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A Report of the Autonomic Symptom Profile in Patients with Fibromyalgia

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Introduction

Autonomic dysregulation is thought to contribute to the pathophysiology and symptoms in patients with fibromyalgia (FM). The majority of studies in FM that have reported autonomic dysregulation have relied on heart rate variability measurement and report increased sympathetic and decreased parasympathetic tone, chronotropic incompetence and impaired autonomic cardiovascular regulation with blunted sympathetic reactivity to acute stress [1–3]. These results may have clinical implications as increased sympathetic tone contributes to symptoms such as muscle tension and pain, fatigue, heightened stress response and unrefreshing sleep, all common patient-reported symptoms in FM [1, 3–6].

The Autonomic Symptom Profile (ASP) is a validated self-report questionnaire that comprehensively assesses autonomic symptoms across 11 subscales and yields a composite autonomic symptom score (COMPASS) [7]. The ASP is unique in comparison to other commonly utilized self-report measures in that it assesses both symptoms and functional status. For example the secretomotor subscale of the ASP assesses secretomotor symptoms e.g. sweating with vigorous exercise, ability to tolerate heat and mucosal secretory dysfunction such as dry eyes and dry mouth [8]. Similarly, the pupillomotor subscale of the ASP assesses of pupillomotor symptoms e.g. light sensitivity, visual blurring and dysfunction pupillomotor functions e.g. trouble focusing eyes and difficulty seeing at night [8]. The ASP also includes a sleep subscale that evaluates presence of sleep disorders such as narcolepsy, obstructive sleep apnea and abnormal sleeping patterns in addition to assessment of sleep quality. This is relevant as sleep and autonomic function are interdependent by virtue of their common controls, regulatory neurochemicals, and functions, but also because unrefreshing sleep is a predominant complaint in patient with FM [9, 10].

There is one previous report utilizing the ASP in patients with FM. In this study, the Spanish version of the ASP was administered to 20 patients with FM and results were compared to those of 30 patients with rheumatoid arthritis (RA) and 30 healthy controls [11]. Patients with FM had the highest COMPASS scores in comparison with patients with RA and healthy controls. Additionally, total COMPASS scores correlated with FIQ total scores suggesting a potential association between FM severity and autonomic dysfunction [11].

Our objective was to assess autonomic symptoms utilizing the ASP and their correlation with the Fibromyalgia Impact Questionnaire – Revised (FIQ-R) in a large sample of patients with FM.

Methods

Participants

A survey including demographics, ASP and FIQ-R was mailed to 1303 patients selected using a random number generator in Microsoft Excel from a list of patients who had agreed to be part of a fibromyalgia registry [12]. The construction of this registry, which has been previously described, entailed recruiting patients with a diagnosis or previous history of fibromyalgia who had presented to Mayo Clinic for clinical care and consented to be included in the registry. The study was approved by the Mayo Clinic Institutional Review Board.

Measures

Autonomic Symptom Profile (ASP)—The ASP is a validated self-report measure that consists of 169 items and yields a total score (COMPASS) reflecting overall severity of autonomic symptoms and 11 weighted subscale scores that reflect autonomic symptoms in the following subscales: orthostatic intolerance, syncope, sexual dysfunction, bladder dysfunction, diarrhea, constipation, upper gastrointestinal, secretomotor dysfunction, sleep dysfunction, vasomotor, and pupillomotor [7]. Total scores range from 0–200 with higher scores indicating worse symptoms.

Revised Fibromyalgia Impact Questionnaire (FIQ-R)—The revised Fibromyalgia Impact Questionnaire (FIQ-R) is an updated version of the FIQ, a validated 21-item self-report questionnaire and has the same three subscales as the FIQ (i.e. function, overall impact, and symptoms). Total scores range from 0–100, with higher scores indicating more severe symptoms [13].

Statistical Analysis

Data were analyzed in two phases. First, bivariate associations between COMPASS total (10 subscales) and COMPASS subscales with the FIQ-R were examined. We excluded the sexual dysfunction subscale of the COMPASS as it is the least robust of the 11 subscales for both males and females. Also, our sample was predominantly female and there is only one question related to sexual function (sexual desire) in females in the measure. Second, scores of the COMPASS subscales were entered in a multiple regression model to determine their shared and unique contributions to fibromyalgia symptoms. Prior to analyses, data were examined for normality, outliers, multicollinearity, and linearity. Alpha was set at .05. Data are reported as mean $\pm$ standard deviation.

Results

Eight hundred fifty-eight of 1303 patients responded to the invitation to participate (66% response rate) and completed questionnaires. Since morbid obesity is a possible confounder for FM symptoms, patients with BMI ≥ 40 were excluded from this analysis ($n = 84$). The sample of remaining respondents were 92% female, 98% Caucasian with a mean age of 56.6 (± 12.7) years and mean BMI of 28.1 (± 5.4). FIQ-R total score for the sample was 52.1 (± 21.1); COMPASS 10 score for the sample was 46.2 (± 21.3).

