Temporomandibular Disorders and Associated Clinical Comorbidities

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Objective: Temporomandibular joint and muscle disorders (TMJD) are ill-defined, painful debilitating disorders. This study was undertaken to identify the spectrum of clinical manifestations based on self-report from affected patients.

Methods: A total of 1511 TMJD-affected individuals were recruited through the web-based registry of patients maintained by The TMJ Association, Ltd, a patient advocacy organization, and participated in the survey as well as 57 of their nonaffected friends. Results were also compared with US population for questions in common with the National Health and Nutrition Examination Survey.

Results: The TMJD-affected individuals were on average 41 years of age and predominantly female (90%). Nearly 60% of both men and women reported recent pain of moderate-to-severe intensity with a quarter of them indicating interference or termination of work-related activities. In the case-control comparison, a higher frequency of headaches, allergies, depression, fatigue, degenerative arthritis, fibromyalgia, autoimmune disorders, sleep apnea, and gastrointestinal complaints were prevalent among those affected with TMJD. Many of the associated comorbid conditions were over 6 times more likely to occur after TMJD was diagnosed. Among a wide array of treatments used (46 listed), the most effective relief for most affected individuals (91%) was the use of thermal therapies—hot/cold packs to the jaw area or hot baths. Nearly 40% of individuals affected with TMJD patients reported one or more surgical procedures and nearly all were treated with one or many different medications. Results of these treatments were generally equivocal. Although potentially limited to the most severe TMJD affected individuals, the survey results provide a comprehensive dataset describing the clinical manifestations of TMJD.

Discussion: The data provide evidence that TMJD represent a spectrum of disorders with varying pathophysiologies, clinical manifestations, and associated comorbid conditions. The findings underscore the complex nature of TMJD, the need for more extensive interdisciplinary basic and clinical research, and the development of outcome-based strategies to more effectively diagnose, prevent, and treat these chronic, debilitating conditions.

Key Words: chronic pain, TMJ, migraine, chronic fatigue syndrome, fibromyalgia, allergies, IBS

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Temporomandibular joint and muscle disorders (TMJD) affect from over 10 million to as many as 36 million adults in the United States.[1–4] Symptoms range from mild pain and jaw dysfunction that may resolve over time to chronic conditions of intractable pain and limitations in jaw function that are severely debilitating. TMJD primarily affect females in a ratio that increases with the degree of severity of the condition. A 1996 National Institutes of Health Technology Assessment Conference on Managing Temporomandibular Disorders defined TMJD as "a collection of medical and dental conditions affecting the joint and muscles of mastication, as well as contiguous tissue components." As noted above, the reported prevalence of TMJD varies considerably across studies, given the lack of a standardized classification and definitions. In 2001, the Agency for Healthcare Research and Quality estimated that TMJD result in 17.8 million lost working days per year for every 100 million working adults in the United States and that the financial costs are in the billions of dollars.[5]

Recent research reveals that TMJD represent a complex family of heterogeneous disorders influenced by genes, sex, age, environmental, and behavioral triggers.[1] It is becoming increasingly apparent that TMJD may be associated with multiple clinical manifestations and a variety of systemic disorders that extend beyond the jaw.[6,7] To a large extent, these conditions remain poorly understood, and there exists a plethora of approaches for diagnosis and to classify them.[1,8–13]

This study was undertaken to identify the spectrum of clinical manifestations and therapeutic strategies associated with TMJD, from the perspective of the affected individuals. The TMJ Association, Ltd (http://www.tmj.org), a national nonprofit patient advocacy organization, maintains an extensive registry of affected individuals. People with TMJD who were listed on the web-based registry constituted the target population for a survey. The survey was undertaken on the premise that the results might provide insight into the pathophysiology of TMJD as well as relevant information concerning the diagnosis and treatment of these disorders. Specifically, the study had 2 objectives: first, to describe the spectrum of clinical manifestations associated with TMJD based on self-reported experiences of affected individuals; second, to compare the prevalence of comorbid conditions and symptoms of affected individuals to a comparable group of unaffected individuals, similar in age and sex.

