The effect of dietary glutamate on fibromyalgia and irritable bowel symptoms

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ABSTRACT

Objective. *To examine the effects of a challenge with monosodium glutamate (MSG) as compared to placebo on the symptoms of fibromyalgia (FM), in participants who initially experienced >30% remission of symptoms on an excitotoxin elimination diet.*

Methods. *Fifty-seven FM patients who also had irritable bowel syndrome (IBS) were placed on a 4-week diet that excluded dietary additive excitotoxins including MSG and aspartame. Thirty-seven people completed the diet and 84% of those reported that >30% of their symptoms resolved, thus making them eligible to proceed to challenges. Subjects who improved on the diet were then randomised to a 2-week double-blind placebo-controlled crossover challenge with MSG or placebo for 3 consecutive days each week. The primary outcome measure was total symptom score. Secondary outcome measures included visual analogue pain scales (VAS for FM and IBS), an IBS Quality of Life Questionnaire (IBS QOL) and the Fibromyalgia Impact Questionnaire-Revised (FIQR). Repeated measures ANOVA was used to analyse crossover challenge results.*

Results. *The MSG challenge, as compared to placebo, resulted in a significant return of symptoms (total symptom score, $p<0.02$); a worsening of fibromyalgia severity as determined by the FIQR ($p<0.03$); decreased quality of life in regards to IBS symptoms (IBS QOL, $p<0.05$); and a non-significant trend toward worsening FM pain based on visual analogue scale (VAS, $p<0.07$).*

Conclusion. *These findings suggest that dietary glutamate may be contributing to FM symptoms in some patients. Future research on the role of dietary excitotoxins in FM is warranted.*

Introduction

Fibromyalgia (FM) is characterised by widespread pain in ≥3 of 4 body quadrants including the axial spine, as well as other debilitating symptoms (1). An internet survey of 2596 FM patients, reported the rank order of symptoms by intensity as: morning stiffness, fatigue, non-restorative sleep, pain, memory problems, difficulty concentrating, trouble falling asleep, and muscle spasms (2). The extreme number of symptoms experienced in FM can lead to great burden in patients' daily lives (3). Sub-threshold depressive symptoms also appear to be more prevalent in FM (4); and some authors have suggested that psychological suffering may amplify the burden of FM, and possibly effect treatment outcomes (5).

Fibromyalgia commonly overlaps with other illnesses including irritable bowel syndrome (IBS), chronic fatigue syndrome (CFS), overactive bladder, migraine, tempomandibular joint disorder (TMD) and restless leg syndrome (6). In fact, up to 81% of FM patients also suffer from IBS, making this the most common co-morbidity in FM (7). The symptoms in these disorders suggest a possible common causal pathway which may be linked to central sensitisation (6).

A key neurotransmitter in central sensitisation is glutamate (8); which is the most ubiquitous excitatory neurotransmitter in mammals (9). In animal models, experimentally high glutamate levels have been shown to overexcite a neuron to the point of death (10). The ability of glutamate, and two other amino acids (L-aspartate and L-cysteine) to induce neuronal cell death, has led to coining of the term 'excitotoxins' (11-12). These amino acids are commonly found in processed foods in their free, non-bound form as food additives (13).

Smith published a case series about four patients who reported improvement in FM symptoms after removal of the dietary excitotoxins monosodium glutamate (MSG) and aspartame, with a return of symptoms upon reintroduc-

tion (14). Similarly, another case series described improvement in FM symptoms after two patients discontinued consumption of aspartame (15). However, to date, no formal research has evaluated the possible role of dietary excitotoxins on FM symptoms.

The objective of this study was to determine if FM patients with IBS, who demonstrated >30% remission of symptoms on an excitotoxin elimination diet, would have a significant return of symptoms using a crossover, double-blind, placebo-controlled MSG challenge.

Materials and methods

Recruitment

Men and women age 18-75 years, with FM and IBS, were recruited from the greater Portland, Oregon area. The multi-step recruitment strategy is described elsewhere (16). Eligibility included: a physician diagnosis of FM per 1990 American College of Rheumatology (ACR) criteria (17), fulfillment of the Rome III criteria for IBS (18), access to telephone/email, willingness to discontinue medications that significantly affect glutamatergic signaling in the brain (gabapentin, pregabalin and lamotrigine), and willingness to consume all food at home for one month. Exclusion criteria included: a current diagnosis of inflammatory bowel disease, colon cancer, endometriosis, current or planned pregnancy, asthma requiring hospitalisation in the past, alcohol/substance abuse, or onset of IBS symptoms directly following major abdominal surgery. This research study was approved by the Human Subjects Protection Programs at both Oregon Health & Science University and the University of Arizona.

