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Distinguishing fibromyalgia from rheumatoid arthritis and systemic lupus in clinical questionnaires: an analysis of the revised fibromyalgia impact questionnaire (FIQR) and its variant the symptom impact questionnaire (SIQR) along with pain locations

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Abstract

Introduction The purpose of this study was to explore a dataset of subjects with fibromyalgia (FM), rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE), who had completed the Revised Fibromyalgia Impact Questionnaire (FIQR) and its variant the Symptom Impact Questionnaire (SIQR), for discriminating features that could be used to differentiate FM from RA and SLE in clinical surveys.

Methods The frequency and means comparing FM, RA, and SLE participants on all pain sites and SIQR variables were calculated. A multiple regression was then conducted to identify the significant pain site and SIQR predictors of group membership. Thereafter a stepwise multiple regression identified the order of variables in predicting their maximal statistical contribution into group membership. Partial correlations assessed their unique contribution, and lastly a two-group discriminant analysis provided a classification table.

Results The dataset contained information on the SIQR and also pain locations in 202 FM, 31 RA and 20 SLE subjects. As the SIQR and pain locations did not differ much between the RA and SLE patients they were grouped (RA/SLE) to provide a more robust analysis. The combination of 8 SIQR items and 7 pain sites correctly classified 99% of FM and 90% of RA/SLE subjects in a two group discriminant analysis. The largest reported SIQR differences (FM minus RA/SLE) were seen for “tenderness to touch”, “difficulty cleaning floors” and “discomfort on sitting for 45 minutes”. Combining the SIQR and pain locations in a stepwise multiple regression analysis revealed that the 7 most important predictors of group membership were: mid lower back pain (29%;79% vs. 16%), tenderness to touch (11.5%; 6.86 vs. 3.02), neck pain (6.8%;91% vs. 39%), hand pain (5%; 64% vs. 77%), arm pain (3%; 69% vs. 18%), outer lower back pain (1.7%; 80% vs. 22%), and sitting for 45 minutes (1.4%; 5.56 vs. 1.49).

Conclusions A combination of 2 SIQR questions (“tenderness to touch” and “difficulty sitting for 45 minutes”) plus pain in the lower back, neck, hands and arms, may be useful in the construction of clinical questionnaires aimed at patients with musculoskeletal pain. This combination provided a correct diagnosis in 97% of subjects, with only 7 of 253 subjects misclassified.

Introduction

Rheumatoid arthritis (RA), systemic lupus erythematosus (SLE) and fibromyalgia (FM) are usually easily discriminated on clinical examination, but have several overlapping features that make their differentiation more problematic in epidemiological surveys. For instance, pain, fatigue and morning stiffness are commonly reported in all 3 disorders. This current report was stimulated by the increasing interest in developing questionnaires that can accurately predict the occurrence of FM in both epidemiological and clinical settings [1,2,3,4,5]. During the evaluation of an updated version of The Impact Fibromyalgia Questionnaire (the FIQR), we compared its properties in FM subjects to those in subjects with RA, SLE and major depressive disorder [6]. Although the primary intent of this analysis was to validate the FIQR as a useful instrument in assessing the overall impact and severity of FM, it was incidentally noted that it had some diagnostic utility in differentiating FM from SLE and RA [6]. A slightly modified version of the FIQR, the SIQR, was used for the SLE and RA groups; the SIQR is identical to the FIQR but does not contain any reference to fibromyalgia [6]. For instance the total SIQR score discriminated between FM and these 3 disorders, with FM having a total FIQR score of 56.6 whereas RA had a score of 27.9 and SLE had a score of 29.5 and MDD had a score of 17.3. We also reported on pain in 24 locations in the FIQR study to confirm that FM subjects who had not been seen recently still had widespread pain. While this pain location questionnaire was not used in FIQR scoring, the number of pain locations was, as expected, much higher in FM subjects -16 pain sites compared to RA - 6 sites, SLE - 7 sites, MDD - 4 sites and Healthy Controls -1.6 sites. The objective of this current analysis was to identify individual SIQR symptoms

and pain locations that best discriminated between FM and RA/SLE subjects in this dataset. Doing so provides some pointers as to which pain sites and common symptoms may best discriminate between FM and RA/SLE in patient questionnaires.

Materials and methods

The data analyzed are taken from the revision of the FIQ, the FIQR, and its non-FM variant, the SIQR [6]. That study compared a sample of Healthy, FM, RA, SLE and MDD subjects. All data were analyzed in *STATISTICA* (version 8). In this current study we compared the data on 202 FM subjects, 20 SLE subjects and 31 RA subjects. The depressed group was not used because the sample number of 11 was too small for classification purposes.