METHODS

Study participants were recruited through the web-based registry of The TMJ Association, Ltd, which consists of individuals who have contacted the association for

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information or to share their TMJD experiences. After obtaining approval from the Medical College of Wisconsin Institutional Review Board, invitations to participate in the web-based survey were mailed electronically to 10,000 association registrants. Individuals were asked to respond by first providing informed consent to participate. Non-respondents were contacted electronically 1 additional time 4 to 6 weeks after the initial invitation was sent. Six months later, a telephone survey of a randomly selected sample of nonresponders (N = 100) was used to determine whether the invitation had been received and the reasons for nonresponse. The principal reported reasons for non-response included: technical difficulties, concerns that the survey would be too time consuming, or emotional distress elicited by the questions. An estimated 3500 (35%) of the 10,000 TMJD registrants contacted actually received the invitation. Of those 3500 recipients, 43% responded to the survey.

After electronically indicating consent, respondents were assigned unique but anonymous identifying numbers and completed a web-based questionnaire. Respondents were asked to provide demographic information, information on experiences with pain and other physical and psychological symptoms, opinions about factors that caused TMJD, medical and dental histories related to treatments for TMJD, medication use, comorbid conditions, and information on quality of life. The questions about the comorbid conditions were: "have you been diagnosed with…" and the respondents with TMJD were asked whether they had the condition "before or after their TMJ problems began." When appropriate, responses to pain intensity or medication usage were phrased as either occurring in the last 4 weeks or currently. No personal identifiers were collected. Respondents were also requested, but not required, to invite and enroll 1 same-sex friend, similar in age (± 5 y), but not affected by TMJD, to serve as a control participant for purposes of comparison. Friend-controls were used to efficiently control for social, lifestyle, and economic factors that could potentially confound the study findings. Although friend-controls may lead to overmatching, they do not bias the results but rather reduce the efficiency of the analysis. A choice of a closely matched control is particularly important in an internet survey. To validate the characteristics of the friend-controls, general US population controls of the same age and sex from the National Health and Nutrition Examination Survey (NHANES 2003-2004) were used. These data were used to ascertain whether the NHANES controls had a similar prevalence of comorbid conditions for the corresponding conditions in the 2 surveys. The NHANES data was appropriately weighted to be a representative sample of the US population of the same age and sex.[14] Only 57 TMJD-affected individuals invited and enabled a friend to participate and complete the questionnaire. Control participants were not personally identified and information on control participants was linked to the TMJD-affected participant's information by using the number provided to the respondent at time of enrollment. Information on control participants included demographic, medical, and dental histories.

After appropriate cleaning and sorting of the responses, the data were converted to an ACCESS database and exported to SAS (version 9.1.3) and STATA (version 10.1) for analysis. The analyses provide both a description of the characteristics and experiences of TMJD-affected individuals and a comparison of affected individuals with unaffected controls in a matched case-control analysis. For the matched case-control approach, a 1-to-4 control-to-affected individuals' match was conducted based on age, sex, and educational attainment. Age and sex were particularly important to eliminate these factors from affecting the results. In addition, the NHANES 2003-2004 was used to validate whether the controls had a similar prevalence to a weighted representative sample of the US population of the same age and sex.[14] Not all participants responded to all the questions therefore, the denominators on which the analyses are based vary to some extent. Consequently, results are presented as percent of respondents in that section of the questionnaire.

Statistical analyses include descriptive statistics, *t* tests, χ^2 or Fisher exact tests, and Mann-Whitney *U* tests. Prevalence of comorbid conditions pre-TMJD and post-TMJD occurrence was determined from 2 questions. The first question asked was whether the person had ever been diagnosed with the following symptoms or conditions (from a list of 132). The second asked question was whether they had developed the condition before or after their TMJD problems. Conditional logistic regression was used in the matched case-control study to obtain estimates of the odds ratio and to adjust for covariates.

