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The differential impact of neuropathic, musculoskeletal and neurovascular orofacial pain on psychosocial function

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Abstract

Background: While the psychosocial morbidity of orofacial pain (OFP) is widely recognized, the differential impact of musculoskeletal, neuropathic and neurovascular symptoms on pain and psychosocial function in individuals with and without coexisting OFP conditions is unclear.

Materials and methods: This was a comparative cross-sectional study of 350 consecutive patients attending an OFP clinic; 244 completed standardized self-report measures of pain experience, mood, and generic and oral health-related quality of life (HRQoL). The impact of musculoskeletal, neuropathic and neurovascular symptoms on measures was assessed using linear and logistic generalized linear models.

Results: Two hundred patients were diagnosed with a neuropathic condition: 125 with musculoskeletal pain and 101 with (neurovascular) headache disorders. 23% of patients presented with multiple OFP conditions; this was more common in patients with neurovascular (62%) than neuropathic (21%) and/or musculoskeletal orofacial symptoms (28%). Patients with neurovascular symptoms experienced significantly higher levels of pain, evidenced less pain self-efficacy and had poorer overall health. Neuropathic OFP was significantly associated with greater psychological and social oral health disability. Multiple OFP symptoms were not linked to pain severity or psychosocial function, although health scores were worse for patients with neurovascular pain and neuropathic/musculoskeletal symptoms compared with patients with only neurovascular symptoms.

Conclusions: The profile and degree of psychosocial morbidity in patients with OFP is significantly related to the types of presenting orofacial symptoms. Patients with neurovascular pain present with higher pain levels and have poorer health while those with neuropathic pain have higher oral functional morbidity; both may require more complex multidisciplinary management.

KEYWORDS

headache, health-related quality of life, musculoskeletal pain, neuropathic, orofacial pain, psychosocial

1 | INTRODUCTION

Orofacial pain (OFP) is a complex, heterogeneous set of syndromes characterized by presentation of pain in the region of the face and oral cavity, arising from structures innervated by the trigeminal nerve system. Chronic OFP (COFP; ie pain > 3 months) is a common problem, with an estimated prevalence in the United Kingdom of 7%.[1] COFP is often very debilitating, dramatically affecting physical and psychological health, social function and economic well-being of individuals.[2-6]

Broad symptomatic classifications of OFP distinguish between musculoskeletal pain (temporomandibular disorders; TMD)—comprising disorders of the temporomandibular joint (TMJ) and of the musculoskeletal structures (eg masticatory muscles), neuropathic syndromes—which include continuous (eg post-traumatic trigeminal neuropathy; PTTN) and episodic pain conditions (eg trigeminal neuralgia; TN), and neurovascular disorders—such as migraine and other headache disorders.[7] Although most patients referred to OFP clinics present with musculoskeletal pain and/or neuropathic symptoms, neurovascular pain is also frequently encountered.[8] Further, both clinical and population-based studies suggest a high rate of comorbid headache disorders in patients with TMD,[9-11] and to a lesser extent, in those with neuropathic OFP.[8,9,12] This can complicate diagnosis and pose considerable management challenges for treating clinicians.

Studies investigating the psychological burden of COFP and (impaired) health-related quality of life (HRQoL) in affected patients have typically focussed on the effects of specific OFP diagnoses, most obviously TMD[6] and conditions associated with neuropathic pain such as PTTN and TN.[2,13] A limited number of studies have directly compared patients with TMD and orofacial neuropathic pain conditions; these observed comparable psychosocial (dys)function, although sample sizes were small and only included patients with single diagnoses.[4,5] Some studies have reported elevated levels of depression or disability in TMD patients with comorbid migraine or other headache compared with a sole diagnosis of TMD[9,14,15] or neurovascular pain only.[16] However, very little research has considered the differential impact of musculoskeletal, neurovascular and neuropathic symptoms on patient well-being in individuals presenting with one or more OFP symptom type.