The SIQR questionnaire is provided in Table 1. The SIQR differs from the original FIQ [7] in having modified function questions and new items on memory, tenderness, balance and environmental sensitivity. It consists of three domains: Function (9 items), Overall Impact (2 items) and Symptoms (10 items) that are scored 0 – 10, with 10 being most severe (Table 1). The 24 pain locations that were used to confirm that FM subjects still had widespread pain were as follows: left shoulder, right shoulder, left jaw, right jaw, left upper back, right upper back, left arm, right arm, left hand, right hand, left lower back, right lower back, left hip, right hip, left thigh, right thigh, left knee, right knee, left foot, right foot, mid upper back, mid lower back, front of chest and neck, see Table 2. These locations were designed to reflect a distribution of widespread pain in terms of 10 axial pain locations above and below the waist (neck, left and right jaw, left and right upper back, left and right lower back, mid upper back, mid lower back and chest), 8

proximal limb locations (shoulders, arms, hips and thighs) and 6 distal limb locations (hands, feet and knees).

Subjects

The data from this study was from the same subjects who had completed the FIQR and SIQR questionnaires for the previously published paper [6]; ethical approval for re-analysis of this data was not required by our institutional guidelines. All participants had completed online informed consent and and the study was conducted in accordance with the Declaration of Helsinki.

Statistical analyses

First, frequency and means comparing FM, RA, and SLE participants on all pain sites and SIQR variables are presented and analyzed. Second, multiple regression was conducted to identify the significant pain site and SIQR predictors of group membership (FM and RA/SLE). A two step analytic and variable reduction procedure was used. Standard multiple regression identified the significant and unique predictors of group membership, thereby reducing the number variables from thirty-five to fifteen. Then a stepwise multiple regression was performed which ordered these fifteen variables according to their maximal statistical contribution in predicting FM and RA/SLE membership. Partial correlations assessed their unique contribution, and a two-group discriminant analysis provided a classification table [8].

Results

Pain site frequency

The 10 left and 10 right side pain locations (right and left: jaws, shoulders, upper outer back, lower outer back, arms, hands, hips, thighs and feet) were highly correlated (range rs = 0.66 - 0.85; mean r =0.77). To avoid multicollinearity and reduce the number of variables, the left and right sides were averaged to form 10 variables, which together with the 4 axial sites (mid upper back, mid lower back, neck, front of chest), formed the 14 pain sites used as predictors. Table 2 shows the percentages of Healthy, FM, RA, SLE and RA subjects and RA combined with SLE (RA/SLE) who reported pain at these 14 pain site locations. The data for healthy subjects are also included to provide a base line for comparison. The first 4 columns show the pain sites percentages in Healthy, RA and SLE subjects; to discern if there was much difference between RA and SLE the fifth column shows the calculated difference between these two groups. The sixth column shows the combined RA and SLE figures (RA/SLE) and the last column shows the FM minus RA/SLE difference; a measure of discriminatory sites. Interestingly there was not a very large discordance between pain sites in RA and SLE, except for neck pain which was endorsed by 55% of SLE subjects versus 29% of RA subjects ($p<0.0001$). As might be expected hand pain was more common in RA, but unexpectedly foot and knee pain was more common in SLE subjects. FM subjects generally reported many more pain locations than RA/SLE except, as might be expected, for the hands and feet. FM subjects frequently reported pain in the extremities and thus a report of hand and/or foot pain does not necessarily discriminate FM from RA/SLE. The last two rows show the average percent of subjects with pain in peripheral and axial locations. FM subjects more often reported axial pain with frequencies of 77%

in axial locations compared to frequencies of 21% in RA/SLE ($p<0.0004$). Interestingly peripheral pain locations were more prevalent in FM than RA/SLE (55% versus 28%, $p<0.0002$). A notable pain location was the thigh; this was never reported in RA/SLE, whereas FM subjects had pain in this region in 55% of subjects. Jaw pain was reported in 36% of FM subjects but only in 7% of RA/SLE subjects $p<0.0001$). It is relevant to note that the FM minus RA/SLE differences are really "zero order relations" and do not necessarily identify unique differences after control for other predictors; see later. The fairly close concordance of pain sites in RA and SLE provides some justification for merging them into a single group (RA/SLE) to increase statistical power and permit regression and discriminant analyses.

SIQR item frequency

Table 3 shows the SIQR scores of Healthy, FM, SLE and RA subjects and RA combined with SLE (RA/SLE). The computed Total SIQR score (last row) and the function, overall and symptom averages are also computed. As in the case of the pain site frequency table, the last column (FM minus RA/SLE) provides some indication of the possible items that are most discriminatory between FM and RA/SLE. The highest differences (≥ 3.5) were seen for difficulty cleaning floors, discomfort on sitting for 45 minutes and tenderness to touch, all of which were more severe in FM. The averaged total SIQR score in FM was 56.6 versus 28.6 in RA/SLE ($p<0.0001$). The RA minus SLE column showed very little difference between RA and SLE (all <0.8), with the exceptions of environmental sensitivity (-2.9; 1.6 vs 4.5; $p<0.001$), which was more of a problem for the SLE group, and climbing one flight of stairs (1.3; 3.6 vs 2.3; $p=0.06$) which was more

difficult for the RA group. Overall these results, along with the pain site frequency findings, provide reasonable justification for merging the RA and SLE groups in the following analyses.

