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Original Research Article

Relationships Between Temporomandibular Disorders, MSD Conditions, and Mental Health Comorbidities: Findings from the Veterans Musculoskeletal Disorders Cohort

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Abstract

Objective. Temporomandibular disorders (TMDs) have been associated with other chronic painful conditions (e.g., fibromyalgia, headache) and suicide and mood disorders. Here we examined musculoskeletal, painful, and mental health comorbidities in men vs women veterans with TMD (compared with non-TMD musculoskeletal disorders [MSDs] cases), as well as comorbidity patterns within TMD cases. **Design**. Observational cohort. **Setting**. National Veterans Health Administration. **Subjects**. A cohort of 4.1 million veterans having 1+ MSDs, entering the cohort between 2001 and 2011. **Methods**. Chi-square tests, *t* tests, and logistic regression were utilized for cross-sectional analysis. **Results**. Among veterans with any MSD, those with TMD were younger and more likely to be women. The association of TMD with race/ethnicity differed by sex. Odds of TMD were higher in men of Hispanic ethnicity (OR = 1.38, 95% CI = 1.27–1.48) and nonwhite race/ethnicity other than black or Hispanic (OR = 1.29, 95% CI = 1.16–1.45) compared with white men. Odds of TMD were significantly lower for black (OR = 0.54, 95% CI = 0.49–0.60) and Hispanic women (OR = 0.84, 95% CI = 0.73–0.995) relative to white women. Non-MSD comorbidities (e.g., irritable bowel syndrome, mental health, headaches) were significantly associated with TMD in male veterans; their pattern was similar in women. Veterans with back pain, nontraumatic joint disorder, or osteoarthritis had more MSD multimorbidity than those with TMD. **Conclusions**. Complex patterns of comorbidity in TMD cases may indicate different underlying mechanisms of association in subgroups or phenotypes, thereby suggesting multiple targets to improve TMD. Longitudinal comprehensive studies powered to look at sex and racial/ethnic groupings are needed to identify targets to personalize care.

Key words: Temporomandibular Disorders; Comorbidity; Central Sensitization; Painful Conditions; Musculoskeletal Disorders; Headache

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Introduction

Temporomandibular disorders (TMDs), which are craniofacial in nature, have been identified as part of a constellation termed chronic overlapping pain conditions (COPC) [1]. Estimated rates of TMD are 5–12% in adults [2–4]. Epidemiological studies have shown TMD to be more common in women; however, longitudinal data on incident TMD and a recent community survey found no sex differences [4–9]. Women have reported cyclical TMD pain that is highest perimenstrually, suggesting a role for sex hormones [10]. The association of age and TMD-related outcomes has varied across studies [4–9,11]. A u-shaped distribution of TMD pain was reported from a recent community survey of orofacial pain, with peaks in younger (age <25 years) and older (age 55–65 years) persons [4]. This age pattern was previously seen in TMD diagnoses in patients from a tertiary clinic [12]. There were two distinct age peaks in TMD, with the most common TMD diagnosis among persons younger than age 25 years being disc displacement without degenerative disorders, and among older persons inflammatory-degenerative disorders (or arthritis). Racial/ethnic group findings have also been mixed, depending on the included study groups, age range, and specific TMD-related outcomes, with higher TMD prevalence in whites than nonwhites often reported. However, different racial patterns for TMD incidence were observed in a restricted age sample (18–44 years) [9], and another study reported sex–age–race/ethnicity interactions [13].

TMD is a member of chronic overlapping pain conditions (COPCs), as defined by the National Institute of Neurological Disorders and Stroke (NINDS) [1], which are also known to be comorbid with multiple mental health conditions. As examples, TMDs have been associated with fibromyalgia [14], primary headache/migraine [15], neck pain [16], depression and anxiety [17,18], and post-traumatic stress disorder (PTSD) [19–21]. A vital part of this research has been phenotyping or identifying subgroups in order to examine etiology. One of the strongest predictors of first-onset TMD identified in the Orofacial Pain Prospective Evaluation and Risk Assessment Study (OPPERA) was the number of prior comorbid pain conditions [22]. Similarly, using case–control data, 91.5% of TMD cases were identified as pain-sensitive and experiencing global pain symptoms [23].