Group diet training

All subjects participated in a 2-hour group diet training session with detailed diet information, including food label reviews, guidance for dietary substitutions, unusual sources of excitotoxins, shopping tips, food cost controls, and ideas for preparing meals. Participants received a hard copy of all information presented and a detailed list of food additives to avoid.(Appendix A)

Clinic visit and individual diet counseling

All participants completed a tender point exam, anthropometric measures, and study questionnaires at the baseline clinic visit. Subjects taking pregabalin, gabapentin or lamotrigine, were weaned off the medications under the supervision of the study physician (RB) over the week prior to the clinic visit. All other medications were to be kept consistent throughout the study, and any changes in use were reported weekly. Since gelatin is a source of excitotoxic amino acids (19), medications or supplements in gelatin capsules were opened, and consumed without the capsule.

A 24-hour diet recall was completed to guide each person through the reporting of their "normal" diet. Individual product substitution ideas were given for replacing foods with additive excitotoxins, as well as recommendations on how to maintain food consumption patterns as similar to their normal diet as possible. All participants began the diet the following Monday, after removing excitotoxins from the household and purchasing diet-appropriate foods over the weekend.

Dietary Intervention

During the 4-week diet intervention, all participants had access to professional dietary counseling if questions arose. Food/symptom diaries were kept for weeks 1 and 4 in order to promote dietary compliance and to help limit recall bias on post-diet study questionnaires. Food/symptom diaries were also completed on Monday/Tuesday/Wednesday of both challenge weeks to assure continued dietary compliance and to aid with symptom recording over this period. Participants were counselled to continue recording symptoms for the entire week if symptoms persisted. An investigator-designed excitotoxin food frequency questionnaire (FFQ) was used to estimate dietary compliance during the 4-week diet and 2-week challenge period. The FFQ consisted of 33 food items commonly containing excitotoxins. These were scored 1-5 based on frequency of consumption, and then summed to form a score. (Appendix B)

MSG-placebo challenge tests

A randomised, crossover, double-blind, placebo-controlled challenge series was used to test the hypothesis. Participants returned to the clinic on Monday of week 5 to complete post-diet questionnaires. Those who experienced >30% remission of symptoms progressed onto the 2-week challenge period, where they were randomised to receive a mixed flavour juice either alone (placebo) or with 5 grams of MSG, over 3 consecutive days (Monday/Tuesday/Wednesday) of each week. The Aji-no-moto MSG® used in this study was purchased from a single Chinese supermarket. The mixed flavour juice consisted of carrot, mango and orange juice, and in preliminary testing masked the flavour of MSG well due to its unique combination of flavours and generally undesirable taste. Five grams was chosen as the dose based on previous challenge studies with MSG (20-21); which concluded that very few people react with flushing, sweating, tightness in the chest, and rapid heartbeat (collectively called Chinese Restaurant Syndrome) when given 5 grams of MSG. Since toxicity reactions are based on dose, and it is possible to receive excitotoxins over multiple days, we challenged participants over three days in order to mimic this "real life" exposure pattern. After a minimum 8 hr fast, participants were challenged with 16 ounces of the mixed flavour juice (with or without MSG) on Monday/Tuesday/Wednesday morning of each calendar week. Participants were then monitored for 2 hours. Outcome data were collected the following Monday after each challenge week. Additionally, participants were contacted via telephone two months after challenges to assess dietary compliance and symptom occurrence.

Outcome measures

The primary outcome for this study was a 28-symptom checklist (Appendix C) which included the symptoms of FM, IBS, and four 'Chinese Restaurant Syndrome' symptoms (rapid heartbeat, flushing, sweating, and tightness in the chest) (22). Each symptom reported was scored as one point on the measure. Hence, to improve the score,