Pain site and SIQR predictors of FM and RA/SLE membership and classification analyses

A preliminary standard multiple regression was performed with the 14 pain site variables and 21 SIQR variables to identify which variables were *uniquely* and statistically associated with FM-RA/SLE group membership. This analysis identified 11 significant variables: neck $p<0$ .0009; arms $p<0$ .002; hands $p<0.003$; lower back $p<0$. 046, thigh $p<0.033$, feet $p<0.007$, tenderness to touch $p<.0001$, cleaning floors $p<0.002$; sitting for 45 minutes $p<0.003$; depression $p<0.01$; and anxiety $p<0.034$. Four other variables, mid lower back ($p<0.08$), feeling overwhelmed ($p<0.065$), poor memory ($p<0.09$), and environmental sensitivity ($p<.09$) were marginally significant and were retained in the final regression analysis model so as not to preclude their possible contribution in a final analysis. The 7 pain site and 8 SIQR variables were then entered in a forward stepwise regression analysis (Table 4) in order to identify which variables, best discriminated FM and RA/SLE group. Table 5 shows their unique contribution (partial correlations) when the other 14 variables are controlled for. Lastly, discriminant function analysis was used to classify FM and RA/SLE individuals according to this final variable list (Table 6).

Forward stepwise regression analysis of pain sites and SIQR predictors of group membership

A forward stepwise regression model (Table 4) with 15 predictors combined to produce a Multiple R=0.809 (see last row column 2) accounting for 65% of variance associated with group membership (see column 3). Additional hierarchical regression analyses (not shown) indicate that this 65% variance can be further decomposed into 30% of variance shared between SIQR and pain sites, 24% unique to pains sites, and 11% unique to SIQR. With regard to the 15 predictors, the first 7 predictors particularly (mid lower back pain, neck pain , arm pain, hand pain, outer lower back pain, tenderness to touch and sitting for 45 minutes) accounted for almost 60% of this variance. These 7 most important predictors of group membership in order of magnitude (variance accounted for and FM – RA/SLE differences indicated) were: mid lower back pain (29%;79% vs. 16%), tenderness to touch (11.5%; 6.86 vs. 3.02), neck pain (6.8%;91% vs. 42%), hand pain (5%; 64% vs. 77%), arm pain (3%; 69% vs. 16%), outer lower back pain (1.7%;80% vs. 22%), and sitting for 45 minutes (1.4%; 5.56 vs. 1.49). Mid and lower back pain, though having strong zero order correlation and quite different percentages in Table 2 have smaller partial correlations Table 5 because of their shared variance as indicated by their quite strong correlation with each other (r=0.56). In fact, while mid lower back pain was the first variable to enter into the step wise regression being responsible for 29.1% of variance (Table 3, column 4), the corresponding partial coefficient, indicating unique contribution, was only -0.129 (Table 5, column 3). On the other hand, tenderness to touch and neck contributed both substantial and unique variance. It is of note that hand and foot pain, which were not much different in Table 2 and have low zero order correlations in Table 5
(-0.162 and -0.021), had stronger unique and statistically significant partial relations

(0.237 and 0.176); thus indicating stronger associations with RA/SLE. It is also relevant to note that the magnitude of the FM minus RA/SLE pain site differences in Table 2 and correlations in Table 5 (which are zero order relations) are not completely reflected by the results of the multivariate regression analysis as exemplified by the partial correlations in Table 5. Of the 14 pains sites in Table 3, the 5 most important pain sites in Table 5, that discriminate between FM and RA/SLE, are mid and outer lower back, neck, arms, and hands. Similarly of the 23 SIQR items, the important variables are "tenderness to touch" and "sitting in a chair for 45 minutes." While SIQR "tenderness" was a strong predictor of group, SIQR "pain" did not distinguish between FM and RA/SLE. Overall, these variables suggest that the relationship between predictors and group membership can be best described by a number of specific pain locations plus a high level of tenderness to touch.

Other unique predictors and considerations

Pain, Tenderness, and Pain Sites in FM and RA/SLE

Given that SIQR tenderness was an important discriminator of RA/SLE groups and SIQR pain was not, further analyses were conducted to provide some insight as to how pain, tenderness and pain sites are functioning in relation to each other and also to FM and RA/SLE.

a. Mean differences in SIQR tenderness and SIQR pain in FM and RA/SLE

A repeated measures 2X2 ANOVA (FM, RA/SLE x Tenderness, Pain) was performed on the means for FM and RA/SLE. A main effect [$F(1,251)=84.87; p < 0.0001$)] showed

that FM compared with RA/SLE subjects reported significantly more tenderness (6.86 vs. 3.02; $p< 0.001$) and pain (6.01 vs. 3.94;
$p<0 .008$). An interaction [$F(1,251)=20.17, p<0.0001$)] comparing the two patient groups shows this approximates to a 4 point difference for tenderness relative to a 2 point difference for pain; these differences may in part account for why tenderness but not pain was a stronger predictor in classifying subjects in the discriminant analysis. Additionally, the FM group reported higher tenderness than pain (6.86 vs. 6.01; $p<0.001$) while RA/SLE reported slightly higher pain than tenderness (3.94 vs. 3.02; $p=0.019$). Thus "tenderness" was rated higher by FM subjects while pain was rated higher by RA/SLE subjects (see Figure 1). A chi-square test indicated that 58% vs. 25% of FM and RA/SLE indicated a greater tenderness than pain score ($p<0.001$).

