calandre et al., 2010).

Although depression and anxiety have been extensively studied in persons with FMS, also general psychopathology is prevalent in fibromyalgia relative to other chronic conditions (Epstein et al., 1999; Gormsen et al., 2010; Shaver et al., 1997), acute disorders (Gatchel, 1996) or asymptomatic subjects (Arnold et al., 2008; Dersh et al., 2002; Hellström & Jansson, 2001; Winfield, 2000) and, for example, post-traumatic stress disorder may affect 50% of subjects suffering from FMS (Fietta et al., 2007), whereas obsession, somatization disorders and alexithymia are reportedly present in up to 55%, 71%, and 47%, respectively (Centonze et al., 2004). High prevalence of positive testing for bipolar disorder among patients with FMS has also recently been reported (Wilke et al., 2010).

1.2 Does the McGill Pain Questionnaire capture clinically relevant information?

Verbal rating scales are among the most commonly used methods for assessing pain intensity. Due to the ease with which they can be administered and because they are generally easy to comprehend, compliance rates for verbal rating scales are comparable to those obtained for other measures of pain intensity (Jensen et al., 1986, 1989). In addition, verbal rating scales are positively co-related to other measures of pain intensity and are sensitive tools to assess treatment outcome (Fox & Melzack, 1976; Ohnhaus & Adler, 1975; Rybstein-Blinchik, 1979), and thus can be considered as valid indicants of pain intensity (Ahles et al., 1984; Downie et al., 1978; Jensen et al., 1986, 1989; Kremer et al., 1981; Littman et al., 1985; Ohnhaus & Adler, 1975; Woodforde & Merskey, 1972).

The McGill Pain Questionnaire (MPQ) (Chen & Treede, 1985; Dubuisson & Melzack, 1976; Melzack, 1975, 1985) is a widely employed verbal pain assessment tool. The MPQ comprises 20 subscales or sets of verbal descriptors designed to evaluate the sensory, affective, evaluative and miscellaneous dimensions of pain.

A number of studies have shown that the MPQ can capture clinical characteristics of pain that predict the occurrence of distinct underlying pathogenic mechanisms. For example, Gruschka and Sessle (1984) administered the MPQ to 102 patients presenting with toothache, in order to test the sensitivity of this tool to distinguish between dental pain originating from reversible or irreversible tooth pulp inflammation. In that study, patients suffering from pain derived from necrotic or irreversibly inflamed tooth pulp scored significantly higher on the total Pain Rank Index, as well as on the sensory, evaluative and miscellaneous Pain Rank Indices, although no differences were found as to the affective-motivational dimension, in such a manner that the MPQ alone was capable of predicting diagnosis in 73% of patients. Melzack and co-workers (1986) used a similar approach to distinguish between trigeminal neuralgia and atypical facial pain patients, and they were able to correctly classify 91% of the patients based on 7 descriptors of the MPQ.

In the present study, we hypothesized that the MPQ might indeed be capable of capturing distinctive pain characteristics in homogeneous subgroups of patients with FMS. However,

understanding complex relationships between subjects across multiple variables may be difficult, and in particular the MPQ comprises a considerable number of items to address several dimensions of the complex experience of pain. Data visualization techniques attempt to solve these difficulties by transforming high-dimensional data into lower dimensional topologies that may be better understood visually. A relatively novel approach to discover similarity relations between data objects in high-dimensional signal space is the Self-Organizing Maps (SOMs), a relatively recent methodology for unsupervised machine learning. A SOM is an artificial intelligence technique, first introduced by Teuvo Kohonen (1995), that is commonly used to non-linearly project multidimensional input data into a bi-dimensional output space, thus providing the investigator with a visual image of the data that better depicts their structure and relationships. A simple SOM layout typically consists of an input neuron layer, a competition layer and an output layer. The SOM builds a two-dimensional regular lattice where the location of a map unit, or neuron, is indicative of relative distances between data points in the high-dimensional space, in such a way that mapping or data structure from the high-dimensional space onto map units are preserved. Based on this property, the SOM can serve as a very efficient, powerful and highly visual tool for cluster analysis of high-dimensional data (Kohonen, 1995). This has been the selected use for the SOM in the present work. The SOM algorithm, also known as the Kohonen feature map algorithm, is a well known artificial neural network algorithm that is based on unsupervised learning, in contrast to many other neural networks using supervised learning.