Chronic pain may be best understood as a "disease" rather than a symptom [24]. Comorbidity among painful conditions has generated a theory of centralized pain sensitization, whereby chronic pain results in hyperalgesia and allodynia [25–28]. A recent review on genetic predictors for musculoskeletal disorders (MSDs) reported elevated cytokines in patients with widespread pain and that persons with TMD had increased levels of pro-inflammatory cytokines, which correlate with greater pain sensitivity, perceived stress, and depression [29]. The OPPERA team has identified and explored clinical, psychological and sensory phenotypes of TMD [30], including intermediate phenotypes for TMD onset [22], which mapped to different patterns of genetic risk factors for TMD [31,32]. The potential use of these risk factors as diagnostic markers is an important step for creating effective treatments [31]. Chronic pain has been described as a classic case of gene–environment interaction [33]. Large observational, neurobiological, and genetic studies are needed to further explore mechanisms underlying COPC.

Fifty-five percent of veterans who used Veterans Health Administration (VHA) services between 2001 and 2011 had at least one musculoskeletal disorder [34]; TMD was one of the 1,700 ICD9 codes used to create the MSD cohort. Vanecek and colleagues found a significant association of TMD and PTSD symptoms in a US military sample [19]. Uhac and colleagues found an association between war stress and TMD in Croatian War veterans [20]. Mottagi and colleagues showed that Iranian veterans with PTSD had significantly poorer TMD functional status than control subjects [21]. These observations, however, may be complicated by the polytrauma triad of traumatic brain injury (TBI), PTSD, and pain commonly observed in Afghanistan and Iraq War veteran VHA users [35]. This paper focuses on comorbidities in men vs women veterans with TMD (compared with non-TMD MSD cases) as well as variation in the comorbidity patterns of TMD cases.

Methods

We used data from the Musculoskeletal Disorder Cohort (MSD) cohort (subset of members with first MSD diagnoses between 2001 and 2011 to ensure follow-up, 4.1 million veterans), which is detailed in depth elsewhere [34]. Briefly, the Musculoskeletal Disorders Cohort Study was created to examine potentially painful conditions, their treatment and cost. VHA electronic health records (EHRs) were searched to identify veterans with ICD9-CM codes for MSD diagnoses as defined by experts (including TMD). Two or more outpatient visits occurring within an 18-month period or one or more inpatient visits with an MSD diagnosis were required to be included in the cohort [36]. Persons with more than one MSD diagnosis were considered to have MSD multimorbidity. Comorbid non-MSD diagnoses were defined in the same manner within 12 months before the first MSD diagnosis date or up to six months after the first MSD diagnosis date. Clinical diagnoses were selected based upon previous literature and conditions common in the VHA. TMD was defined as ICD codes 524.29, 524.6, 524.60, 524.61, 524.62, 524.63, 524.64, and 524.69. The MSD cohort study received local institutional review board approval.

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Table 1. Description of veterans with and without TMD, by sex (proportions)

	Women, %		Men, %	
Variable	TMD (N = 2,844)	Without TMD (N = 250,519)	TMD (N = 9,782)	Without TMD (N = 3,864,843)
Age <25 y	11.0	7.5****	6.6	2.3****
Age 25–34 y	30.6	19.6	15.2	5.8
Age 35–44 y	24.2	19.8	13.3	7.4
Age 45–54 y	20.4	23.6	17.5	15.1
Age 55–64 y	5.7	10.6	20.3	25.4
Age 65–74 y	0.8	3.9	10.2	16.5
Age 75+ y	7.4	15.1	16.9	27.5
White race	62.8	59.3***	66.3	74.3****
Black race	17.0	25.6	15.3	14.4
Hispanic race	6.2	5.3	7.7	4.8
Other race	3.2	2.9	3.3	2.5
Unknown race	10.8	1.8	7.4	4.1
Married	41.2	33.8****	52.6	56.5****
Not married	22.6	22.1	17.4	10.6
Seperated/divorced	32.2	35.8	24.9	24.5
Widowed	2.5	0.6	1.0	0.4
Unknown	1.5	7.8	4.2	8.1
Migraine	15.0	8.3****	3.5	1.1****
Tension headache	0.6	0.2***	0.4	0.1****
Cluster headache	0.00	0.01	0.02	0.01
Headache NOS	8.7	5.1****	6.5	2.2****
Traumatic brain injury	0.8	0.9	2.4	1.2****
Irritable bowel syndrome	3.6	1.8****	1.0	0.4****
Major depression	31.5	27.0****	20.6	15.5****
PTSD	12.8	9.9****	13.6	8.2****
Anxiety disorders	14.3	10.7****	10.0	6.1****
Alcohol use disorder	3.0	3.9*	8.1	7.7
Nonalcohol substance use disorders	2.3	2.5	4.2	3.7**
Nontraumatic joint disorder	11.0	32.7****	9.0	28.0****
Back disorders	11.1	28.5****	8.3	25.9****
Osteoarthritis	4.1	11.6****	3.6	19.9****
Neck pain	5.5	7.1**	3.0	5.2****
Fibromyalgia	2.6	3.0	0.8	1.0*
Traumatic joint disorders	0.8	1.9****	0.9	1.4****
MSD multimorbidity				
TMD vs nontraumatic joint	21.4	31.0	15.6	27.9
TMD vs back disorders	27.8	37.8	21.5	33.2
TMD vs osteoarthritis	27.0	35.7	20.3	25.2