RESULTS

A total of 1511 TMJD-affected individuals participated in the survey (43%). Table 1 presents the demographic information for these respondents who were predominantly female (90%), attended some college or graduated (80%), married (57%), employed (70%), and were 41 years of age on average.

Respondents were given a list of putative causes of TMJD and asked to indicate which of the listed items they

TABLE 1. Profile of TMDS-affected Respondents

	Percent	
Characteristic	**Female (N = 1358)**	**Male (N = 153)**
No.	89.9	10.1
Race		
White	95.7	95.3
Black	1.4	1.4
Asian	2.1	2.7
American-Indian	0.8	0.7
Marital status		
Single, never married	28.6	30.1
Married	57.2	56.2
Divorced	11.7	9.2
Widowed	1.0	2.0
Unknown	1.5	2.6
Educational attainment		
Less than high school	0.3	0.0
High-school graduate	20.2	15.7
Some college	61.3	60.8
College degree or higher	18.0	22.9
Employment status		
Employed	68.9	79.2
Age of respondents (y) (as of July 1, 2006)		
< 22	3.2	0.6
22-33	29.9	28.8
34-46	34.7	30.1
46+	32.2	40.5

TABLE 2. Pain Experienced by TMJD-affected Survey Respondents

Characteristic	Female (%)	Male (%)	*P* (Male Versus Female)	Pain Rating Mean (SE)*	
				At TMJ Diagnosis	Now
Age of initial pain (y)					
< 18	35.5	26.8	0.41	6.3 (0.1)	4.5 (0.1)
18-39	53.6	51.0	0.60	6.8 (0.1)	4.4 (0.1)
40 +	10.9	22.3	0.57	6.7 (0.2)	3.2 (0.2)
Time from symptom onset to diagnosis (y)					
Mean (SD)	4.2 (6.3)	4.5 (10.1)	0.43	NA	NA
Median	1	1			
Severity of pain in past 4 wk					
None or mild	37.5	39.8	0.24	6.0 (0.2)	2.6 (0.1)
Moderate	38.0	30.1		7.0 (0.1)	4.6 (0.1)
Severe	24.5	30.1		7.3 (0.2)	6.6 (0.2)
Extent to which pain interfered with work					
Not at all	23.9	21.6	0.87	5.8 (0.2)	2.6 (0.1)
Mildly or moderately	53.3	54.9		6.9 (0.1)	4.2 (0.1)
Very much or extremely	22.8	23.5		7.0 (0.2)	6.5 (0.2)

*On 0-10 scale (0 = none and 10 = worst pain ever).
NA indicates not applicable; TMJD, temporomandibular joint and muscle disorders.

personally believed caused or contributed to their disorder and whether they had been told by their healthcare providers that these were causative. The most frequently identified putative causes listed by respondents were trauma (65%), stress (49%), and teeth clenching (47%). Other less frequently listed factors believed to be causative included arthritis (17%), orthodontics (11%), dental problems (9%), and heredity (9%). For each of the putative causative factors listed, there was close agreement between what the respondents thought and what they were told by their healthcare providers. The exception to this was that 16% of respondents reported that providers had indicated that the causes of TMJD were unknown, but none of the respondents concurred with this assessment.

An important issue in any survey is how the diagnosis of TMJD was obtained. The participants reported that 95.4% of the diagnoses were made by a dentist (73.6%) or medical doctor (21.8 %). Pain was assessed on a 0 = no pain to 10 = worst-pain-ever 11-point scale. Table 2 presents an overview of the sex-specific pain experienced by TMJD-affected individuals and includes the level of pain using this scale. There were no statistically significant sex differences. Approximately 50% of both men and women had onset of TMJD-related pain as young adults (18 to 39 y). Overall, the average age of onset of symptoms was 25 years. One-third of women and one-fourth of men had first experienced pain as children (< 18 y of age). On average, a diagnosis of TMJD was made 4 years after the onset of pain symptoms (median 1 y, 75th percentile 5 y). Eighty percent of the participants reported a pain score of 4 or more initially (mean pain score 6.6) and 53% reported a pain score of 4 or more (mean pain score 4.3) in the last 4 weeks. Fifty-six percent reported severe pain "off and on all day" and 23% indicated that the pain extensively interfered with their work-related activities.