2. Methods

2.1 Setting and data collection

A total of 30 consecutive FMS subjects (28 females, 2 males) aged 29-82 years (58 ± 10.38) participated in the study. Subjects were recruited through advertisements, FMS associations and informative presentations. All participating subjects had been diagnosed with FMS on according to the 1990 ACR classification criteria at least one year prior to the initiation of this study. The study was approved by the Ethical Review Board of the University of the Basque Country, and all participants provided their written, informed consent.

Subjects were interviewed individually by a trained psychologist. Sociodemographic data were collected first, and self-applied questionnaires were then administered for clinical assessment in the same session, including the MPQ, FIQ, Medical Outcomes Study – Short Form 36 (SF-36) and SCL-90-R (c.f. below). Participants were not asked to discontinue medication prior to study.

We used the validated Spanish translation of the MPQ (Lázaro et al., 1994), which includes a total of 78 descriptors of pain. In this version, five out of the 78 descriptors are computed into a Present Pain Index (PPI) measuring overall pain intensity. A zero score was assigned here if no descriptor was chosen. PRIs on sensory, affective-motivational, evaluative and miscellaneous dimensions of pain were obtained from weighted MPQ item scores. A total, cumulative PRI was also calculated. Subjects were also asked to assess the level of pain using the Visual Analog Scale (VAS), that is, by placing a mark on a line 10 cm long at an appropriate distance between two endpoints signaling no pain at all and the most intense pain imaginable (Huskisson, 1974; Scott & Huskisson, 1976).

The Fibromyalgia Impact Questionnaire (FIQ) is a 20-term, self-administered questionnaire that assesses both psychological and physical symptoms of FMS and allows for a broad

quantification of interference of the condition on daily living tasks and quality of life (Burckhardt et al., 1991). It is quickly administered and easily evaluates a broad range of clinical characteristics associated to FMS. The total FIQ score can adopt values ranging from 0 to 10, where higher scores denote greater severity or impact. The FIQ is held to be a sensitive tool to monitor progression of the FMS and response to treatment in clinical trials (Dunkl et al., 2000). We used the Spanish language version validated by Monterde and co-workers (2004).

The Spanish version of the SF-36 (Alonso et al., 1995) was administered to assess overall health status. The physical component summary (PCS) and the mental component summary (MCS), whose values can range from 0 to 100 where higher values relate to better quality of life, were calculated.

The 90 Symptom Checklist Revised (SCL-90-R) (Derogatis, 1994) is a self-reported inventory that inquires patients on the level of distress generated by 90 hypothetical situations, and provides scores on 9 psychopathological dimensions, namely somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation and psychoticism, plus additional scores assessing the severity of the above dimensions. SCL-90-R has proved useful for assessing emotional status in chronic pain patients, since it is an inexpensive way to access a significant amount of data on a range of psychopathological dimensions (Torres et al., 2010). Here, we used the validated version for Spanish language (González de Rivera et al., 2002). For each subscale, composite normalized T-scores with a mean of 50 and standard deviation of 10 were obtained on the basis of standardized norms for nonpsychiatric patients provided in the test manual (González de Rivera et al., 2002). The global severity index (GSI), positive symptom total (PST) and positive symptom distress index (PSDI) were also obtained.

2.2 Analysis with Self-Organizing Maps

Raw scores from all 20 MPQ items were normalized prior to SOM analysis, and scores from items contributing to the four studied subscales were fed to separate SOMs. Geometry of the two-dimensional SOMs was set to 10 rows x 20 columns, and the grid of the SOM units was selected as hexagonal from the beginning. Competition layer neurons were initialized randomly as a pre-processing step, and the SOM was then trained by iteratively calculating similarity measures as Euclidean distances.