The objective of the present study was to assess pain severity and behaviours, psychological and affective function, and oral and generic health in a large sample of OFP patients presenting with individual or combined musculoskeletal, neuropathic and/or neurovascular symptoms.

2 | MATERIAL AND METHODS

2.1 | Design and sample

This was a cross-sectional, clinical study. The study sample was drawn from 350 consecutive patients attending the OFP Clinic at a south London hospital from February 2016-January 2017. Patients were aged 18 years and above, presenting with OFP. The majority of patients (319, 91.1%) were newly referred patients, while 31 (8.9%) had previously been referred to (and attended) the service. Diagnostic and functional data from subsamples of the patient group have been presented elsewhere.[8,13] Informed consent for (anonymized) questionnaire data to be used for research was obtained from all patients and ethical approval for the study provided by the National Research Ethics Service Committee, London Dulwich (No. 15/L0/1108).

2.2 | Clinical examination and diagnosis

Clinical examination of the patients was performed by trained clinicians in OFP with assessment by a neurologist when required. Diagnoses related to neuropathic and neurovascular pain were made according to the International Classification of Headache Disorders-III,[17] while all TMD diagnoses were made using the Diagnostic Criteria for Temporomandibular Disorders.[18] Data for patients were collected prospectively and included sociodemographic information, diagnoses and clinical profile.

2.3 | Measures of pain, psychological function and HRQoL

Patients were asked to provide a 0-10 visual analogue scale (VAS) rating of pain severity at the time of consultation and complete a number of self-report, standardized questionnaires intended to measure affective function and HRQoL at their clinic appointment or electronically via IMPARTS (an initiative funded by King's Health Partners to "integrate mental and physical healthcare in research, training and clinical services").

Anxiety was measured using the 7-item Generalized Anxiety Disorder-7 (GAD-7)[19] scale, a reliable and valid measure of anxiety in primary care, the general population and secondary care, while the 9-item depression module from the Patient Health Questionnaire (PHQ-9),[20] a well validated and widely used screening and severity measure for depressive symptomatology (including suicidal ideation) in primary care and physically ill populations in secondary care, was also employed. On both scales, ordinal frequency response categories for each item (symptom) ranged from 0 ("not at all") to 3 ("nearly every day"), with a total score range of 0-21 for GAD-7 and 0-27 for PHQ-9. IMPARTS patients (n = 41) only completed all questionnaire items if they responded affirmatively to either of the initial two items (ie scored ≥ 2); 24 (GAD-7) and 25 (PHQ-9) patients did not, and as such, their data were not considered in analyses of (continuous) GAD-7 and PHQ-9 scores.

Oral health was assessed with the Oral Health Impact Profile-14 (OHIP-14),[21] a validated 14-item scale that includes seven conceptual dimensions of oral HRQoL. Each item has 5 frequency response categories (ranging from 0 for "never" to 4 for "very often"), and the measure allows for a total summative severity (0-56) and extent scores (number of items with "often" or "very often" responses)

to be calculated as well as summative scores for each dimension. Generic HRQoL was examined using the EQ-5D-5L,[22] a health status questionnaire comprising five domains (mobility, self-care, usual activities, pain/discomfort and anxiety/depression), each measured on a 5-point ordinal scale (ranging from 0 for "no problems" to 4 for "extreme problems"), yielding an overall health state valuation (ranging from −0.285 for "extreme problems in all domains" to 1.000 for "no problems in any domain") derived from an English population-normed value set.[23] Patients also self-rated their "health today" on a 0-100 ("worst health"-to-"best health") vertical (EQ-)VAS.