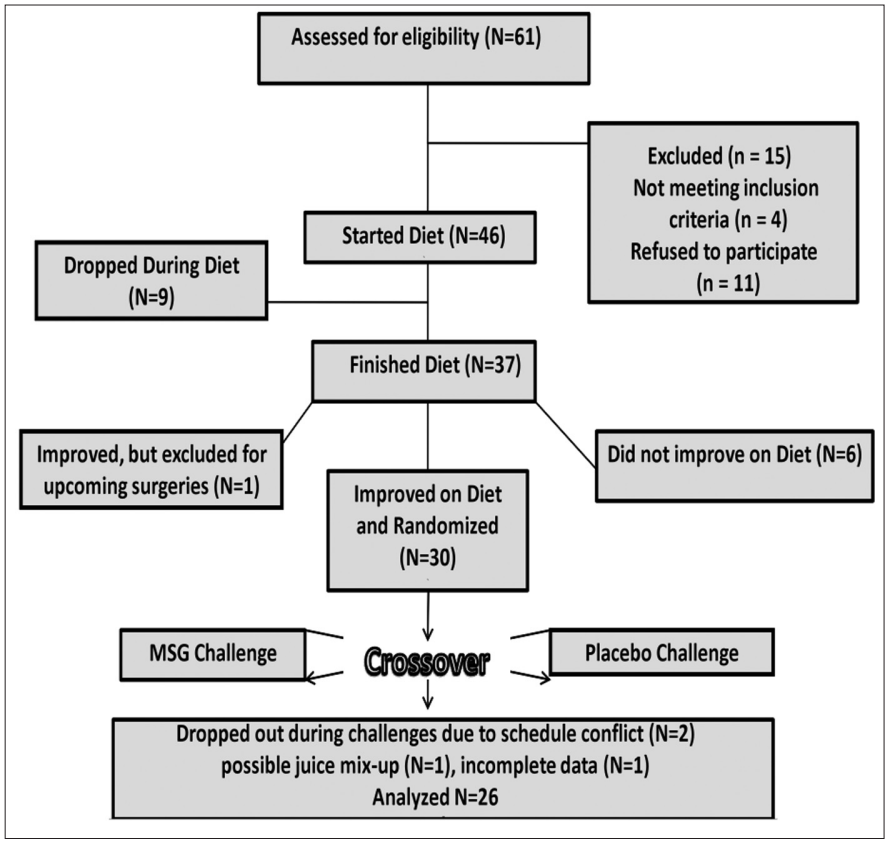

Fig. 1. CONSORT diagram of the clinical trial.

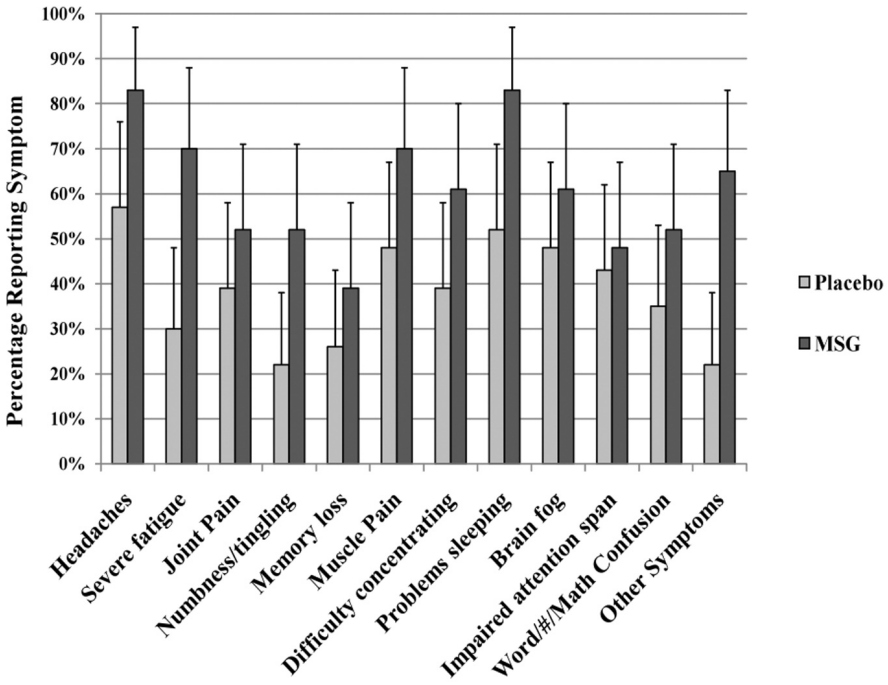

Fig. 2. Percentage of participants responding with each fibromyalgia symptom evaluated as part of the total symptom score on the MSG challenge week as compared to the placebo week.

one or more symptoms had to resolve. Secondary outcome measures included two 20 cm Visual Analogue Pain Scales (VAS) for FM and IBS; the Fibromyalgia Impact Questionnaire-Revised (FIQR), a measure of function, symptoms and overall impact of FM (23); and an IBS Quality of Life (QOL) Questionnaire (24). Higher scores on the FIQR indicate greater negative impact of FM. The decision was made to code the IBS QOL questionnaire backwards so that a higher score indicated a worse QOL, so that all measures could be consistent.