The unified distance matrix (U matrix) method is the most commonly used method to render the SOM. The U matrix consists of a regular neuron grid where each cell or node represents a neuron, and distances between neighboring neurons provide a bi-dimensional representation of the distance of the corresponding reference vectors. The basic idea of this method is based on the principle of representing the distance matrix between the all the reference vectors associated to the SOM units by using colorings or shades of gray, where a dark shade of gray between neurons denotes a large distance and thus a gap between the vectors in the input space, whereas light shades represent close relationships between neighboring units. Analogously, light areas in a U matrix can be seen as a representation of clusters whereas dark areas denote cluster separators. Thus a U matrix representation of a SOM can be a practical way to easily visualize clusters in the input space when no a priori information exists on the input data. Here, U matrices yielded by the four maps were used to decide on the presence of patient clusters on each analyzed MPQ dimension and the convenience of further statistical analyses.

2.3 Characterization of FMS patient subpopulations

Subjects located on each side of a cluster separator were considered as belonging to separate clusters. Subsequently, the resulting patient clusters were compared as to a number of clinical and psychological determinants, in order to verify the capability of the SOM analysis to discriminate between clinically distinct patient subpopulations. Firstly, we wished to know whether FMS patient subgroups discriminated by the SOM analysis on the basis of their scoring profiles on a given pain dimension also exhibited differential profiles on other dimensions of pain or differences in intensity of experienced pain. Secondly, we compared identified patient clusters in terms of severity of the disease and impact on health-related quality of life. Finally, we assessed whether or not patients with FMS belonging to different clusters also differed in associated psychological comorbidity.

3. Results

We used self-organizing maps to test whether verbal pain descriptors on the MPQ that address sensory, affective-motivational and evaluative dimensions of pain would be able to discriminate between clinically distinct FMS patients.

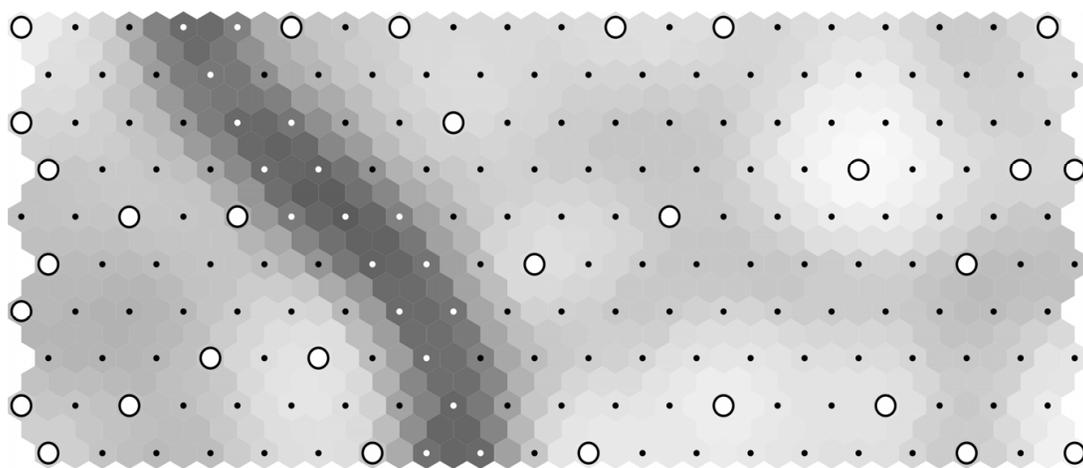


Fig. 1. U-matrix representation of responses from patients with FMS on MPQ items addressing the affective-motivational dimension of pain. Neurons of the network are marked as dots, whereas open circles indicate neurons representing patients with FMS. The cluster separating zone, represented here by the dark gap, segregates two patient subgroups which are termed here as cluster 1 (right side of the map) and cluster 2 (left side).