Patients who reported experiencing OFP at the time of consultation were asked to complete measures gauging pain experience and behaviours. Specifically, the degree of confidence patients has in performing activities across different areas (eg work, leisure) while in pain was assessed with the 10-item Pain Self-Efficacy Questionnaire (PSEQ).[24] Responses were scored on a 7-point ordinal scale ranging from 0 ("not at all confident") to 6 ("completely confident") for each item, with a total score range of 0-60. The 13-item Pain Catastrophizing Scale (PCS)[25] was employed to assess patients' tendency to attend to pain stimuli, overestimate their threat value and underestimate the ability to handle that threat. Items were rated on a 5-point ordinal rating scale ranging from 0 ("not at all") to 4 ("all the time"), yielding a total score ranging from 0 to 52.

2.4 | Data analysis

The relationship of symptom type with demographic and clinical variables and impact on pain-related, psychosocial and HRQoL indicators were calculated using generalized linear models (GLM) with linear or logistic models according to (response) variable of interest; magnitudes of effects were described by (unstandardized) beta (B) values and odds ratios (OR), respectively, with 95% confidence intervals (CI) provided for each. Post hoc tests and tests involving dichotomous dependent variables were administered using chi-square for categorical variables and univariate analysis of (co-)variance (AN(C)OVA) for continuous variables. Where continuous data deviated markedly from a Gaussian distribution, bootstrapping (bias-corrected and accelerated; based on 2000 bootstrap samples) was employed to calculate CI and associated *P* values. To control for possible type I errors due to multiple tests of associations, the false discovery rate (FDR) approach was applied to the set of regression models and (post hoc) tests concerning OHIP-14 subscales, with control set to 5%.[26] Otherwise, the criterion for statistical significance was set at $P < .05$. Statistical analyses were completed with SPSS (IBM, version 25.0).

3 | RESULTS

3.1 | Sociodemographic and clinical data

A little under three-quarters of patients were female with a wide range of ages (18-80 years), averaging just under 50 years old (Table 1). Time since symptom onset varied widely, although almost all (295, 95.2%) had experienced OFP symptoms for 3 months or longer. The mandibular and maxillary divisions were most commonly affected with symptoms lateralized in a little under three-quarters of patients. More than 200 patients (201, 58.8%) presented with neuropathic orofacial symptoms—just over half of these had PTTN, reflecting the speciality of the clinic. Smaller numbers presented with musculoskeletal orofacial symptoms (most receiving a diagnosis of Myalgia or TMJ Disc Displacement with/without reduction) and neurovascular symptoms (most commonly Migraine or Other primary/secondary headache syndromes). Notably, 5 (1.4%) patients had a diagnosis of idiopathic persistent orofacial pain and another 4 (1.1%) had no confirmed diagnosis; these patients were excluded from further analyses.

3.2 | Orofacial pain symptoms

Almost one in four patients (77, 22.5%) presented with more than one (broad) type of orofacial symptom (Figure 1); this occurred more often in patients with neurovascular (63/101, 62.4%) than musculoskeletal (57/125, 45.6%; $P = .001$) or neuropathic pain (42/201, 20.9%; $P = .001$). Forty-three (42.6%) patients with neurovascular pain also had musculoskeletal symptoms, while only 28 (27.7%) had concurrent neuropathic symptoms.

There was no relationship between presence of any one symptom type with gender, time since onset or comorbid (non-pain) medical conditions ($P > .054$), although patients with neuropathic symptoms tended to be older, B = 5.85, CI = 1.50,10.20, $P = .008$, and presence of TMD symptoms was significantly associated with (comorbid) chronic body pain, OR = 2.38, CI = 1.15,4.89, $P = .019$.

Approximately 70% (244, 70.9%) of patients with a diagnosed neuropathic, musculoskeletal and/or neurovascular orofacial condition(s) completed one or more functional measures. Non-completion of questionnaires was due to time constraints in the clinic itself and was not related to age, gender, division affected, symptom laterality or OFP symptom type (Table 1; for all comparisons between completers and non-completers, $P > .115$).