b. SIQR pain and SIQR tenderness prediction of Total Pain Site

A second analysis, using standard multiple regression, was conducted to determine how tenderness and pain *uniquely* and together predicted total pain site scores in the FM and RA/SLE groups separately. In FM subjects, pain ($\beta= 0.277$, $p=0.0002$) and tenderness ($\beta=0.181$; $p=0.013$) were *both* independent predictors of total pain site scores ($R= 0.389$; $p=0.001$). In the RA/SLE group *only* pain ($\beta= 0.472$, $p=0.003$) but not tenderness ($\beta=0.042$, $p=0.78$) predicted total pain sites ($R=0.497$, $p=0.001$). This demonstrates that while SIQR pain predicts pain sites in both groups, tenderness to touch predicts pain sites only in the FM group.

Along with the regression analyses, the latter analyses point to several conclusions. First, FM subjects report higher tenderness than pain scores whereas the reverse is true of RA/SLE subjects who report higher pain than tenderness scores. Second, tenderness to touch seems to be an important "between group" variable in discriminating between FM and RA/LE, whereas pain is not. Third, *both* pain and tenderness are independent predictors of pain sites in FM whereas *only* pain is a predictor of pain sites in RA/SLE. Collectively, these analyses show that tenderness to touch plays a unique role in differentiating FM from RA/SLE, and is a unique predictor of pain sites in FM but not in RA/SLE subjects. With regard to RA/SLE subjects, pain is rated higher than tenderness, and is correlated with pain sites, whereas tenderness is not. These findings indicate that variables predicting *between* group identification do so in a different way than they do in predicting *within* group *severity* differences. Notably, tenderness to touch plays a unique role in both *differentiating* FM from RA/SLE subjects and in predicting FM *severity* (in addition to pain) among FM subjects.

Discussion

This analysis of FIQR/SIQR items and 24 pain locations provides some potentially useful pointers to questions that could be used in the construction of epidemiological questionnaires in surveys of musculoskeletal pain. The questions in the SIQR reflect the domains, (pain, tenderness, fatigue, multidimensional function and sleep), that OMERACT (Outcome Measures in Rheumatology Clinical Trials) has recommended as core dimensions to be assessed in all fibromyalgia clinical trials [9]. The SIQR includes

domains that are also deemed to be important by OMERACT (i.e. fatigue, dyscognition, stiffness, depression and anxiety). The SIQR items relating to balance and environmental sensitivity have not been evaluated in the OMERACT process, but are some of the commonest complaints of FM patients [10].

While the classification criteria for RA, SLE and FM all require a physical examination, epidemiological surveys seldom provide for subject examination, thus the development of discriminatory questionnaires is problematical. The one physical examination criteria for FM, as per the 1990 ACR classification criteria, is the finding of ≥11 out of 18 designated tender points [11]. Reporting on tenderness of joints is part of the ACR and DAS scoring system in the evaluation of RA severity [12,13]. One might logically surmise that the symptom of tenderness to touch that is “whole body”, as in FM, would be more severe than focal joint tenderness in RA; that is what was found in this analysis. Although the finding of inflammatory arthritis in 2 or more joints is one of the 11 criteria used in SLE classification [14], tenderness per se is not part of these criteria. Thus it was of interest to note that in this analysis tenderness to touch in SLE was similarly rated in RA and SLE (2.9 versus 3.4).

Overall the combination of seven pains sites and eight SIQR items together produced a multiple R of 0.81 (65 % variance) accounting for substantial variance in group membership with a correct classification rate of 97%. From a conceptual perspective it is interesting to note that the largest component of this variance (30%) was shared by pain sites and SIQR items; indicating that pain locations and SIQR dimensions are

intimately connected in differentiating FM from RA/SLE. The additional unique contribution of pain sites (24%) and SIQR items (11%), particularly “tenderness to touch”, suggest that epidemiological surveys should consider both of these items to maximize their effectiveness. But neither pain sites nor SIQR alone seem sufficient in differentiating groups. The role of SIQR pain was different and also significant when examining *within* group correlations rather than *across* groups (pooled across groups) as described above. Both SIQR pain and SIQR tenderness significantly predicted pain site scores in FM, while only SIQR pain predicted total pain site scores in RA/SLE. Furthermore, the means for SIQR “tenderness to touch” and SIQR “pain”, were different, thus showing discriminant validity between FM and RA/SLE.

A notable finding in this study was that the SIQR question on “tenderness to touch” along with neck pain, arm pain and hand pain were important symptoms to consider when developing questionnaires to distinguish between FM and RA or SLE. In all analyses, tenderness contributed equally with other specific pain sites in classification of FM and RA/SLE subjects. SIQR “pain” did not help distinguish between FM and RA or SLE, possibly because the pain site location captures pain ratings, thus making SIQR “pain” redundant. This notion is supported by the observation that tenderness was correlated with pain (0.55), but was more strongly associated with group diagnosis than pain (0.52 vs. 0.35).

