Weather-related changes in severity of fibromyalgia symptoms reported by patients indicate response to concentrations of environmental toxins

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1. Introduction

The Fibromyalgia Wellness Project* is an experimental web-based project for symptom reduction sponsored by the National Institutes of Health. A pool of 883 subjects reported severity levels of nine symptoms on a 0-10 scale, for the period October 1, 2009 to September 1, 2010. The reported symptoms included:

1. Pain
2. Stiffness
3. Fatigue
4. Concentration problems
5. Memory problems
6. Anxiety
7. Depression
8. Gastrointestinal problems
9. Sleep problems

A total of 15 subjects were selected from this pool who reported these symptom severity levels at least 70 times.

These severity levels were compared with values of 500 mb geopotential heights for the location of the patients' residence and day of the reported ratings*. The atmospheric pressure at any height of the atmosphere is equal to the weight of the overlaying air. The 500 mb height is the average pressure calculated at approximately 18,000 feet. This height varies with the temperature of the column of air below this surface. Lower heights correspond to a lower column temperature.

The value of Kendall's tau-b (τ) was used to measure the association of 500 mb height (HT500) and severity level of each symptom. 1-day, 3-day, and 5-day moving averages of HT500 were obtained, and the best fit was found by smoothing with a 5-day moving average (HT500S). Table 1 displays the values of τ for each subject and symptom. Positive values of τ indicate a positive association of symptom severity level with HT500S. Shaded and bolded areas indicate significant adjusted *p*-values for the subject and symptom according to the Holm-Sidak test.

Table 2 contains the global *p*-values for the association of each symptom and HT500S according to the unweighted Simes test, and the status of global null hypothesis rejection for each symptom according to the Simes test weighted by sample size. Significant associations were found for HT500S and each symptom.

The Fibromyalgia Wellness Project treated each subject as a separate entity, and no data was used from other subjects in its behavioral recommendations. Here also each subject was considered as a separate

study, in the spirit of meta-analysis. We wish to know the consistency in the direction of the effect of HT500S on each symptom. Homogeneity for each symptom was assessed with ODA*.

For all of the N ratings for each subject and symptom, each pair of $N(N\text{-}1)/2$ observations was compared. For x_i as the value of the ith observation of symptom x, and y_i as the value of the ith observation of HT500S, a concordant pair (x_i, y_i) and (x_j, y_j) is such that $x_i > x_j$ and $y_i > y_j$, or $x_i < x_j$ and $y_i < y_j$. A discordant or inverted pair is such that $x_i < x_j$ and $y_i > y_j$, or $x_i > x_j$ and $y_i < y_j$. Tied pairs are such that $x_i = x_j$ or $y_i = y_j$.

A weight $W_{ij} = 2N/(N^2\text{-}N)$ was assigned to each pair, and the quantity Q_c was computed as the sum of the W_{ij} over all the concordant pairs. Similarly, Q_v and Q_t were obtained for the inverted and tied pairs, respectively. The Q were then rounded to the nearest integer. This procedure has the effect of translating the proportion of intra-subject ratings comparisons back into the original unit N.

The rounded Q constitute a 15x3 table for each symptom. The ties Q_t were excluded and the resulting 15x2 table was analyzed as a rectangular table by ODA. The significance levels from this analysis, for each symptom, are displayed in Table 3. It is seen that the results for all symptoms, except for anxiety and gastrointestinal problems, are heterogeneous and are inconsistent in terms of the direction of effect of HT500S with these symptoms.

(new) A cluster analysis of the fibromyalgia symptoms was then performed. The Q table was used to compare each pair of symptoms via Fisher's exact test (Table 4). High values of p indicate that the effects for each comparison are indistinguishable, while low values of p indicate that the effects are

distinguishable. The $p < .10$ criterion was used in light of the reversal of the usual role of significance testing.

Three clusters of symptoms were then determined by inspection. The clusters include:

1. Pain and stiffness. There are considered to be **Rheumatic symptoms (R)**.
2. Fatigue, concentration problems, memory problems, and sleep problems. These are classified as **Physical and Cognitive fatigue (F)**.
3. Anxiety, depression, and gastrointestinal problems. These are labeled as **Mood disorders (M)**.

Table 5 contains the results of the clustered symptoms. The – or + sign appended to the symptom cluster refers to the sign of tau obtained from Table 1. For instance, subject D had a value of tau = -.249 for pain, and tau = -.347 for stiffness. This subject was considered R-. These individuals suffer pain and stiffness when HT500 is low. Conversely, R+ individuals suffer pain and stiffness when HT500 is high. Similarly, F- individuals experience physical and cognitive fatigue when HT500 is low, and M+ individuals suffer mood disorders when HT500 is high.