Frequency of Pharmacologic and Surgical Treatments

Table 3 summarizes the TMJD respondents' categories of pharmacologic agents that had been prescribed to address TMJD symptoms and the number of major jaw surgeries that they had undergone. Anti-inflammatory agents had been prescribed to almost three quarters of respondents. Opioids were used by almost one-half of respondents. Both antidepressants and antianxiety medications were prescribed to 50% and 41% of respondents, respectively. A substantial number of respondents (n = 394) reported having undergone major surgeries intended to address TMJD symptoms. Of these, 54% had undergone 1 to 3 surgeries, 30% had 4 to 9 surgeries, and 15% had 10 or more surgical procedures.

Furthermore, these surgical procedures could be classified as those that were less invasive (ie, arthrocentesis and arthroscopy) and those that were more invasive (ie, condylectomy, condylotomy, coronoidectomy, disc plication, eminectomy, and maxillary or mandibular osteotomy). Of the 394 respondents, 54% reported that the less-invasive techniques made them somewhat or significantly better whereas 17% perceived no change and 26% said they were somewhat or significantly worse with these procedures. Of the more invasive procedures, only 32% expressed some improvement and only 6% expressed significant improvement. In contrast, 28% reported no change and 46% considered themselves worse or significantly worse after surgery.

TABLE 3. Frequency of Pharmacologic and Surgical Treatments Reported by TMJD Respondents

Pharmacologic Treatments	No.	Percent (N = 1066)
Anti-inflammatory agents	781	73.3
Nonprescription pain relievers	597	56.0
Antidepressants	538	50.5
Opioids	515	48.3
Antianxiety agents	435	40.8
Muscle relaxants	430	40.3
Number of surgical treatments		Percent (N = 394)
1-3	214	54.3
4-9	119	30.2
10 or more	61	15.5

TMJD indicates temporomandibular joint and muscle disorders.

Effectiveness of Treatments

TMJD-affected respondents were also asked to rate the effectiveness of a wide range of diverse nonsurgical, nonpharmacologic treatments that were recommended, prescribed, or administered by their healthcare providers. Table 4 summarizes these responses by categorizing the therapy according to the frequency of treatment ($\geq 50\%$, 20% to 49%, and $< 20\%$). The effectiveness of a treatment was reported by the respondent as an improvement in symptoms as listed in Table 4 as "percent improved." The most frequently used intervention (65% of respondents) was thermal therapy (hot or cold compresses) to the jaw; these were also found by most respondents (74%) to result in a reduction of symptoms. The second most frequently recommended therapy was jaw exercises (60%), although these were reported to be effective for the relief of symptoms in less than one-half of respondents for whom these were recommended.

Prevalence of Comorbid Conditions

TMJD-affected respondents were asked to identify other conditions that they have experienced and to indicate whether these conditions occurred before or after the onset of TMJD as summarized in Figure 1. The prevalence is categorized as either before-onset or post-onset TMJD. All differences in prevalence were significant at P value less than 0.0001. The prevalence relative risk—the prevalence after divided by the prevalence before—was highest for fibromyalgia (8.8 fold), trigeminal neuralgia (8.0 fold), and swallowing difficulties (6.3 fold); and lowest for migraine headache (3.7 fold), tension headache (2.6 fold), and allergies (1.8 fold).

Figure 2 summarizes the significant differences ($P < 0.001$) in the prevalence of comorbid conditions between the subset of TMJD-affected individuals compared with controls (4:1 matched case-control analysis). Not unexpectedly, TMJD-related pain and joint symptoms were significantly different between cases and controls. However, a number of other conditions occurred significantly more frequently among TMJD-affected individuals, including headaches, allergies, depression, fatigue, degenerative arthritis, fibromyalgia, autoimmune disorders, sleep apnea, and gastrointestinal symptoms. Given the relatively low number of control participants, we sought to validate the prevalence by comparing the prevalence in the controls with the prevalence in the US population. When the questions in the NHANES 2003-2004[14] corresponded to a question we asked, we determined weighted population-based estimates for NHANES participants of the same age and sex. The respective prevalence rates were as follows: tinnitus (26.4% US vs. 10.5% controls); chronic pain (27.2% US vs. 35% controls); severe headaches/migraines (22.3% US vs. 24% controls); and degenerative arthritis (8.6% US vs. 14.0% controls).