3.3 | Pain severity, psychological function and HRQoL

Psychosocial data for the patient sample are shown in Table 2. More than 70% (176, 72.4%) reported experiencing OFP at the time of consultation, with almost two-thirds of the sample presenting with moderate (101, 43.3%) or severe pain (49, 21.0%). PHQ-9 and GAD-7 scores varied widely, with 29.5% and 18.6% reporting depression and anxiety symptom levels that were moderate or severe (>10), respectively. Mean OHIP-14 severity suggested poor oral health relative to the United Kingdom dentate population, with more than two-thirds of patients (67.2%) scoring above the upper 90th percentile value (17).[27] Physical pain, psychological discomfort (self-conscious, tense)

TABLE 1 Sociodemographic and clinical information for patients attending the orofacial pain clinic. Values represent frequency (percentage) unless otherwise stated

	All (n = 350)	Questionnaire completers (n = 249)
Gender (Female)	256 (73.1)	180 (72.3)
Age (Mean years, (SD))	48.5 (14.1)	49.0 (14.2)
Time since onset (median months (range))	18 (1-420)	18 (1-396)
Site affected		
Ophthalmic division (V1)	64 (18.7)	43 (17.7)
Maxillary division (V2)	136 (39.8)	95 (39.1)
Mandibular division (V3)	157 (45.9)	111 (45.7)
Other (eg pre-auricle)	120 (35.1)	84 (34.6)
More than one site affected	107 (31.3)	71 (29.2)
Symptom laterality		
Left only	129 (38.5)	90 (37.3)
Right only	117 (34.9)	88 (36.5)
Both left and right	89 (26.6)	63 (26.1)
OFP diagnosis		
Neuropathic pain		
Post-traumatic Trigeminal Neuropathy	111 (31.7)	75 (30.1)
Persistent Dento-Alveolar Pain 2	31 (8.9)	24 (9.6)
Spontaneous Neuropathy	20 (5.7)	13 (5.2)
Persistent Dento-Alveolar Pain 1	2 (0.6)	2 (0.8)
Burning Mouth Syndrome	11 (3.1)	9 (3.6)
Trigeminal Neuralgia Classical	16 (4.6)	14 (5.6)
Trigeminal Neuralgia Non-classical	17 (4.9)	11 (4.4)
Occipital Neuralgia	10 (2.9)	8 (3.2)
Geniculate Neuralgia	1 (0.3)	0 (0.0)
Musculoskeletal pain (Temporomandibular Disorders; TMD)		
Pain-related TMD		
Myalgia	69 (19.7)	51 (20.5)
Arthralgia	3 (0.9)	2 (0.8)
Mixed (myalgia and arthralgia)	4 (1.1)	3 (1.2)
TMJ intra-articular disorders		
Disc Displacement with/without Reduction	34 (13.7)	15 (14.9)
Neurovascular pain (Headache Disorders)		
Trigeminal Autonomic Cephalgia		
Unspecified	3 (0.9)	3 (1.2)
Cluster Headache	1 (0.3)	0 (0.0)
SUNCT	4 (1.1)	4 (1.6)
SUNA	1 (0.3)	1 (0.4)
Paroxysmal Hemicrania	2 (0.6)	1 (0.4)
Hemicrania Continua	10 (2.9)	8 (3.2)
Migraine	59 (16.9)	41 (16.5)
Other Primary/Secondary Headaches	45 (12.9)	31 (12.4)
Idiopathic pain		
Persistent Idiopathic Facial Pain	5 (1.4)	3 (1.2)
No diagnosis (or provisional only)	4 (1.1)	3 (1.2)
Other (Bodily) Chronic Pain	75 (25.2)	53 (25.2)
Comorbid Medical Condition(s)	118 (39.6)	89 (42.6)