Nevertheless, while pain and tenderness uniquely predict pain sites, they did not account for much variance in pain site location. A more refined measure of pain

locations, such as a pain VAS, or one that specified the nature or quality of the pain in greater detail, or one which included axial, distal and proximal subscale scores may provide more useful information than a simple count of presence or absence of pain.

We are not aware of other survey questionnaires that have asked about “tenderness to touch”. However, the recent preliminary diagnostic FM criteria paper did find that a widespread pain index and muscle tenderness were the most important variables in the classification of cases and non cases of FM, although tenderness was not used in the final formulation of the criteria [4]. It seems possible that the question, “tenderness to touch”, may be a useful surrogate for a tender point evaluation in musculoskeletal pain surveys sine a physical examination. It is also worthy of comment that “tenderness to touch” was associated with a diagnosis of FM even when psychological variables such as depression, anxiety and "feeling overwhelmed" were controlled for in multivariate regression analyzes; thus challenging the still common notion that tenderness in FM can be explained in terms of a psychiatric condition or a psychosomatic reaction. Looking backwards to the 1990 ACR study, the finding of “tenderness to touch” is redolent of the "skin-fold tenderness" test which provided an odds ratios of 8.8 and 6.5 for the diagnosis of primary FM and secondary FM over controls [11].

Although FM subjects had higher pain scores than RA/SLE subjects (6.0 versus 3.9), pain was not a useful between group discriminator. We surmised this was due to pain locations being a better discriminator. The SIQR only asks about pain in the general sense and maybe more specific questions would be useful in epidemiological surveys.

For instance, Perrot has reported on the development of a rapid screening tool for FM and found that positivity on ≥ 5 out of 6 questions *(I have pain all over my body, My pain is accompanied by continuous and very unpleasant general fatigue, My pain feels like burns, electric shocks or cramps, My pain is accompanied by other unusual sensations throughout my body, such as pins and needles, tingling or numbness, My pain is accompanied by other health problems such as digestive problems, urinary problems, headaches or restless legs, My pain has a significant impact on my life, particularly on my sleep and my ability to concentrate, making me feel slower generally)* had a sensitivity of 90.5% and a specificity of 85.7% in differentiating FM from a composite group of non-FM group with RA, ankylosing spondylitis and osteoarthritis.

There are several limitations to this study. The numbers of RA and SLE subjects were small compared to the FM population (51 versus 202). The pain locations were designed to reflect a composite of widespread pain and peripheral pain. In this respect it may have been useful to include the wrists and ankles; joints that are commonly involved in RA. The RA and SLE subjects were specifically screened for not having concomitant FM, and thus this study does not provide any useful information on that common combination, which is now appreciated to skew the results of questionnaires such as the DAS [15]. The subjects in this study were not screened for hand osteoarthritis, a condition that is found in about 80% of the elderly individuals [16]; however hand pain was the only pain location that was more prevalent in RA/SLE than FM.

While researching background information for this manuscript, it became apparent that there has been very little information published regarding musculoskeletal pain in SLE patients. A typical description is

”joint involvement in SLE is similar to that of rheumatoid arthritis, primarily affecting the small joint of the hands, wrists and knees …….. patients’ symptoms (pain and stiffness) are usually out of proportion to the degree of synovitis present on physical examination” [17]. An inconsistency of symptoms and objective findings is always suggestive of central sensitization, as exemplified by FM. While FM is a common accompaniment of SLE [18], the SLE subjects in this study were specifically screened not to have concomitant FM; the success of this screening was validated by the relatively low FIQR/SIQR scores compared to FM (29.6 in SLE versus 56.6 in FM). The only SIQR question that significantly differentiated RA from SLE was sensitivity to “loud noises, bright lights, odors and cold”. This maybe a reflection of sensitivity to sunlight in SLE, but this cannot be inferred from this dataset. The only pain location that significantly differentiated RA from SLE was neck pain with 55% prevalence in SLE versus 29% in RA. Other notable, non significant, differences were a higher prevalence of foot pain (63% vs 46%) and knee pain (53% vs 39%) in SLE compared to RA. These differences may be due to the relatively small number of RA and SLE subjects, but if confirmed in a larger dataset, these differences could point to differences in the musculoskeletal symptoms of SLE and RA that have hitherto been opaque.

Conclusions

This study analyzed data from subjects with FM, SLE and RA who had completed the FIQR/SIQR and identified sites of pain out of 24 locations. A combination of 2 SIQR question (“tenderness to touch” and “difficulty sitting for 45 minutes”) plus pain in 4 locations (lower back, neck, hands and arms) identified the correct diagnosis in 97% of subjects. Overall, this report provides some pointers for distinguishing FM patients from patients with RA or SLE in clinical questionnaires and raised some potentially novel issues regarding musculoskeletal symptoms in SLE.

Abbreviations

ACR, American College of Rheumatology; ANOVA, analysis of variance; DAS, disease activity score in rheumatoid arthritis; FIQ, fibromyalgia impact questionnaire; FIQR, revised fibromyalgia impact questionnaire; FM, fibromyalgia; MDD, major depressive disorder; RA, rheumatoid arthritis; SIQR, symptom impact questionnaire; SLE, systemic lupus erythematosus.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

RF and RB contributed equally to the design of the study, analysis of the data, and writing the manuscript.