The comorbid conditions tended to appear in clusters in the TMJD cases. Among the 9 most prevalent comorbid conditions—migraine, tension headache, depression, degenerative arthritis, chronic fatigue, dizziness, tinnitus, gastrointestinal issues, and allergies—the average number for the cases is 4.5 (SE = 0.2) and the average number for the controls is 1.5 (SE = 0.3). The difference between the cases and the controls increased slightly with age (0.05 comorbid conditions increase per year of age, $P < 0.003$).

TABLE 4. Reported TMJD Treatment Effectiveness by Frequency of Use

Treatment	No.	Percent Treated	Percent Improved
Most frequent treatments ($\geq 50\%$ treated)			
Heat or cold compresses	751	65	74
Flat-plane/stabilizing splint (orthotic)	602	52	56
Jaw exercises	687	60	49
Moderately frequent treatments (20%-49% treated)			
Jacuzzi or hot bath	281	24	71
Trigger point	242	21	62
Relaxation	298	26	61
Posture training	256	22	60
Physical therapy	433	38	60
Chiropractic therapy	380	33	58
Repositioning splint, orthotic	373	32	56
Cortisone injections	231	20	52
Pain management	321	28	50
Stress management	304	26	49
Acupuncture	225	20	48
Electrostimulation	239	21	46
Biofeedback TENS unit	314	27	43
Equilibration	227	20	34
Least frequent treatments ($< 20\%$ treated)			
Yoga	165	14	63
Craniosacral therapy	180	16	60
Marcaine injections	122	11	57
Osteopathic manipulation	93	8	56
NTI appliance	170	15	54
Neural-cranial restructuring	48	4	52
Steroid injections	172	15	49
Botox injections	85	7	48
Passive motion exercises/ device	109	9	48
Acupressure	136	12	48
Light therapy	72	6	42
Aqua flow mouth piece	135	12	41
Elastic mandibular advancement appliance	53	5	38
Magnabloc injections	38	3	37
Saline injections	71	6	37
Bridge work (partial/ fixed/removable)	90	8	36
Psychological therapy	189	16	35
Psychiatric therapy	132	11	34
Radiation therapy	22	2	32
Dentures	44	4	32
Styloid blocks	44	4	32
Teeth crowned	163	14	31
Facial flex	38	3	29
Tooth extraction	172	15	28
Magnetic therapy	85	7	27
Aromatherapy	105	9	27
Root canal	161	14	27
Oxygen therapy	25	22	16
Oral sensor	26	22	8
Others	216	19	70

NTI indicates nociceptive trigeminal inhibition; TENS, transcutaneous electrical nerve stimulation; TMJD, temporomandibular joint and muscle disorders.

DISCUSSION

This study provides an extensive self-reported characterization of the TMJD population together with a