Table 6 displays the success rate for each subject for each symptom. This is the ratio of concordances to the sum of concordances and inversions.

These results are consistent with distributions of aerosols (particles suspended in air) and gases. **Here are some citations involving low levels of HT500:**

Miyake et al. (1962): “It was found that the specific radioactivity in rain water or the air activity was much higher when there was a trough at the 500-mb level [low HT500] or above and the core of a jet stream was located above or a little south of Tokyo.”

Miyake et al. (1960): “There is little correlation between the surface weather conditions and fallout while a considerably higher correlation was found among a trough at 500 mb, position of jet stream and air activity… These facts will account for the increase of the concentration of radioactive debris in the air and the rain with the passage of a trough line at 500 mb across an observation point.”

Chen et al. (1970): ”The dates of occurrence of peak concentrations of fallout particles generally coincided with (a) the arrival times of air masses at 500 mb and/or 300 mb after completing a cycle around the world, and (b) the passage of 500 mb troughs at Fayetteville… All these peaks have a direct correlation with the passage of the 500 mb trough. The dynamic explanation of this process is that to the immediate west of the upper-level trough, we usually find low-level divergence and upper-level convergence with the descending motion. It is this descending motion that brings down upper air and thus tends to increase the particle concentration. Miyake et al. (1960) also reported that similar meteorological conditions play an important role in the transport of radioisotopes from the stratosphere to the troposphere. They noted that the Sr-90 concentration in the ground-level air showed an increase after the passage of a 500 mb trough.”

The radioactive properties of these particles are irrelevant for us here, it is the size that is important:

E.A. Martell (1965): “The size distribution and interaction of radioactive and natural aerosols in the stratosphere”. At this time most of the artificial radioactivity above 27 km was associated with particles

below 0.02 (micron) radius. By comparison, radioactive debris only several months old in this altitude range shows most of the radioactivity on particles between 0.02 (micron) and 0.15 (micron) radius (DREVINSKY & PECCI, 1965)."

Here are some citations involving high levels of HT500:

M. Koerber (2008): www.ladco.org/reports/pm25/pre2008/synoptic_typing_analysis.pdf : "An upper-level ridge [high HT500] or flat flow generally produces higher PM2.5 concentrations (i.e., above 30 µg/m3), while a trough or zonal flow produces lower concentrations (i.e., generally below 20 µg/m3)." [PM2.5 refers to particles that are less than 2.5 micrometers in diameter.]

Strohm et al. (2004): "Regional stagnation associated with surface and aloft high pressure [high HT500] tends to produce the best conditions for regional build-up of PM2.5 concentrations as well as provide conditions that favor the highest PM2.5 concentrations during an event."

Table 7 indicates symptoms caused by inhalation or ingestion of toxic substances in the environment that are shared with fibromyalgia. Note the large amount of overlap between fibromyalgia symptoms, and symptoms of toxic exposure.

So we conclude:

Daily variation of fibromyalgia symptoms obtained from the FM Wellness Project is associated with concentrations of environmental toxins in the breathable atmosphere. For R-, F-, and M- individuals, the toxins associated with their symptoms originate from a distant location, travel in the upper levels

of the atmosphere, and are of a size of 0.3 micrometers or less in diameter. For R+, F+, and M+ individuals, the toxins original from a local source, travel in lower levels of the atmosphere, and are of a size 0.3 – 2.5 micrometers in diameter.

Fibromyalgia is a disease characterized by increased sensitivity to environmental toxins. The symptoms suffered by FM patients are due to the toxic properties of these toxins themselves. They are NOT "fibromyalgia symptoms".

The FM patient should limit her inhalation and ingestion of these toxins by purifying the air with an air filter, purifying water with a water filter, and changing diet by eating foods with low amounts of these toxins. She should reduce dermal exposure by increasing the amount of baths and showers, and assist her body in detoxification with exercise, and with natural supplements such as spirulina and chlorella.

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M. Koerber (2008): www.ladco.org/reports/pm25/pre2008/synoptic_typing_analysis.pdf

Table 1. The values of Kendall's tau-b and its associated *p*-value for each subject's ratings of fibromyalgia symptoms and 5-day moving average of 500 mb geopotential heights (HT500S) for her location. Shaded results are significant at the familywise .05 level for each symptom according to the Hochberg (1988) extended Simes procedure.