Note: Age and time since onset data were available for 349 (249) and 310 (223) patients, respectively; data concerning site affected and symptom laterality were available for 342 (239) and 335 (241) patients, respectively; data concerning body pain and comorbid medical condition were available for 298 (210) patients; percentages reflect the proportions from available data only; diagnoses are not mutually exclusive across patients—98 (28.0%) and 71 (28.5%) patients had received more than one diagnosis in the total cohort and questionnaire completer subsample, respectively—as such, percentages in each column do not add up to 100%; TMJ = Temporomandibular Joint; SUNCT = Short-Lasting Unilateral Neuralgiform Headache Attacks with Conjunctival Injection and Tearing; SUNA = Short-Lasting Unilateral Neuralgiform Headache Attacks with Cranial Autonomic Symptoms; Other Primary/Secondary Headaches includes tension-type headache; Co-medical conditions included (but were not limited to) hypertension, diabetes, hypothyroidism, multiple sclerosis, epilepsy, hiatus hernia, cardiovascular disease and/or malignancy.

and psychological disability (difficulty to relax, embarrassment) were the domains most often highlighted by patients. EQ-5D-5L health state valuation scores suggested overall health was compromised in patients in comparison with age-matched healthy UK populations.[23] Patients evidenced significant pain catastrophizing; the group mean markedly higher than that observed in a large nonclinical sample.[25] Self-efficacy for coping with pain was, on average, in the mid-range, although more than a third (37.7%) scored 30 or less, indicating low confidence.

3.4 | Impact of neuropathic, musculoskeletal and/or neurovascular on psychosocial function

The associated risk of reporting experienced orofacial pain at the time of consultation was more than three times greater in patients with neurovascular symptoms (OR = 3.39, CI = 1.46, 7.90), with no significant effect of either neuropathic (P = .574) or musculoskeletal symptoms (P = .727). There were also significant effects of neurovascular symptoms on VAS pain, PSEQ scores and EQ-VAS (Table 3), reflecting higher levels of pain, decreased pain self-efficacy and poorer health, respectively, in those with neurovascular symptoms. By contrast, there were highly significant effects of neuropathic symptoms on OHIP-14 scores, indicative of a greater cost of these symptoms to oral health. Affective function was not related to OFP symptom type, including PHQ-9 suicidal ideation (for all symptom types, P > .350). Significant effects remained after FDR correction and in subsequent (GLM regression) analyses that also controlled for VAS pain, except for neurovascular symptoms on pain self-efficacy (P = .102). Post hoc analyses showed moderate-to-severe levels of VAS pain were significantly more likely in patients with neurovascular symptoms (79.7%) than those without (57.9%; OR = 2.85, CI = 1.47, 5.54, P = .002) and significant differences between patients with and without neuropathic symptoms (after controlling for VAS pain severity) on functional limitation, psychological discomfort, psychological disability, social disability and handicap subscales of the OHIP-14 (Figure 2).

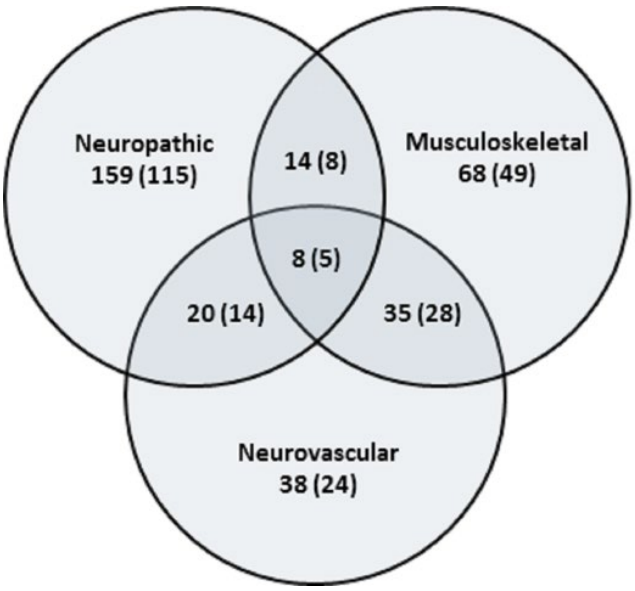

FIGURE 1 Number of patients (completing functional measures in parentheses) with neuropathic, musculoskeletal and/or neurovascular orofacial symptoms (n = 342)