Statistical methods

Data were analysed using SAS 9.1.3 software (SAS Institute Inc., Cary, NC). Pre-post diet change scores were analysed with student *t*-tests for normally distributed variables or Wilcoxon signed rank test for non-normally distributed measures. The outcomes of the crossover challenge were analysed using repeated measures ANOVA for crossover designs (25-26). The FFQ scores were non-normally distributed, so the Friedman test for non-parametric data was used, controlling for person.

Results

Study-flow is depicted in a consort diagram (Fig. 1). Of the 46 subjects who started the diet, 9 dropped out within the first 2 weeks due to: schedule conflict, 2 (2%); life event, 1 (1%); distance, 2 (2%); too sick to shop/cook, 2 (2%); or too much life stress, 2 (2%). Those who improved on the diet had a mean (SD) age of 53 (13) years, BMI of 31 (6) kg/m^2, were diagnosed with FM symptoms 18 (11) years prior to study enrolment, and had an average of 16 (2) of a possible 18 tender points. At baseline, the majority reported alternating-type IBS (76%) and fewer people reported constipation-type (15%) or diarrhoea-type IBS (9%). Participants who improved on the diet were similar to those who did not improve (Table I). Nine participants were weaned off their anticonvulsant medication(s) prior to starting the diet; 8 of 9 completed the diet, and all 8 of these reported >30% remission of symptoms. They had been taking: Lamotrigine 1 (<1%), Gabapentin 4 (11%), Pregabalin 3 (1%), or both Gabapentin and Pregabalin 1 (<1%). The dose of all medications was constant throughout the study, with the exception of one participant prescribed a beta-blocker. Approximately 30% of participants chose to discontinue all supplements found in gelatin cap-

sules for the month rather than opening them. The supplements most frequently discontinued were fish oil capsules, vitamin D and vitamin E.

Thirty-seven participants completed the diet, and 84% (n=31) reported >30% remission of symptoms. On average, 11 symptoms remitted and eight participants (22%) no longer had ≥11 tender points by the end of the month. Improvements in outcome measures following the diet were all significant ($p<0.0001$). Table II reports pre-post outcome changes from the dietary intervention.

The 31 people who reported >30% remission of symptoms were eligible to go onto the double-blind crossover challenge. One woman did not proceed to the challenges due to scheduled neck and shoulder surgery. Two participants dropped out during the first challenge week, both citing schedule conflict and stress issues. One participant refused the final visit due to distance and fuel costs, and did not provide final study forms.

Data were analysed for 26 participants who completed both challenge weeks. A possible mix-up in MSG *vs*. placebo assignment was identified by the research assistant for one subject during challenges, so this data was excluded from the analysis. The excitotoxin FFQ score did not differ between challenge weeks (mean SD) of (2.9(3) *vs*. 3.3(4) respectively), $p<0.27$)), demonstrating that participants followed the diet similarly both weeks, consuming ~1 food with excitotoxins/week. Food/symptom diaries corresponded to the FFQ.

Table III lists outcome measures for MSG *versus* placebo challenge. The total symptom score differed between challenge weeks (mean(SD) of 12(6) *vs*. 9(5), $p<0.02$), demonstrating a significant return of symptoms from MSG challenge as compared to placebo. The total FIQR score significantly worsened during MSG challenge week as compared to placebo (mean(SD) of 48(22) *vs*. 36(19), $p<0.03$). The VAS for FM pain was higher after challenge with MSG as compared to challenge with placebo (mean(SD) of 11(5) vs. 8(4)), but was only marginally significant ($p<0.07$) (Table III). The IBS-QOL questionnaire also worsened during MSG challenge week (26(20) *vs*.18(15),

Table I. Descriptive characteristics of study population at baseline and relation of measures with improvement from diet.