SOM analysis of the MPQ items corresponding to the sensory, evaluative and miscellaneous domains of the test failed to suggest the existence of clinically distinct patient subsets. Therefore, no further analysis was conducted on these dimensions. However, SOM analysis of the responses to items 15 through 17, i.e. those addressing the affective-motivational domain of pain, consistently revealed the existence of two distinct subject clusters (figure 1), which will be referred to as *cluster 1* and *cluster 2* hereafter.

Cluster 1 comprised 17 out of the 30 subjects of the sample, whereas 13 subjects were found to fall within cluster 2. General characteristics of both clusters are provided in table 1. No statistically significant differences were found between clusters with respect to age, gender, years since diagnosis, or active status. The two FMS patient clusters were indistinguishable in terms of MPQ scores on sensory-discriminative, evaluative and miscellaneous

dimensional scores (table 2). As well, no significant between-clusters differences were found as to Present Pain Index scores or intensity of pain as measured by the VAS.

	cluster 1 n=13	cluster 2 n=17
Mean age (s.d.)	51.85 (7.76)	50.35 (12.21) ⁽¹⁾
Women (%)	100	88.2 ⁽²⁾
Mean years from diagnosis	4.76 (1.32)	3.94 (0.95) ⁽¹⁾
Active status	23.2%	41,2% ⁽²⁾

Table 1. Sociodemographics of patients with FMS classed as cluster 1 and cluster 2. Differences between groups were not significant ⁽¹⁾ Student's *t* test; ⁽²⁾ Mann-Whitney *U* test).

	cluster 1	cluster 2
McGill Pain Questionnaire		
Sensory PRI	21.00 ±4.912	22.15 ±4.298
Affective-motivational PRI	4.41 ±1.906	6.08 ±1.935 *
Evaluative PRI	7.71 ±2.054	7.85 ±2.267
Miscellaneous PRI	3.24 ±0.903	3.46 ±0.660
Total PRI	36.35 ±8.299	39.54 ±5.348
Number of words	14.00 ±1.852	16.54 ±1.450 **
PPI	2.82 ±0.809	3.08 ±1.038
Pain intensity (VAS)	6.76 ±1.15	7.05 ±0.92
Total FIQ score	6.83 ±1.296	7,90 ±1.277 *
SF-36		
Physical component Summary	39.81±9.206	29.77±7.224 **
Mental component Summary	50.60±25.436	22.22±9.149 **

Table 2. Summary of measures of pain and assessment of clinical status in FMS patient clusters. * $p < 0.05$ and ** $p < 0.01$ as compared to cluster 1.

Not surprisingly, the two subpopulations segregated by SOM analysis on the basis of affective dimensional scoring profiles differed significantly ($p < 0.05$ at the Student's *t* test) in their affective Pain Rating Index (table 2). Specifically, cluster 1 patients exhibited lower scores (4.41 ±1.906) than cluster 2 patients (6.08 ±1.935). In addition, the total number of words chosen by cluster 1 patients was significantly lower (14.00 ±1.852) than cluster 2 patients (16.54 ±1.450). Clinical status in both patient clusters was assessed here by using the FIQ and the SF-36. Cluster 2 patients exhibited significantly more severe FMS in terms of total FIQ scores

(7,90±1.277) as compared to cluster 1 patients (6.83±1.296, $p < 0.05$ at the Student's *t* test). Health-related quality of life was also significantly poorer in cluster 2 patients as assessed by the physical component summary (29.77±7.224) and the mental component summary (22.22±9.149) derived from the SF-36 items, relative to cluster 1 patients (39.81±9.206 and 50.60±25.436, respectively).

Psychological status was assessed by means of the SCL-90-R. The profile exhibited by FMS patients classed as cluster 1 was fully within normal levels for nonpsychiatric population (figure 2). In contrast, subjects in cluster 2 exhibited generally higher levels of psychopathology. Composite normalized T-scores in these patients were significantly higher and well above the diagnostic cutoff value of 60 on dimensions somatization, obsession-compulsion, depression, anxiety, paranoia, and psychoticism. On the global severity index (GSI), positive symptom total (PST) and positive symptom distress index (PSDI), cluster 2 patients also scored above the diagnostic level, although differences with respect to cluster 1 scores were not statistically significant.