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Table 1: The Symptom Impact Questionnaire (SIQR)

<u>Domain 1</u>: For each question, place an "X" in the box that best indicates how much difficulty you have experienced in doing the following activities during the past 7 days. If you did not perform a particular activity in the last 7 days, rate the difficulty for the last time you performed the activity. If you can't perform an activity, check the last box.

Brush or comb your hair	**No difficulty**	□ □ □ □ □ □ □ □ □ □	**Very difficult**
Walk continuously for 20 minutes	**No difficulty**	□ □ □ □ □ □ □ □ □ □	**Very difficult**
Prepare a homemade meal	**No difficulty**	□ □ □ □ □ □ □ □ □ □	**Very difficult**
Vacuum, scrub or sweep floors	**No difficulty**	□ □ □ □ □ □ □ □ □ □	**Very difficult**
Lift and carry a bag full of groceries	**No difficulty**	□ □ □ □ □ □ □ □ □ □	**Very difficult**
Climb one flight of stairs	**No difficulty**	□ □ □ □ □ □ □ □ □ □	**Very difficult**
Change bed sheets	**No difficulty**	□ □ □ □ □ □ □ □ □ □	**Very difficult**
Sit in a chair for 45 minutes	**No difficulty**	□ □ □ □ □ □ □ □ □ □	**Very difficult**
Go shopping for groceries	**No difficulty**	□ □ □ □ □ □ □ □ □ □	**Very difficult**

<u>Domain 2</u>: For each of the following 2 questions, check the <u>one</u> box that best describes the overall impact of any medical problems over the last 7 days:

My medical problems prevented me from accomplishing goals	**Never**	□ □ □ □ □ □ □ □ □ □ □	**Always**
I was completely overwhelmed by my medical problems	**Never**	□ □ □ □ □ □ □ □ □ □ □	**Always**

<u>Domain 3</u>: For each of the following 10 questions, check the <u>one</u> box that best indicates the intensity of the following common symptoms over the last 7 days:

Please rate your level of pain	**No pain**	□ □ □ □ □ □ □ □ □ □ □	**Unbearable pain**
Please rate your level of energy	**Lots of energy**	□ □ □ □ □ □ □ □ □ □ □	**No energy**
Please rate your level of stiffness	**No stiffness**	□ □ □ □ □ □ □ □ □ □ □	**Severe stiffness**
Please rate the quality of your sleep	**Awoke rested**	□ □ □ □ □ □ □ □ □ □ □	**Awoke very tired**
Please rate your level of depression	**No depression**	□ □ □ □ □ □ □ □ □ □ □	**Very depressed**
Please rate your level of memory problems	**Good memory**	□ □ □ □ □ □ □ □ □ □ □	**Very poor memory**
Please rate your level of anxiety	**Not anxious**	□ □ □ □ □ □ □ □ □ □ □	**Very anxious**
Please rate your level of tenderness to touch	**No tenderness**	□ □ □ □ □ □ □ □ □ □ □	**Very tender**
Please rate your level of balance problems	**No imbalance**	□ □ □ □ □ □ □ □ □ □ □	**Severe imbalance**
Please rate your level of sensitivity to loud noises, bright lights, odors and cold	**No sensitivity**	□ □ □ □ □ □ □ □ □ □ □	**Extreme sensitivity**

Scoring:

1. Sum the scores for each of the 3 domains (Function, Overall and Symptoms).
2. Divide domain #1 score by three, divide domain # 2 score by one (i.e. it is unchanged) and divide domain score # 3 by two.
3. Add the 3 resulting domains scores to obtain the total SIQR score (range is 0 to 100)

Table 2: Percentage pain site response for RA, SLE and FM with the calculated differences between groups (including the combined RA and SLE group)

Location	Healthy *(n=204)*	FM *(n=202)*	RA *(n=31)*	SLE *(n=20)*	RA minus SLE	RA/SLE *(n=51)*	FM minus RA/SLE
Shoulders	14%	76%	32%	25%	7%	29%	48%
Jaws	4%	36%	3%	10%	-7%	7%	30%
Arms	6%	69%	23%	10%	13%	16%	53%
Hands	5%	64%	81%	73%	9%	77%	-13%
Hips	11%	79%	29%	28%	2%	28%	51%
Thighs	4%	55%	0%	0%	0%	0%	55%
Knees	10%	64%	39%	53%	-14%	46%	18%
Feet	12%	50%	46%	63%	-17%	54%	-4%
Lateral upper back	6%	82%	15%	23%	-8%	19%	64%
Lateral lower back	8%	80%	23%	20%	3%	22%	59%
Mid upper back	4%	77%	13%	15%	-2%	14%	63%
Mid lower back	16%	79%	10%	25%	-15%	18%	62%
Front of chest	4%	54%	10%	15%	-5%	13%	42%
Neck	16%	91%	29%	55%	-26%	42%	49%
Peripheral	7%	55%	28%	29%	-1%	28%	26%
Axial	9%	77%	17%	25%	-9%	21%	56%

Note: Minus scores in the RA minus SLE column indicate that the SLE group had higher scores on that item. Minus scores in the FM minus RA/SLE column indicate that the RA/SLE group had higher scores on that item.