	Improved on diet*		
	No n=6	Yes n=31	*p*-value**
Characteristic	Mean (SD)	Mean (SD)	
Age (years)	42.5 (16)	53.4 (13)	0.08
Height (inches)	66.9 (2)	64.5 (3)	0.06
Weight (kg)	75.9 (20.5)	82.7 (16.8)	0.41
BMI (kg/m^2)	26.4 (7)	30.8 (6)	0.12
Number medications used	4.8 (2)	5.8 (5)	0.65
Number supplements used	3.5 (3)	2.9 (4)	0.72
Symptom duration (yrs)	18.8 (10)	18.1 (11)	0.89
Time since diagnosis (yrs)	17.2 (10)	12.5 (7)	0.19
Tender point number	17.3 (1)	16.4 (2)	0.19
Myalgic score	39.8 (6)	34.3 (7)	0.09
FFQ score at baseline	43.7 (24)	41.0 (15)	0.73
FFQ score at 4 weeks	3.7 (2)	4.7 (6)	0.70
Total symptom score	19.3 (5)	20.5 (4)	0.52
Number of other symptoms	1.3 (1)	1.4 (1)	0.97
VAS for FM	12.1 (4)	13.3 (3)	0.45
VAS for IBS	9.6 (4)	10.4 (5)	0.69
FIQR	57.0 (22)	58.9 (14)	0.79
IBS QOL	30.1 (24)	33.1 (17)	0.72
Characteristic	Number (%)	Number (%)	
Sex			
Female	6 (100%)	28 (90%)	N/A
Male	0	3 (10%)	
Menopause status			
Pre-menopausal	4 (67%)	7 (25%)	0.07
Post menopausal	2 (33%)	21 (75%)	
Type of IBS (n=54)			
Constipation	1 (17%)	4 (13%)	0.79†
Diarrhoea	1 (17%)	3 (10%)	
Alternating	4 (67%)	23 (77%)	
Precipitating onset (n=51)			
None identified	0	3 (10%)	N/A
Trauma	3 (50%)	12 (39%)	
Infection	2 (33%)	10 (32%)	
Major life stress	1 (17%)	6 (19%)	

BMI: Body Mass Index; FFQ: Food Frequency Questionnaire; VAS: Visual Analogue Pain Scale; FIQR: Fibromyalgia Impact Questionnaire Revised; IBS: Irritable Bowel Syndrome; QOL: Quality of Life.

Table II. Average change in outcome measures after one month on the excitotoxin elimination diet.

Measure n=37	Change score* Mean (SD)	*p*-value**
Weight loss (kg)	1.9 (4.3)	0.002†
BMI change (kg/m^2)	0.3 (0.7)	0.002†
TP number change	2.5 (3.6)	0.0003†
Myalgic score change	9.5 (8.6)	<0.0001
Total symptom score change	11.4 (5.2)	<0.0001†
VAS for FM change	5.4 (5.7)	<0.0001
VAS for IBS change	4.6 (6.3)	<0.0001
FIQR change	22.2 (20.6)	<0.0001
IBS Quality of life change	12.9 (14.1)	<0.0001

*Change score computed from average baseline minus average post diet score.
**Students t-test or †Wilcoxon signed rank test.
TP: Tender Point Exam; VAS: Visual Analogue Pain Scale; FIQR: Fibromyalgia Impact Questionnaire Revised; IBS: Irritable Bowel Syndrome; QOL: Quality of Life.

Table III. Challenge results for fibromyalgia and irritable bowel syndrome measures among those who improved on the Excitotoxin Elimination Diet.

n=26*	Challenge		*p*-value**
	MSG Mean (SD)	Placebo Mean (SD)	
Excitotoxin FFQ	2.9 (3)	3.3 (4)	0.27***
Total symptom score	11.9 (5.5)	8.7 (5.1)	0.02
VAS FM	10.6 (4.8)	8.1 (4.2)	0.07
VAS IBS	8.4 (5.3)	6.3 (4.9)	0.19
FIQR overall	48.0 (22.4)	35.7 (19.4)	0.03
IBS QOL overall score	25.5 (20.4)	17.5 (14.7)	0.05†

*Excluding one possible challenge mix-up and one man's missing data. **Repeated measures ANOVA. ***Friedman test. *p*-value indicates participants followed diet similarly both weeks. †Square root transformation of data.
FFQ: Food Frequency Questionnaire; VAS: Visual Analogue Pain Scale; FIQR: Fibromyalgia Impact Questionnaire Revised; IBS: Irritable Bowel Syndrome; QOL: Quality of Life.