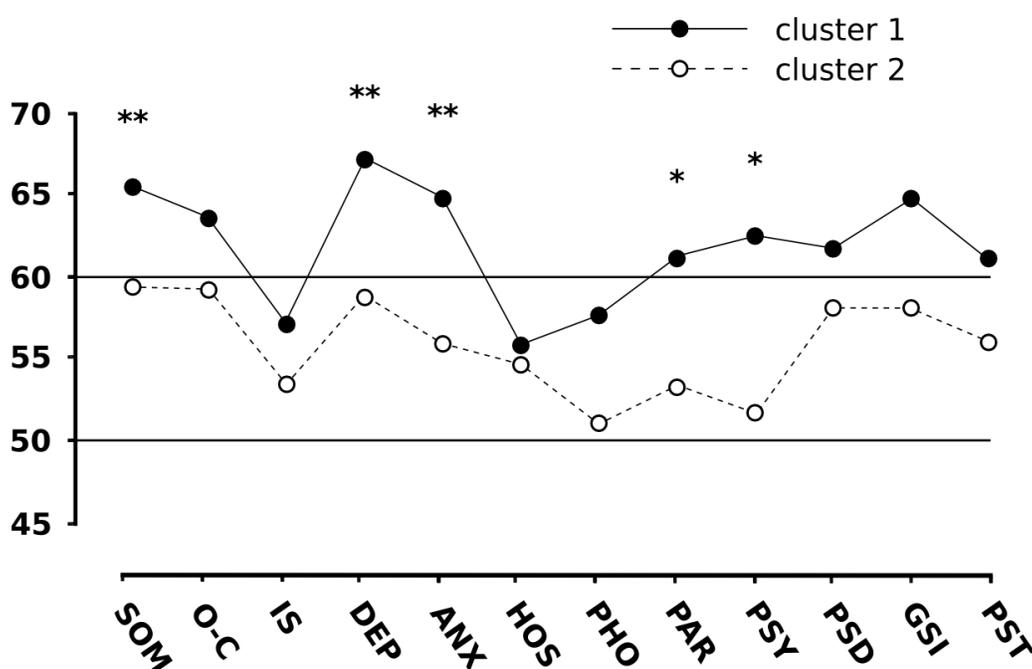


Fig. 2. Psychological profiles based on composite, normalized T-scores of the SCL-90-R in the two FMS patient clusters identified by SOM analysis. Scores of cluster 2 patients are generally higher and above diagnostic level on subscales somatization, obsession-compulsion, depression, anxiety, paranoia, and psychoticism.

4. Discussion

4.1 What is in the affective-motivational dimension of pain?

Pain descriptors have long been analyzed to differentiate medical from psychiatric diagnoses or to differentiate among medical diagnostic categories. Back in the 70's, Veilleux and Melzack (1976) proposed that the pattern of sensory and affective pain descriptors used by patients may be clinically useful, since patients with persisting pain complaint within a psychiatric population used more sensory than affective descriptors to describe their pain, whereas patients with rather transient pain used more affective than sensory descriptors.

These investigators suggested that a pattern dominated by sensory descriptors may indicate traditional methods of pain control, whereas psychiatric approaches may be more appropriate when affective descriptors prevail (Veilleux & Melzack, 1976).

Pain affect can be defined as the emotional arousal and disruption engendered by the pain experience. Arousal produced by pain, which may be experienced as frightening or distressing, can interfere in daily activities and habitual modes of response. Measures of pain affect can be complex and heterogeneous, and can be different from measures of pain intensity (Gracely, 1992; Jensen et al., 1989). In a sense, pain may not be different from other sensory-perceptual experiences in that, in the same way that identifying a pitch or a melody can be distinguished from what that sound means to us or how it makes us feel, pain intensity or location may be considered as different from its affective or motivational interpretation. The emotional response to pain is closely related to the meaning the patient gives to the pain experience. Hence, pain is likely to engender more suffering when it is perceived as indicative of threat to the subject's physical, psychological, or social integrity than when it is not considered to be a threat. It is thus not hard to understand that among cancer patients, the emotional aspects of pain can eventually come to dominate the whole clinical picture. According to their affective dimensional scores, cluster 2 FMS patients as characterized here are thus likely to associate negative affect to their perception of pain and disease.