		Pain		Stiffness		Fatigue		Concen		Memory		Anxiety		Depress		Gastro		Sleep	
Subject		τ	*p*	τ	*p*	τ	*p*	τ	*p*	τ	*p*	τ	*p*	τ	*p*	τ	*p*	τ	*p*
A	AZ N=144	-.058	.385	-.078	.230	-.157	.018	-.099	.128	-.030	.638	.117	.065	**.207**	**.002**	-.014	.828	.077	.249
B	MS N=119	**-.217**	**.002**	-.159	.018	-.045	.507	-.082	.233	-.174	.012	-.074	.281	-.132	.057	-.041	.548	.019	.779
C	OR N=77	-.085	.334	.069	.423	-.115	.167	**.244**	**.004**	.071	.382	.073	.398	.111	.233	.021	.797	-.141	.086
D	CA N=268	**-.249**	**<.001**	**-.347**	**<.001**	**.156**	**<.001**	**.149**	**.002**	**.150**	**.001**	**.201**	**<.001**	**.254**	**<.001**	**.191**	**<.001**	.129	.004
E	OR N=168	.022	.697	.091	.112	.046	.409	**.185**	**<.001**	**.194**	**<.001**	.164	.006	.121	.048	.067	.251	.108	.081
F	PA N=81	.094	.251	.218	.010	.123	.131	.036	.668	.015	.865	.033	.714	-.087	.327	-.028	.747	-.121	.135
G	MN N=297	**-.309**	**<.001**	**-.349**	**<.001**	**-.221**	**<.001**	**-.400**	**<.001**	**-.353**	**<.001**	-.001	.993	-.121	.005	-.067	.150	**-.144**	**<.001**
H	UT N=71	.103	.250	.116	.200	.112	.222	.139	.112	.220	.012	-.036	.673	-.035	.693	.080	.366	-.051	.551
I	MD N=76	-.130	.125	-.093	.270	.171	.043	.140	.116	.238	.008	.240	.006	.138	.116	**.258**	**.004**	.137	.107
J	ID N=99	.016	.830	.001	.998	-.060	.418	-.181	.020	-.133	.088	.022	.774	.048	.537	.093	.237	-.050	.508
K	MT N=118	.052	.449	**-.293**	**<.001**	-.146	.040	-.070	.349	.007	.926	-.003	.966	.070	.332	-.058	.417	.112	.100
L	ID N=83	.122	.127	.035	.660	-.110	.180	-.047	.551	-.123	.116	-.005	.953	-.226	.005	.061	.442	.049	.531
M	TN N=101	-.161	.041	-.175	.023	.027	.710	**.270**	**<.001**	**.251**	**.002**	-.032	.685	-.049	.544	-.009	.914	.035	.655
N	TN N=99	-.011	.874	.126	.083	**-.347**	**<.001**	.092	.226	.091	.247	.025	.738	.072	.332	.010	.892	.028	.726
O	TX N=107	-.123	.085	-.136	.058	-.027	.704	.011	.877	-.006	.939	.053	.453	.057	.411	**-.220**	**.002**	-.098	.173

Table 2. Meta-analysis results: Global *p*-values for each symptom obtained by Simes' test* and null hypothesis rejection for each symptom obtained by Simes' test weighted by sample size**.

	Pain	Stiffness	Fatigue	Concen	Memory	Anxiety	Depress	Gastro	Sleep
Simes	3.6E-12	1.6E-15	2.6E-6	2.0E-20	1.1E-15	1.7E-4	7.5E-7	7.2E-4	.009
Weighted Simes	yes	yes	yes	yes	yes	yes	yes	yes	yes

Table 3: Meta-analysis results: Significance obtained by ODA-based homogeneity tests for each symptom, with HT500S as the response variable (15 subjects, 1908 ratings per symptom).

Pain	Stiffness	Fatigue	Concen	Memory	Anxiety	Depress	Gastro	Sleep
.004	**<.001**	**<.001**	**<.001**	**<.001**	.689	**<.001**	.087	**.024**

Table 4. Distinguishability of symptoms in response to HT500S, and cluster assignments according to Fisher's exact test ($p < .10$ criterion).

	Stiffness	Fatigue	Concen	Memory	Anxiety	Depress	Gastro	Sleep
Pain	.574	.064	.006	.004	<.001	<.001	<.001	.002
Stiffness		.015	<.001	<.001	<.001	<.001	<.001	<.001
Fatigue			.351	.295	<.001	.013	.036	.175
Concen				.940	.018	.124	.236	.674
Memory					.025	.155	.285	.760
Anxiety						.468	.275	.055
Depress							.743	.266
Gastro								.449

Table 5: Cluster analysis results for HT500S ($p < .001$ overall).