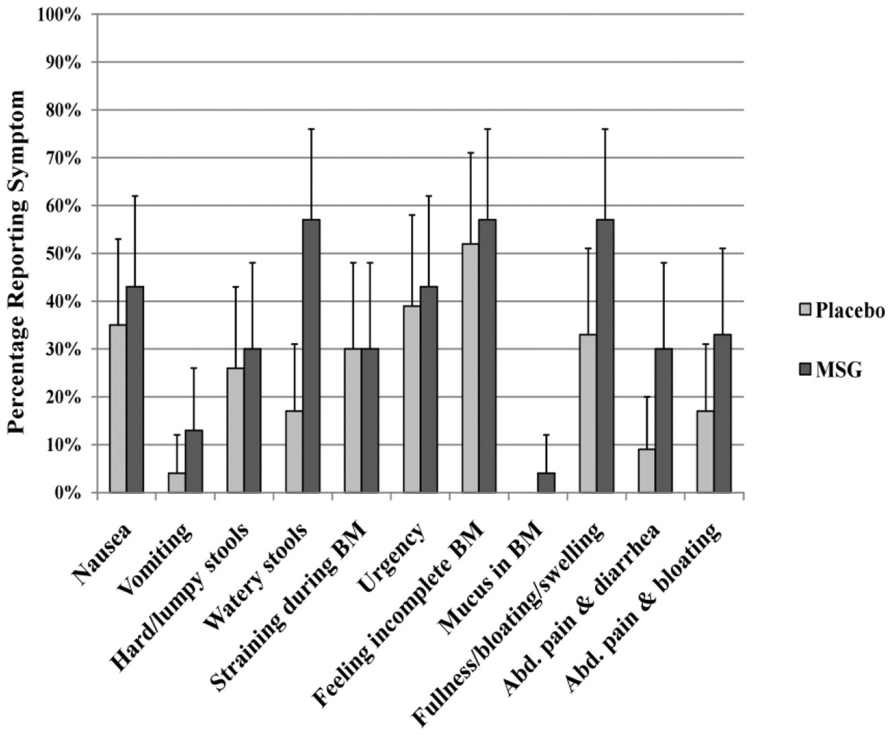

Fig. 3. Percentage of participants responding with each irritable bowel syndrome symptom evaluated as part of the total symptom score on the MSG challenge week as compared to the placebo week.

$p<0.05$), but the visual analogue pain scale for IBS did not significantly differ between challenge weeks (8(5) *vs*. 6(5), $p<0.19$) (Table III).

The only symptoms reported during the 2-hour observation period on the first day of challenges were headache, visual disturbance, dizziness and nausea. Most participants (n=19, 73%) reported onset of symptoms during the evening hours of the first day of MSG challenge or the following morning; symptoms worsened over time, peaking on day 3.

All FM symptoms returned more frequently during MSG challenge as compared to placebo challenge. Figure 2 illustrates the FM symptom differences during challenge weeks. The GI symptoms which returned more frequently during MSG challenge as compared to placebo were watery stools (57% *vs*. 17%), abdominal fullness/bloating/swelling (57% *vs*. 33%) and abdominal pain with diarrhoea (30% *vs*. 9%) (Fig. 3). Of the four 'Chinese Restaurant Syndrome' symptoms, only sweating and flushing occurred more frequently during MSG challenge as compared to placebo (52% *vs*. 30%; 33% *vs*. 17% respectively) (Fig. 4).

All "other" symptoms were reported more frequently during MSG challenge as compared to placebo challenge except for lung congestion and esophageal spasms which only occurred during placebo week. The "other" symptoms most frequently reported included restless leg syndrome (22%), visual disturbances (17%), tempomandibular joint disorder (13%), difficulty regulating body temperature (13%), migraine (13%), balance problems (13%), and sensitivity to environmental stimuli (13%).

Study participants were contacted by telephone 2 months after study completion; and were queried about continued dietary compliance and whether symptoms had returned. Of those who improved on the diet, 97% reported that they were still avoiding excitotoxins, and that symptoms which were eliminated on the diet only returned when accidentally consuming foods containing excitotoxins.

Discussion

Few dietary interventions have been tested in FM patients (27-31). A review of these studies has been published previously (32). Benefit has been noted from raw food vegan diets; however, due to their highly restrictive nature, participants were unable to continue the diets post-study, which limits their applicability.