The Affective subscale of the McGill Pain Questionnaire (MPQ) is by far the most widely used measure of pain affect. The results of the present study demonstrate that segregation of patients with FMS on the basis of the affective-motivational dimension of pain results in reliable segregation on other indicators of physical and psychological status. Patients classed as cluster 2, which exhibited higher scores on the pain affect scale, also reported poorer clinical status as revealed by the FIQ and the MCS and PCS, and showed psychological comorbidities in a number of subscales addressed by the SCL-90-R. In contrast, patients of cluster 1 showed no psychological distress and lower levels of severity of disease. A reasonable interpretation of this finding is that the affective dimension of the MPQ provides a good indication of psychological distress and mood disturbances associated to FMS. In connection with this, it may be argued that, since mood is known to modulate perceived pain intensity (Von Graffenried et al., 1998), higher scores on the affective dimension could be considered to indicate the contribution of pain affect to perceived pain intensity. However, we failed to find significant differences between clusters as to sensory-perceptual or evaluative dimensions of pain and intensity of pain as measured by the VAS. This appears to suggest that psychological factors may be influencing the clinical status of patients with FMS irrespective of sensory aspects and intensity of pain. As a consequence, interventions addressing associated psychopathology might be expected to improve FMS and health-related quality of life without necessarily alleviating the perceived levels of pain.

4.2 Clues to therapeutic intervention

It is reasonable to assume that treatment can be enhanced if it is appropriately tailored to the patient characteristics and that therapeutic interventions targeted at specific needs identified in patient subgroups should be substantially more effective than therapies prescribed just by matching to medical diagnosis. This is why research into the heterogeneity and individual variability in patients with FMS is of such great importance, as is the identification of

distinctive features of relevant patient subgroups. The clinical practice should also respect this heterogeneity and should aim at developing interventions that best match the needs of the individual patient. There has been a growing awareness of the importance of psychological factors in reports of pain (Gatchel & Turk, 1999). For example, physical factors fail to predict pain severity or life interference in patients with low back pain or rheumatoid arthritis, whereas assessment of helplessness and hopelessness can help to predict reported pain and behavior in response to pain (Flor & Turk, 1988). In addition, variables other than medical diagnoses and identified physical pathology may affect treatment outcome (Jensen et al., 1994, 2001). In particular, perceptions of control over pain is inversely correlated with pain, depression, and physical disability, whereas catastrophizing and beliefs about being disabled may be directly associated.