NOS = not otherwise specified; PTSD = post-traumatic stress disorder; TMD = temporomandibular disorder.
**** $P < 0.0001$; *** $P < 0.001$; ** $P < 0.01$; * $P < 0.05$ for significance of difference of TMD and no TMD groups within sex.

TMD Cases

For an in-depth description of the patterns of disorders, comorbidity groupings were created as follows: 1) select MSD conditions: fibromyalgia, nontraumatic joint disorders, traumatic joint disorders, and/or osteoarthritis; 2) select non-MSD conditions: migraine headache, tension headache, headache not otherwise specified, traumatic brain injury, and/or irritable bowel syndrome (IBS); 3) substance use disorders: alcohol and/or nonalcohol substance use disorder; and 4) mental health disorders: major depression, PTSD, and/or anxiety disorders.

Statistical Analyses

Chi-square and *t* tests were used to examine bivariate associations. Multivariable logistic regression was used with TMD as the outcome to model demographic and clinical variables simultaneously (N = 3,874,625; those with any missing variables were dropped from analysis). A priori two-way interactions were tested with sex, race/ethnicity, and/or age based on previous veteran studies. Models were stratified by sex for clarity and parsimony, rather than the inclusion of multiple significant gender interaction terms. Patterns of comorbidity were examined through sex-specific cross-tabulations with chi-square tests within TMD cases.

Results

There are 12,626 persons with TMD in the cohort, which is only 0.31% of the overall MSD sample. Median pain on the day of entry into the MSD cohort was 3/10 for

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persons with TMD (below the VHA cutoff for "actionable pain" on the Numeric Rating Scale which is 4/10). TMD ranked ninth out of 16 MSD diagnostic groupings on cohort baseline pain. The top three individual MSD conditions for those with TMD were the same as for the overall MSD cohort (nontraumatic joint disorder, back pain, and osteoarthritis).

Age, race/ethnicity, and marital status were significantly associated with TMD in men and women with MSD (Table 1). Stratification by sex revealed that both men and women with TMD were younger than those with other MSD. Men with TMD were more likely to be nonwhite, whereas women with TMD were more likely to be white. Women with TMD were more likely to be married, whereas men were less likely to be married. The bivariate odds ratios associated with TMD were largely similar between men and women. All non-MSD and mental health conditions, including other pain conditions, with the exception of cluster headache (in both sexes), and TBI (in women), were significantly associated with higher odds of TMD. With respect to MSD multimorbidity, persons with TMD had lower rates of an additional MSD compared with those with nontraumatic joint disorder (men: 15.6% vs 27.9%; women: 21.4% vs 31.0%), back pain (men: 21.5% vs 33.2%; women: 27.8% vs 37.8%), and osteoarthritis (men: 20.3% vs 25.2%; women: 27.0% vs 35.7%). These differences are likely a function of age, as we observed that persons with TMD were younger.

Multivariable models were likewise stratified by sex (Table 2). Two conditions were excluded: 1) cluster headache due to very low prevalence and 2) TBI due to the inclusion of the headache (a painful condition and common sequelae of TBI). In women veterans, younger age, being married or having unknown marital status, and being white or of unknown race were positively associated with TMD. Black and Hispanic women had significantly lower odds of TMD than whites. Conditions with higher odds of TMD included migraine and headache not otherwise specified (NOS), IBS, and anxiety disorders, whereas major depression, PTSD, tension headache, and nonalcohol substance use disorders were not significantly related with TMD. Alcohol use disorder had significantly lower odds of TMD.

In men, being younger, unmarried or with unknown marital status, and of Hispanic, other, or unknown race were associated with significantly higher odds of TMD (Table 2). Conditions associated with significantly higher odds of TMD were migraine, tension and headache NOS, IBS, major depression, PTSD, and anxiety disorders. Alcohol and nonalcohol substance use disorders were associated with lower odds of TMD.