This is the first study of an excitotoxin elimination diet and glutamate challenge in FM patients and contributes the following observations: 1) use of the excitotoxin elimination diet in free-living individuals is feasible; 2) the diet resulted in clinically significant symptom improvement in 84% of participants tested; 3) oral challenge with MSG compared to placebo resulted in significant symptom return in those who responded to the excitotoxin elimination diet; and 4) continued dietary compliance post-study suggests the diet is not overly restrictive for longer term use. These results indicate that excitotoxins may elicit symptoms in some FM patients.

We hypothesised that the excitotoxin elimination diet could affect central sensitisation by altering excitatory neurotransmission in the CNS. Authors have reported significant correlation between plasma glutamate levels and tender points in FM (33), as well as increased CSF glutamate levels in FM patients as compared to controls (8, 34-35). Additionally, magnetic resonance spectroscopy studies have also demonstrated higher brain levels of excitatory neurotransmitters in the insula, amygdala and posterior gyrus of FM patients as compared to healthy controls (36-39). Passage of glutamate at the blood brain barrier (BBB) is normally limited (9); however, compromised permeability of the BBB such as from infection (40), stress (41-42), and head injury (43); could increase brain levels of glutamate.

One strength of this excitotoxin elimination diet is the very specific focus on controlling the intake of excitatory amino acids, whose biochemical pathways as neurotransmitters have been implicated in the process of central sensitisation (44). This diet is much less restrictive than the raw food vegan diets previously evaluated. Since direct substitutions were made in the diet with similar food items lacking excitotoxins, it is unlikely that an increase in micronutrients could explain or confound the results. Moreover, this study included a double-blind placebo-controlled challenge with MSG, which further supports the hypothesis that diet effectiveness was due to reduced excitotoxic load as opposed to other mechanisms. The challenge scheme mimics real life exposure wherein excitotoxins are commonly consumed daily. Since the excitotoxin elimination diet theoretically lowers the underlying glutamate level, an induction of a toxicity reaction may necessitate dosing over multiple days. Participants in this study reported increasing symptoms over the 3-day MSG challenge, which suggests that the use of a 3-day challenge, or possibly longer, should be considered in future study designs.

We acknowledge several limitations to this research. First, this was a small study, and the findings will need to be replicated in a larger trial. Second, this study only examined self reported outcomes, so future research should include objective measures of physical function, balance, burden assessment, cognitive testing and pain threshold testing. Additional studies should also be pursued to assess the diet's effect on brain levels of excitatory amino acids as measured by NMR spectroscopy, the contribution of nutrient status on susceptibility to excitotoxins, and gluta-

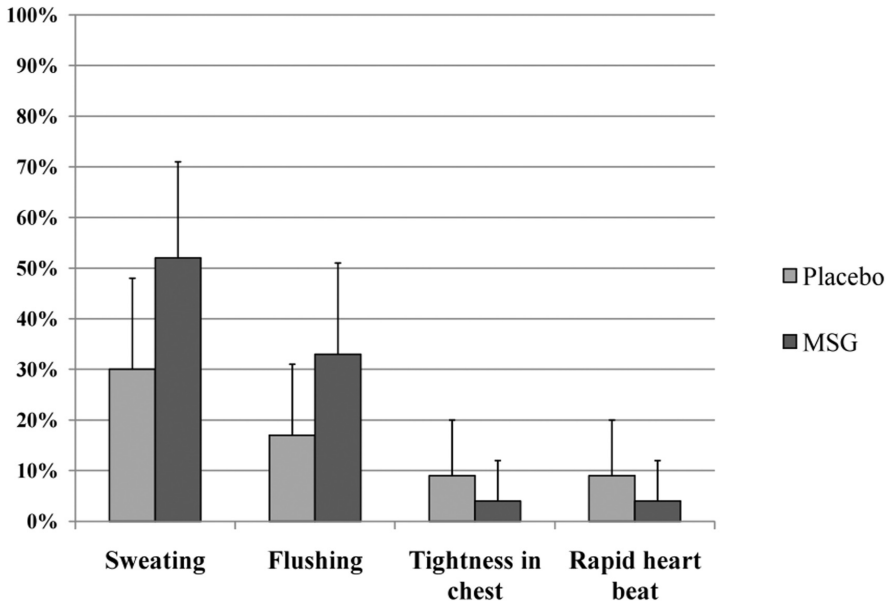

Fig. 4. Percentage of participants responding with each 'Chinese Restaurant Syndrome' symptom evaluated as part of the total symptom score on the MSG challenge week as compared to the placebo week.