FM, fibromyalgia; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus.

Table 3: Individual SIQR questions for RA, SLE and FM with the calculated differences between RA and SLE and between FM and the combined RA and SLE groups

SIQR Question	Healthy *(n=204)*	FM *(n=202)*	RA *(n=31)*	SLE *(n=20)*	RA minus SLE	RA/SLE *(n=51)*	FM minus RA/SLE
Brush or comb hair	0.1	2.4	0.9	0.8	0.1	0.8	1.6
Walk continuously for 20 minutes	0.6	5.7	3.4	2.2	1.2	2.9	2.8
Prepare a homemade meal	0.2	4.3	1.2	1.4	-0.2	1.3	3.0
Vacuum, scrub or sweep floors	0.6	6.5	2.8	2.5	0.3	2.7	3.8
Lift and carry a bag full of groceries	0.4	5.6	2.6	3.3	-0.7	2.9	2.7
Climb one flight of stairs	0.5	5.6	3.6	2.3	1.3	3.1	2.5
Change bed sheets	0.4	5.5	2.4	2.2	0.2	2.3	3.2
Sit in a chair for 45 minutes	0.7	5.6	1.5	1.6	-0.1	1.5	4.1
Go shopping for groceries	0.4	5.6	2.5	2.4	0.1	2.4	3.2
FUNCTION (average)	0.4	5.2	2.3	2.1	0.2	2.2	3.0
Achieve goals	0.7	5.7	2.7	3.1	-0.4	2.8	2.9
Feel overwhelmed	0.7	5.2	2.5	3.3	-0.8	2.8	2.4
OVERALL (average)	0.7	5.5	2.6	3.2	-0.6	2.8	2.7
Pain	1.5	6.0	3.9	4.1	-0.2	3.9	2.1
Energy	2.6	6.8	5.1	5.1	0.0	5.1	1.7
Stiffness	2.1	6.7	4.5	4.1	0.4	4.4	2.3
Sleep	3.8	7.6	5.4	5.5	-0.1	5.5	2.1
Depression	1.7	4.6	1.8	1.8	0.0	1.8	2.8
Memory	1.7	5.9	2.7	3.4	-0.7	3.0	2.9
Anxiety	1.8	4.5	1.9	2.6	-0.7	2.2	2.3
Tenderness	1.0	6.9	3.4	2.5	0.9	3.0	3.9
Balance	0.7	4.8	2.0	1.8	0.2	1.9	2.9
Sensitivity	1.5	6.2	1.6	4.5	-2.9	2.8	3.4
SYMPTOMS (average)	1.8	6.0	3.2	3.5	-0.3	3.3	2.7
TOTAL SIQR SCORE	12.4	56.6	27.9	29.6	-1.7	28.6	28.0

Note: Minus scores in the RA minus SLE column indicate that SLE group had higher scores on that item.
Higher scores indicate more impairment or higher level of symptoms
FM, fibromyalgia; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus.

Table 4 : Stepwise Multiple Regression showing 15 predictors ranked in order of magnitude in predicting group membership (FM or RA/SLE)

Predictors	Step/and number of variables included	Multiple R	Multiple R-square	R-square change	p-level (for predictor variable)
Mid lower back	1	.540	.291	.291	.00000
Tenderness to touch	2	.637	.406	.115	.00000
Neck	3	.689	.474	.068	.00000
Arms	4	.712	.507	.033	.00007
Hands	5	.747	.558	.051	.00000
Lateral lower back	6	.758	.575	.017	.00168
Sitting for 45 minutes	7	.768	.589	.014	.00367
Feeling overwhelmed	8	.775	.601	.012	.00750
Depression	9	.784	.615	.014	.00365
Sensitivity	10	.791	.626	.011	.00855
Thighs	11	.797	.635	.009	.01471
Feet	12	.804	.647	.012	.00529
Cleaning floors	13	.806	.649	.003	.16326
Anxiety	14	.807	.652	.002	.19893
Memory	15	.809	.654	.002	.21899

Note: This forward stepwise regression analysis used 15 predictors which combined to produce a Multiple R=0.809 (last row column 2); this accounted for 65% of variance associated with group membership (column 3).

FM, fibromyalgia; RA/SLE, combined rheumatoid arthritis and systemic lupus erythematosus.