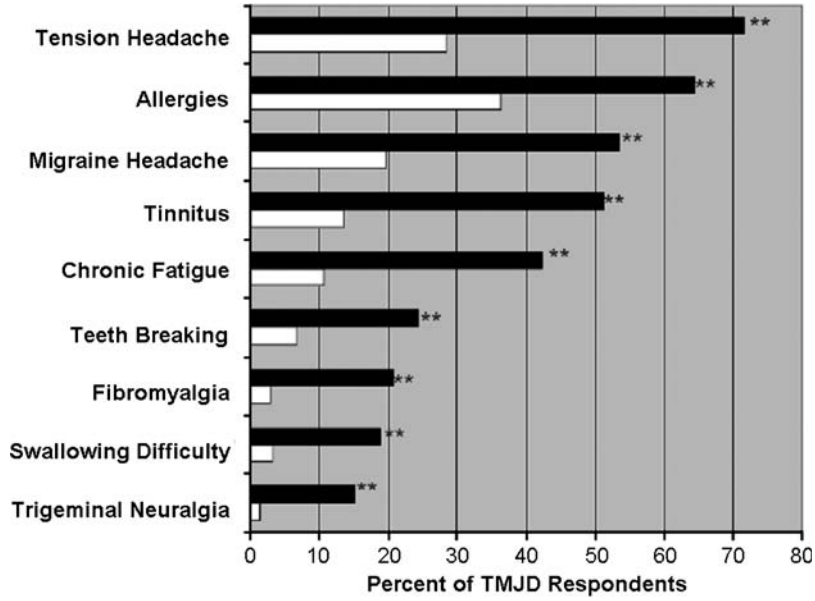

FIGURE 1. Prevalence of comorbid conditions identified by respondents. The prevalence of comorbid conditions that are identified by the survey respondents as existing before (white bar) and before and after (black bar) onset of TMJD are summarized. All comorbid conditions were more prevalent after the onset of TMJD (**$P < 0.0001$). TMJD indicates temporomandibular joint and muscle disorders.

quantitative determination of comorbid conditions and symptoms of affected individuals. We anticipate that this information will be useful to healthcare providers who treat TMJD patients for associated medical conditions.

In the absence of knowledge about pathophysiology, the lack of validated diagnostics and controlled clinical trials on management and treatment of TMJD patients, therapeutic efficacy for TMJD has been defined almost exclusively in terms of symptom relief rather than "cure."[15] Ninety percent of the respondents to this survey were female, and pain was their predominant issue with nearly 20% of respondents having been forced to quit a job or change jobs because of their TMJD-related pain. A remarkable finding of this survey was the wide array

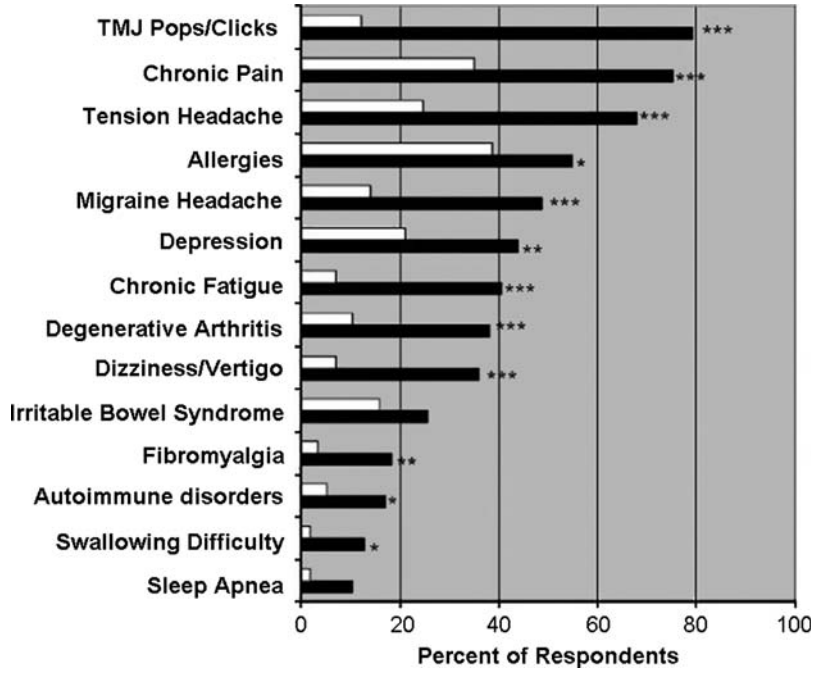

FIGURE 2. Prevalence of comorbid conditions in case-control analysis. In the case-control analysis, the prevalence of comorbid conditions between TMJD-affected individuals (cases; black bar) and the controls (white bar) was found to be significantly greater in the affected individuals (*$P < 0.05$; **$P < 0.01$; and ***$P < 0.001$). TMJ indicates temporomandibular joint.

of treatments reported by these respondents, including nonprescription pain relievers, anti-inflammatory agents, muscle relaxants, narcotic agents, antidepressants, antianxiety medications, and surgery. These treatments were prescribed by multiple healthcare providers including dentists, chiropractors, and physicians.