APPENDIX A
List of Excitotoxic Food Additives Avoided*

– MSG (monosodium glutamate) or potassium glutamate
– sodium guanylate or inosinate
– gelatin
– hydrolyzed oat flour
– hydrolyzed vegetable protein (any kind… soy, corn, wheat, etc)
– plant protein extract
– sodium caseinate
– calcium caseinate
– yeast extract
– autolyzed yeast (extract)
– textured protein
– malt extract (or flavouring)
– any kind of modified food starch
– soy (or whey) protein concentrate or isolate
– smoke flavouring
– bouillon, broth, stock
– flavouring, natural flavouring (any kind), seasoning, spices, and carrageenan can all contain excitotoxins (but don't always)
– L-cysteine
– soy sauce, asian fish sauces
– parmesan and other aged cheeses

*Adapted from work by Russell Blaylock (45)

Appendix A: the list of food additives containing excitotoxins that participants were asked to avoid during the one month excitotoxin elimination diet.

APPENDIX B
Excitotoxin Food Frequency Questionnaire
(An estimate of Frequency of Intake of Foods Excluded on the Diet)

Please indicate if you have eaten a food item in each category in the box corresponding to how frequently that food item is consumed. If you never consume items from a category then leave all boxes blank.

	1-3x/yr	1x/mo	1-3x/wk	1x/day	2+x/day
Protein powder/ shakes					
Body building supplements					
Spice mixes or seasoning packets					
Marinades purchased at grocery store					
Boxed foods including seasoning packets					
Canned goods (canned soup, chili, etc.)					
Frozen meals					
Packaged spaghetti/tomato sauce					
Asian pre-packaged foods					
Soy sauce					
Other Asian sauces (like oyster sauce, etc.)					
Worcestershire Sauce					
Seasoned nuts					
Chips (except plain tortilla or potato chips)					
Crackers (excluding plain Triscuits)					
Salad Dressing or salad dressing mixes					
Caesar salad dressing					
Croutons					
Anchovies					
Parmesan cheese					
Sausage, pepperoni, bacon, ham,					
hot dogs, or deli meat					
Equal (aspartame sweetener)					
Diet Soda or other diet drinks					
Chewing gum					
Breath mints					
Vitamins or medication in gelatin capsules					
Vitamins/medication containing aspartame					
Sugar-free candy					
Jello or Jello pudding					
Gelatin Candy (gummy worms, skittles, etc.)					
Sunny Delight or vegetable juice					
Reduced calorie yogurt					
Regular flavoured yogurt					

Appendix B: the excitotoxin food frequency questionnaire (FFQ) used to assess dietary compliance.

APPENDIX C
Total Symptom Score

– Nausea
– Vomiting
– Hard or lumpy stools
– Watery stools
– Straining during a bowel movement (BM)
– Urgency (having to rush to have a BM)
– Feeling of incomplete bowel movement
– Passing mucus (white material) in a BM
– Abdominal fullness, bloating, or swelling
– Abdominal pain with diarrhoea
– Abdominal pain with bloating
– Headaches
– Severe fatigue
– Joint pain without redness/ swelling
– Numbness/ tingling in extremities
– Memory loss
– Muscle pain
– Difficulty concentrating
– Problems sleeping
– Sudden low blood pressure
– Brain fog
– Impaired attention span
– Confusion with words, numbers, math, etc.
– Sweating
– Flushing
– Tightness in the chest
– Rapid heart beat
– Other

** Other symptoms reported most frequently (and which improved) in this study included: TMD, restless legs, balance problems, tinnitus, muscle spasms/cramping, and migraine

Appendix C is the symptoms used in the 'Total Symptom Score' evaluated in this study.

mate kinetics in FM patients. Third, this study was designed specifically to test a dietary intervention by challenging those who improved on the diet with MSG. Since only diet responders needed to be challenged, no control diet was needed. Future research with a placebo diet group receiving equal attention will help fully quantify the effects of this dietary intervention over placebo response.

In conclusion, this novel research implicates glutamate as a major adverse excitotoxin in some FM patients. Dietary manipulation is a relatively simple and low cost non-pharmacological intervention that warrants further exploration.

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