	Symptom Cluster R		Symptom Cluster F		Symptom Cluster M	
	Pain, Stiffness		Fatigue, Concentration, Memory, Sleep		Anxiety, Depression, Gastro	
	Rheumatic Symptoms		Physical/Cognitive Fatigue		Mood Disorders	
$p <$	.001		.001		.001	
	Group R-	Group R+	Group F-	Group F+	Group M-	Group M+
Subjects	A B C D G I K M O	E F H J L N	A B G J K L N O	C D E F H I M	B F G K L M O	A C D E H I J N
N	1307	601	1066	842	906	1002
Proportion of Ratings, %	68.5	31.5	55.9	44.1	47.5	52.5
Concordances, %	47.9	43.2	44.9	42.6	31.7	39.0
Ties, %	25.8	19.3	25.2	25.8	40.9	34.0
Inversions, %	26.3	37.4	29.9	31.5	27.5	26.9

Table 6. Success rate (C / (C + I), %) for each subject and symptom according to the direction of association with HT500S specified by the ODA model.

Subject		Pain		Stiffness		Fatigue		Concen		Memory		Anxiety		Depress		Gastro		Sleep	
A	AZ N=144	-	53.9	-	55.0	-	60.3	-	56.3	-	51.9	+	57.0	+	63.2	-	51.0	+	56.5
B	MS N=119	-	61.9	-	58.7	-	52.5	-	54.7	-	60.1	-	54.3	-	57.9	-	52.3	+	51.0
C	OR N=77	-	55.2	+	54.0	-	56.3	+	63.2	+	53.8	+	54.3	+	61.5	+	51.1	-	57.5
D	CA N=268	-	65.6	-	70.2	+	59.0	+	58.6	+	58.6	+	61.6	+	65.4	+	62.1	+	57.2
E	OR N=168	+	51.2	+	55.2	+	52.5	+	60.1	+	60.6	+	60.5	+	59.8	+	54.1	+	61.0
F	PA N=81	+	55.2	+	62.8	+	56.7	+	52.0	+	50.9	+	52.4	-	56.3	-	51.7	-	56.6
G	MN N=297	-	67.0	-	69.2	-	62.3	-	71.9	-	69.7	-	50.0	-	56.9	-	55.5	-	58.0
H	UT N=71	+	55.9	+	56.8	+	56.8	+	57.6	+	62.0	-	52.0	-	51.9	+	54.6	-	52.7
I	MD N=76	-	57.1	-	55.1	+	59.5	+	58.5	+	65.0	+	64.0	+	58.2	+	65.2	+	57.7
J	ID N=99	+	50.9	-	50.0	-	53.4	-	61.1	-	58.2	+	51.3	+	53.0	+	56.6	-	52.9
K	MT N=118	+	53.0	-	69.4	-	59.3	-	56.8	-	49.5	-	50.3	+	55.1	-	53.8	+	56.3
L	ID N=83	+	56.6	+	51.9	-	56.2	-	52.5	-	56.5	-	50.2	-	62.3	+	53.3	+	52.6
M	TN N=101	-	60.3	-	60.8	+	51.4	+	68.6	+	68.0	-	52.7	-	56.1	-	50.8	+	52.5
N	TN N=99	-	50.6	+	56.9	-	68.7	+	55.3	+	56.0	+	51.4	+	54.1	+	50.6	+	51.9
O	TX N=107	-	56.9	-	57.7	-	51.5	+	50.6	-	50.3	+	52.9	+	53.1	-	62.1	-	55.5

Table 7. Symptoms caused by inhalation or ingestion of toxic substances in the environment that are shared with fibromyalgia.

Substance	Symptom								
	Pain	Stiffness	Fatigue	Concentration	Memory	Anxiety	Depression	Gastro	Sleep
Aluminum	✓		✓	✓	✓		✓	✓	
Antimony	✓							✓	
Arsenic	✓		✓		✓		✓	✓	✓
Benzene	✓		✓		✓		✓	✓	✓
Beryllium	✓		✓						
Cadmium	✓			✓	✓	✓		✓	✓
Chlorine	✓		✓	✓		✓	✓	✓	✓
Chromium	✓		✓					✓	
Cobalt					✓			✓	
Copper	✓		✓				✓	✓	
Fluorine & Fluorides	✓	✓	✓		✓			✓	
Formaldehyde	✓	✓	✓	✓	✓			✓	✓
Hydrogen Sulfide			✓	✓	✓			✓	
Lead	✓		✓	✓	✓	✓	✓	✓	
Manganese	✓	✓	✓	✓	✓	✓	✓	✓	✓
Mercury	✓	✓	✓	✓	✓	✓	✓	✓	✓
Methylene Chloride			✓		✓		✓	✓	
Nickel	✓							✓	
PCBs	✓		✓	✓	✓		✓	✓	✓
Tin			✓	✓	✓		✓	✓	
Toluene			✓	✓	✓				✓

ATSDR Toxic Substances Portal http://www.atsdr.cdc.gov/toxprofiles/index.asp