It is unclear the extent to which TMJD may be a symptom or manifestation of some other underlying disorder. Several comorbid conditions have been anecdotally described earlier in TMJD patients.[16–20] This study represents the first quantitative evaluation of the prevalence of these various conditions. As almost two-thirds of the patients reported 3 or more of the major comorbid conditions, TMJD do not seem to occur in isolation. The most frequent comorbid conditions included fibromyalgia, chronic fatigue syndrome, irritable bowel syndrome, rheumatoid arthritis, chronic headache, depression, and sleep disturbances. Commonly associated comorbidities will surely provide clues about pathophysiology. For example, a relevant finding was the high prevalence of allergies that preceded the TMJD diagnosis suggesting an autoimmune etiology for a subset of TMJD patients. Although comorbid conditions may be reported differentially depending on sex, age, and education, the comparison group was matched to account for this problem. We asked questions about current comorbid conditions and pain status to avoid recall bias. In addition, we asked the respondents to indicate whether a condition occurred before or after the TMJD pain. To address the concern that respondents to our survey were self-selected and not representative, these control participants were compared with a representative sample of the general US population of the same age and sex obtained from the NHANES 2003-2004 survey.[12] The NHANES information on comorbidities was also obtained from the self-reported medical history part of the NHANES study, not the medical examination portion of the NHANES study, so that it would be more comparable with this study. The similarity of the results with this survey adds validity to our conclusions.

Several groups have provided preliminary evidence that patients with chronic fatigue syndrome, fibromyalgia, and TMJD share key symptoms. Maixner and colleagues have conducted prospective clinical studies on the perception of pain[21–23] and various genetic determinants.[24,25] They have found that TMJD might be in part a manifestation of a generalized pain sensitivity syndrome, as is fibromyalgia, irritable bowel syndrome, chronic pelvic pain, and whiplash-associated disorder.[6,7] Several single nucleotide polymorphisms were found to be associated with the perception of pain in these studies. This hypothesis and observations are consistent with the high prevalence of comorbid conditions reported in this manuscript in TMJD patients.

As with most surveys, the present analysis has limitations. It is a self-selected target population with a response rate of 43%; therefore, respondents may not be representative of all TMJD-affected individuals. It is also possible that only the more severely affected patients were motivated to complete the lengthy and comprehensive survey. In addition, the data were self-reported and not obtained from medical or dental records, therefore, there is potential for selective recall bias. Despite these limitations, the survey results suggest a wide spectrum of clinical manifestations associated with TMJD and the array of therapeutic strategies, primarily targeted for symptomatic relief.

It seems that TMJD represent a spectrum of disorders with varying pathophysiologies, clinical manifestations, and associated comorbid conditions. Although potentially limited to the most severe TMJD-affected individuals, the survey results provide a comprehensive dataset describing the clinical manifestations of TMJD as reported by a large number of individuals who have chronic TMJD. The multiplicity of the reported health problems evident from this study strongly suggests that TMJD are not a localized condition but involve system-wide components. This is consistent with recent observations in a prospective cohort study indicating that individuals with TMJD who develop persistent chronic pain and disability also develop significant widespread pain related to fibromyalgia.[26] It is also consistent with observations that catechol-O-methyltransferase gene polymorphisms have been found to be associated with multiple pain-evoked stimuli.[23,24] If so, a multidisciplinary system approach will be necessary to advance our understanding of this complex disease and a major paradigm shift needs to occur in the way TMJD are viewed in the scientific and clinical communities. It is our view that this paradigm shift will be essential if meaningful strategies are to be developed for the more effective diagnosis, treatment, and prevention of these chronic debilitating conditions.

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