Table 5: Forward stepwise multiple regression analysis showing zero order (Pearson r) and partial correlations

Predictors	Pearson r	partial r	p-level (partial r)
Mid lower back	-.540	-.129	.0458
Tenderness to touch	-.518	-.242	.0002
Neck	-.518	-.275	.0000
Arms	-.447	-.261	.0000
Hands	.162	.237	.0002
Lateral lower back	-.524	-.191	.0030
Sitting for 45 minutes	-.475	-.177	.0060
Feeling overwhelmed	-.314	.274	.0000
Depression	-.378	-.190	.0031
Sensitivity	-.422	-.144	.0258
Thighs	-.474	-.166	.0101
Feet	.021	.176	.0064
Cleaning floors	-.452	-.085	.1914
Anxiety	-.292	.099	.1277
Memory	-.428	-.080	.2190

Note: Minus correlations indicate that FM subjects have higher scores on predictor variable. All Pearson correlations are significant (N=253; $p<0.001$) except Hands ($p<0.01$) and Feet ($p<0.74$)

Table 6: Correct classification as predicted by discriminant analysis using seven pain sites and eight SIQR variables

	FM	RA/SLE	Percent Correct
FM (N=202)	200	2	99.01
RA/SLE (N=51)	5	46	90.20

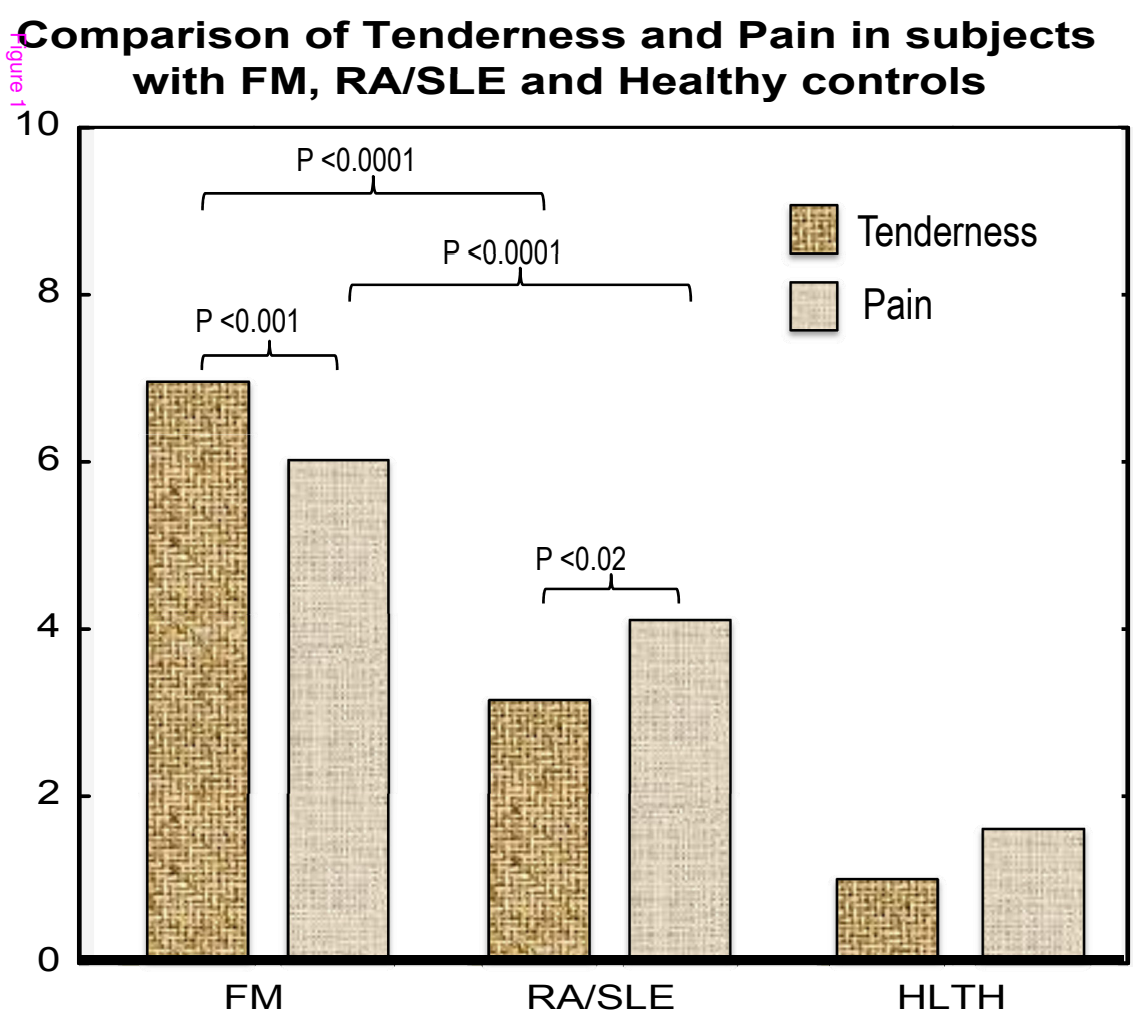
Note: The combined correct classification for FM and RA/SLE = 97.23%

FM, fibromyalgia; RA/SLE, combined rheumatoid arthritis and systemic lupus erythematosus.

Figure 1

The main effect shows that both tenderness and pain are significantly greater in FM than RA/SLE. However, the interaction shows that: a) this difference is greater in FM than RA/SLE, and b) tenderness is more severe than pain in FM, whereas pain predominates over tenderness in RA/SLE. The healthy control values are provided for background comparison

Figure 1


Comparison of Tenderness and Pain in subjects with FM, RA/SLE and Healthy controls
10
8
6
4
2
0
P <0.0001
P <0.0001
P <0.001
P <0.02
Tenderness
Pain
FM
RA/SLE
HLTH