The stratification of TMD cases by diagnostic groupings was then conducted to examine the diagnostic complexity and burden on TMD patients (Table 3). Prevalence differences in TMD's comorbid disorders were observed as a function of these comorbidity groupings; for example, when a TMD case had another MSD (defined here as fibromyalgia, nontraumatic joint disorder, traumatic joint disorder, or osteoarthritis), lower rates of major depression were observed. When a person with TMD also had an identified non-MSD (defined here as migraine, tension headache, headache NOS, TBI, or IBS) substance use disorder or mental health disorder, increases in their comorbid MSD were observed.

Table 2. Multivariate models: Odds of temporomandibular disorders by sex

	Women Veterans			Men Veterans		
Effect	Estimate	95% CL		Estimate	95% CL	
Age <25 y	2.63	2.18	3.16	3.46	3.14	3.82
Age 25–34 y	2.75	2.34	3.23	3.25	3.01	3.50
Age 35–44 y	2.26	1.92	2.66	2.45	2.27	2.56
Age 45–54 y	1.64	1.39	1.93	1.68	1.56	1.80
Age 55–64 y	1.01	0.82	1.25	1.21	1.13	1.29
Age 65–74 y	0.40	0.26	0.62	1.01	0.93	1.09
Age 75+ y	1.00			1.00		
Black race	0.55	0.49	0.60	1.04	0.99	1.11
Hispanic race	0.84	0.72	0.99	1.37	1.27	1.48
Other race	0.92	0.75	1.14	1.30	1.16	1.45
Unknown race	1.23	1.09	1.40	1.36	1.25	1.45
White race	1.00			1.00		
Not married	0.81	0.74	0.90	1.15	1.08	1.22
Separated/divorced	0.80	0.73	0.88	1.00	0.95	1.05
Widowed	0.48	0.37	0.61	0.77	0.69	0.85
Unknown marital status	1.69	1.23	2.32	2.08	1.69	2.55
Married	1.00			1.00		
Migraine	1.53	1.38	1.71	1.72	1.54	1.93
Tension headache	1.54	0.93	2.55	1.88	1.34	2.63
Headache NOS	1.44	1.26	1.65	1.95	1.79	2.12
IBS	1.67	1.36	2.04	1.84	1.50	2.24
Major depression	1.00	0.88	1.14	1.25	1.15	1.36
PTSD	1.06	0.94	1.20	1.18	1.11	1.26
Anxiety disorders	1.20	1.07	1.34	1.35	1.26	1.45
Alcohol use disorder	0.73	0.57	0.93	0.86	0.79	0.94
Nonalcohol substance use disorders	1.04	0.79	1.37	0.86	0.77	0.97

CL = confidence limit; IBS = irritable bowel disease; NOS = not otherwise specified; PTSD = post-traumatic stress disorder.

Discussion

Our analyses confirm and extend the literature through the findings of independent associations of key mental health and painful non-MSD conditions with TMD in a sample of US veterans who all had at least one musculoskeletal disorder. Our observed sex differences in the association between marriage and chronic pain have previously been reported [37], as well as sex differences in race/ethnicity and health [38]. With respect to race, intersectionality, or the simultaneous identification of persons with multiple groups who experience discrimination (e.g., being a woman and a black American), can impact health and sociodemographic outcomes such as employment [39]. The large proportion of women with TMD who had no information on self-identified race

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Table 3. Prevalence of comorbidities in the overall TMD group and in specific disease clusters (proportion of group with comorbidity)