Significant correlations ($p < .0001$) were observed between FIQ-R and COMPASS total scores (Figure 1, Table 1) and subscales (Table 1). Similarly, multiple regression analyses

(Table 1) examining the combined and unique contribution of the COMPASS and its subscales on the prediction of fibromyalgia symptom scores (FIQ-R total) demonstrated that ten COMPASS predictors explain almost a third ($R^2 = .31$) (Table 1) of the variability in fibromyalgia symptom scores. Of the ten predictors, six offered a statistically significant contribution to predicting FM symptoms. These were: Orthostatic Intolerance, Secretomotor, Upper Gastrointestinal, Constipation, Pupillomotor, and Sleep. Secretomotor, Pupillomotor, Sleep, and Orthostatic Intolerance provide approximately equal unique contributions to understanding FM symptoms. Upper Gastrointestinal and Constipation scores accounted for slightly less unique variance in FM symptoms.

Discussion

The results of our study demonstrate that patients with FM report symptoms across multiple self-reported autonomic subscales and these subscales correlate significantly with FM symptom severity as characterized by FIQ-R total. This suggests that patient-reported autonomic symptoms contribute in part to overall patient-reported FM symptom severity.

Our results are similar to those of Solano et al who reported “multiple non-pain symptoms” and correlations between COMPASS and FIQ-R scores [11]. This paper did not report which of the specific subscales of ASP account for the association with the FIQ-R. In our study the subscales of Orthostatic Intolerance, Pupillomotor symptoms, Sleep disturbances and Secretomotor symptoms contributed most to the association of COMPASS with FIQ-R.

Our findings have clinical implications because patients with FM often report symptoms that could be attributable to autonomic dysregulation. For example, patients frequently report lightheadedness that is triggered by upright posture, warm temperatures or stressful events which may indicate the presence of orthostatic intolerance. This could trigger clinical evaluation for the presence of orthostatic disorder with orthostatic blood pressure measurements of a formal tilt-table testing. Similarly, complaints of sweating and inability to tolerate heat may be attributable to secretomotor dysfunction that can be clinically assessed with a thermoregulatory sweat test. Therefore, clinicians who encounter patients with FM who complain of dry eyes, dry mouth, difficulty focusing, photophobia, light sensitivity, visual blurring, bladder and bowel symptoms and sleep difficulties will want to consider the possibility that autonomic dysregulation may be contributing, in part, to these symptoms. In our institution, the clinical suspicion for autonomic symptoms is further assessed by conducting an autonomic reflex screen, the gold standard objective assessment for autonomic deficits [14, 15]. This would guide further work-up for patient and open up avenues that could improve well-being of the patient. However, clinicians also need to bear in mind that patients with FM display somatic hypervigilance and may over report symptoms leading to unnecessary and expensive testing.

Similar to Solano et al who reported a mean FIQ score of $60.5(\pm 13.3)$, patients in our sample had a mean FIQ-R score of $52.1(\pm 21.1)$ indicating moderate to severe symptoms. This is indicative of high symptom burden attributable to FM in patients who present to a tertiary center. Therefore, these results may not be generalizable to patients with FM who report milder symptoms and is one limitation of this report. Also, assessments of symptoms with questionnaires have the limitation of a dependence on patient report which, in this case, may be subject to subjective vigilance.

To our knowledge, this is first report comprehensively evaluating the original (English) version of ASP, COMPASS, and COMPASS subscale scores in a large sample of patients with FM. Clinicians caring for patients with FM who report these symptoms may want to

further assess whether symptoms couple with somatic hypervigilance or with autonomic deficits and utilize objective autonomic measures to further guide evaluation.

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Figure 1. Scatterplot showing the relationship between Composite Autonomic Symptom Scale – 10 subscales (COMPASS total) and the revised Fibromyalgia Impact Questionnaire (FIQ-R) total scores in 774 fibromyalgia patients.

Table 1

Score profiles, Pearson correlations and Unstandardized and Standardized Regression Coefficients for COMPASS Predictors of Fibromyalgia Symptoms (FIQ-R Total)

			Pearson Correlation		Multiple Regression Model					
COMPASS Domains	Max. possible score	Mean	% >0 [†]	Range	Correlation	p	B	S.E.	Beta	p
COMPASS Total (10 Domains)		46.5	0	1.8–122.7	.50	.0001	n/a	n/a	n/a	n/a
Orthostatic Intolerance	40	15.8	16.2	0–40	.39	.0001	.38	.07	.19	.0001
Syncope	20	0.8	83.6	0–12	.15	.0001	−.06	.35	−.01	.8699
Vasomotor	10	2.3	59.2	0–10	.14	.0001	−.41	.24	−.06	.0832
Secretomotor	20	7.2	5.8	0–20	.36	.0001	.84	.18	.16	.0001
Upper Gastrointestinal	10	1.9	42.5	0–10	.60	.0001	1.17	.33	.13	.0005
Diarrhea	20	5.9	36.5	0–20	.22	.0001	.20	.12	.06	.0853
Constipation	10	2.1	41.0	0–10	.21	.0001	.85	.28	.10	.0021
Bladder	20	4.8	13.5	0–20	.18	.0001	−.06	.18	−.01	.7411
Pupillomotor	5	2.1	9.9	0–5	.38	.0001	2.93	.53	.19	.0001
Sleep	15	3.5	17.7	0–15	.27	.0001	1.20	.23	.17	.0001
Constant		n/a	n/a	n/a	n/a	n/a	25.82	1.68	0	.0001

$R^2 = .31$; $F(10, 773) = 34.77$, $p < .0001$; B = unstandardized regression coefficient, S.E. = standard error for unstandardized regression coefficient.

[†] % >0: percent of people with a score greater than 0.