It has long been suggested that high affective scores indicate the necessity of a psychotherapeutic approach (Veilleux & Melzack, 1976). Psychotherapy appears to be mandatory in subgroups of patients displaying measurable distortions of pain affect. An implication of the present results is that only one subset of patients with FMS, namely the one termed here as cluster 2, is likely to benefit from a psychotherapeutic intervention. Thus, in these patients, criteria used to tailor psychotherapeutic interventions may allow for different factors in a biopsychosocial model (Keefe et al., 2004). Treatment tailored to the shared cognitive behavioral factors may enhance treatment effects (Prins et al., 2001; Bazelmans et al., 2006). Indeed, in patients with chronic pain, treatment outcomes tend to be affected by specific cognitive behavioral factors such as passive pain coping and helplessness (Nicassio et al., 1995; Rollman & Lautenbacher, 1993). Cognitive-behavioral therapies can successfully modify key elements of the fear-avoidance model in patients with chronic low-back pain (de Jong et al., 2005; Vlaeyen et al., 2001, 2002). Likewise, factors shared in common by specific FMS patients subsets should be taken into account. For example, approaches aimed at pain acceptance that proved relevant in chronic pain should be considered for FMS (Evers et al., 2001; McCracken et al., 2005). Meta-analyses have concluded that cognitive-behavioral therapy in combination with physical exercise training is the most effective non-pharmacological treatment for FMS (Goldenberg et al., 2004; Hadhazy et al., 2000; Rossy et al., 1999; Sim & Adams, 2000). Behavioral reactions such as avoidance, cognitive reactions including increased attention to bodily sensations and catastrophizing, and physiological reactions such as increased neurovegetative arousal and muscle tension, all are appropriate adaptive short-term reactions. However, they may become detrimental in the long term in response to chronic pain (Evers et al., 2001; Flor & Birbaumer, 1990; Turk & Flor, 1999). For example, muscle tension and neurovegetative hyperactivity, which are physiological reactions to pain, may lead to higher levels of pain and functional disability in the long term if misinterpreted as evidence of physical harm (Bortz, 1984; Flor & Birbaumer, 1990). Catastrophizing is also an important cognitive factor in chronic pain (McCracken & Gross, 1993; Vlaeyen et al., 1995). Exaggeration of negative interpretations of pain may lead to increased levels of pain-related fear, and this may in turn result in increased attention to bodily sensations and hypervigilance to pain (McCracken, 1997). Finally, sustained avoidance of physical activities can worsen musculoskeletal condition, thereby contributing to exacerbate pain (Bortz, 1984). On this basis, a number of treatments have been aimed at modifying the patient's pain experience and disability. Although studies show that the cognitive-behavioral approach alone does not generally

provide significant benefits to FMS patients over group educational or physical exercise programs, it may indeed be beneficial for patients in great psychological distress (Van Koulil et al., 2007).

5. Conclusions

The results of this pilot study based on SOM analysis suggest that the affective-motivational domain of the MPQ discriminates between two FMS patient subpopulations with distinctly different levels of illness severity and associated psychopathology. According to these findings, psychotherapeutic intervention on one subset of patients with FMS with associated psychopathology may result in better clinical status and improved quality of life.

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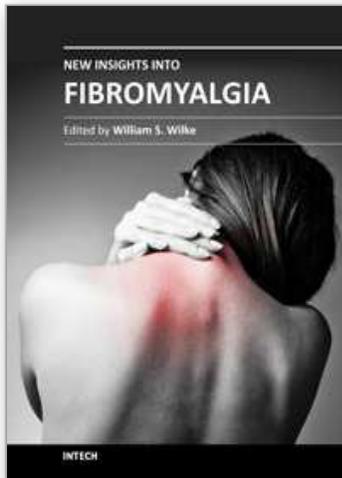
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Given the potential problems that can obscure any scientific enterprise, inconsistent results across studies are bound to occur. How are we to decide what is true? Let's turn to philosophy for a reasonable answer. The mathematician-philosopher Bertrand Russell approached a similar problem in his monograph *The Problems of Philosophy* (Russell B, 1912). He addressed the following question: How do we know that anything is "real"? Is the only reality subjective and simply in our minds, as Bishop Berkley challenged, or can we mostly believe the objective reality? His pragmatic answer: All possibilities may be true, but when the preponderance of evidence indicates that objective reality and knowledge are the most probable case, go with it. If the preponderance of all evidence about the clinical description of fibromyalgia and it's pathogenic mechanisms and treatment strategies indicate a highly probable interrelated hypothesis, go with it. The direction of the literature on the whole trumps the less likely tangents. At the same time, remember Bertrand Russell and his pragmatic answer, and keep an open mind.

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University Campus STeP Ri
Slavka Krautzeka 83/A
51000 Rijeka, Croatia
Phone: +385 (51) 770 447
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Unit 405, Office Block, Hotel Equatorial Shanghai
No.65, Yan An Road (West), Shanghai, 200040, China
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
Phone: +86-21-62489820
Fax: +86-21-62489821

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