	Overall TMD Sample (N = 12,626)		Subset With Select MSD (N = 1,779)		Subset With Select Non-MSD (N = 1,786)		Subset With Substance Use Disorders (N = 1,035)		Subset With Psychiatric Disorders (N = 3,054)	
	Women (N = 2,844)	Men (N = 9,782)	Women (N = 477)	Men (N = 1,302)	Women (N = 684)	Men (N = 1,102)	Women (N = 120)	Men (N = 915)	Women (N = 778)	Men (N = 2,276)
MSD										
Any of the 4 conditions	16.77	13.31	N/A	N/A	23.68	17.51	14.17	9.51	18.12	14.28
Fibromyalgia	2.60	0.79	15.51	5.91	4.82	1.72	3.33	1.20	4.63	1.23
Nontraumatic joint	11.01	8.99	65.62	67.51	14.47	13.07	9.17	6.56	10.93	10.98
Traumatic joint	0.98	1.00	5.87	7.53	1.32	1.00	0.00	0.77	1.29	0.66
Osteoarthritis	4.11	3.55	24.53	26.65	6.43	3.72	5.00	1.53	4.24	2.68
Non-MSD										
Any of the 5 conditions	24.05	11.27	33.96	14.82	N/A	N/A	34.17	16.39	34.96	21.70
Migraine	14.98	3.45	21.80	5.30	62.28	30.58	17.50	4.26	21.59	6.46
Tension headache	0.56	0.36	0.42	0.31	2.34	3.18	2.50	0.98	1.29	0.75
Headache NOS	8.72	6.54	10.48	7.22	36.26	58.08	12.50	8.74	12.85	11.95
TBI	0.77	2.42	1.05	4.30	3.22	21.51	2.50	5.03	2.31	6.77
IBS	3.59	1.01	6.71	1.46	14.91	8.98	6.67	1.09	6.04	2.28
Substance use disorder										
Either alcohol and/or drug use disorders*	4.22	9.35	3.56	6.68	5.99	13.61	N/A	N/A	10.80	21.66
Alcohol use disorder	2.99	8.06	2.31	5.68	4.24	11.62	70.83	86.12	7.84	18.45
Drug use disorder	2.32	4.20	2.10	2.53	3.65	7.17	55.00	44.92	5.66	10.28
Psychiatric disorder										
Any of the 3 conditions†	27.36	23.27	29.56	24.96	39.77	44.83	70.00	53.88	N/A	N/A
Major depression	21.62	9.24	9.22	4.76	13.89	12.34	34.17	19.02	37.40	27.68
PTSD	12.83	13.64	13.63	16.90	19.01	30.67	40.00	34.86	46.92	58.61
Anxiety disorder	14.31	10.01	16.56	9.91	22.66	18.24	40.00	22.40	52.31	43.01

IBS = irritable bowel syndrome; MSD = musculoskeletal disorder; NOS = not otherwise specified; PTSD = post-traumatic stress disorder; TBI = traumatic brain injury.

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deserves further exploration. The age range in the MSD cohort was extremely wide (18–100), with robust numbers of the older old. We observed increased odds of TMD in men and women under age 45 years (compared with the 75+ age group), which may include the key TMD diagnoses of disc displacement without degenerative disorders and inflammatory–degenerative disorders, as reported in a key tertiary clinic study on TMD age [12].

Adjusting for the presence of another disorder statistically does not take into account these complex relationships that suggest the addition of three-way or higher interaction terms, which are difficult to interpret. For example, major depression, anxiety disorders, and migraine are highly comorbid [40]; however, this relationship may be confounded by TBI where post-traumatic migraine or headache NOS results [41]. Although these data contain a comprehensive array of MSDs, the final table illustrates that the associations between conditions are highly complex. Increases in comorbid MSD were observed when a person with TMD had an identified non-MSD (e.g., migraine, tension headache, headache NOS, TBI, or IBS) and substance use or mental health disorder.

Raising awareness of TMD and COPC in the general health care community may help facilitate secondary prevention/early intervention efforts such as TMD screening and/or follow-up of TMD patients for the appearance of other pain conditions. Our data point to specific comorbidities that might be used as markers to identify high-risk patients earlier, allow for more conservative treatments, and potentially reduce the probability of additional pain conditions.

This study has several limitations. There is no comparator group without MSD; therefore, caution must be taken in interpretation. Our bivariate analyses for MSD multimorbidity used the three most common MSDs as comparison groups rather than the full cohort. Given the sex and age distribution of our sample, it is not surprising that the overall rate of TMD was low. We believe that unbiased underrepresentation will not impact our findings on TMD associations. Measurement of TMD by ICD9 codes (of conditions addressed during clinical care) rather than diagnostic workups [42] is also a limitation. Although dental care is restricted, all VHA patients have access to primary and specialty pain care, which would allow them to seek treatment for TMD pain. Patients in the VHA have high rates of comorbidities and chronic pain [43], painful and high-impact conditions that may influence reporting or prioritizing of TMD symptoms.

Conclusions

Patterns of clustering of conditions within both men and women with TMD suggest that a comprehensive compendium of MSD, non-MSD, and mental health disorders should be included in studies. Chronic painful conditions likely involve different mechanisms working simultaneously upon each other; therefore, a longitudinal, biopsychosocial approach powered to examine sex and race/ethnic groupings will likely be most fruitful in the creation of effective prevention and treatment scenarios.

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