3.5 | Impact of multiple OFP symptoms

There were significant differences between those with and without multiple OFP symptom types for VAS pain (M = 5.70, SD = 2.54 versus M = 4.54, SD = 3.12, P = .007) and EQ-VAS (M = 59.65, SD = 24.87 versus M = 69.51, SD = 22.66, P = .006), with all other measures nonsignificant (P > .138). However, once presence of neurovascular pain was accounted for (Figure 3), the effects of multiple OFP symptom types on VAS pain and EQ-VAS were no longer significant (for both, P > .102). There was also no interaction between neurovascular pain

TABLE 2 Affective function, health-related quality of life (HRQoL) and pain severity and behaviour in patients with orofacial pain

	n	Mean (SD)
VAS pain (0-10)	233	4.81 (3.03)
Mood		
PHQ-9 (0-27)	196	5.25 (6.72)
Suicidal ideation (Item 9; 0-3)	195	0.17 (0.53)
GAD-7 (0-21)	210	6.99 (6.32)
HRQoL measures		
OHIP-14 Severity (0-56)	235	25.25 (15.05)
Functional limitation (0-8)	234	2.41 (2.51)
Physical pain (0-8)	238	5.20 (2.58)
Psychological discomfort (0-8)	233	4.52 (2.84)
Physical disability (0-8)	239	2.91 (2.70)
Psychological disability (0-8)	236	3.78 (2.58)
Social disability (0-8)	237	3.28 (2.76)
Handicap (0-8)	238	3.27 (2.61)
OHIP-14 Extent (0-14)	235	5.09 (4.15)
EQ-Health (−0.285 to 1.00)	234	0.665 (0.276)
EQ-VAS (0-100)	237	67.26 (23.49)
Pain behaviours		
PCS (0-52)	153	23.75 (14.48)
PSEQ (0-60)	162	35.43 (16.43)

Note: n values for questionnaires are variable due to a small number of patients not completing all measures.

VAS Pain = pain severity rating at consultation; PHQ-9 = Patient Health Questionnaire – 9; GAD-7 = Generalized Anxiety Disorder - 7; OHIP-14 = Oral Health Impact Profile-14; EQ-Health = EQ-5D-5L health state evaluation; EQ-VAS = current overall health rating; PCS = Pain Catastrophizing Scale; PSEQ = Pain Self-Efficacy Questionnaire.

TABLE 3 Impact of musculoskeletal, neuropathic and neurovascular symptoms on affective function, HRQoL, and pain severity and behaviour in patients with orofacial pain

	Neuropathic		Musculoskeletal		Neurovascular	
Questionnaire	**B (CI)**	***P***	**B (CI)**	***P***	**B (CI)**	***P***
VAS pain (0-10)	−0.34 (−1.41, 0.74)	.523	0.40 (−0.57, 1.38)	.431	**1.27 (0.41, 2.11)**	**.005**
Mood						
PHQ-9 (0-27)	−1.67 (−4.72, 1.42)	.268	−1.63 (−4.23, 0.94)	.210	0.98 (−1.57, 3.62)	.451
GAD-7 (0-21)	−1.74 (−4.36, 0.88)	.192	0.28 (−2.19, 2.74)	.825	1.50 (−0.55, 3.55)	.152
HRQoL measures						
OHIP-14 Severity (0-56)	**8.24 (2.35, 14.12)**	**.006**	4.11 (−1.38, 9.61)	.143	3.06 (−1.64, 7.77)	.202
OHIP-14 Extent (0-14)	**2.28 (0.66, 3.90)**	**.006**	0.91 (−0.60, 2.43)	.237	0.96 (−0.33, 2.26)	.145
EQ-Health (−0.285 - 1.00)	0.023 (−0.088,0.133)	.689	−0.018 (−0.122, 0.085)	.729	-0.036 (−0.122, 0.051)	.423
EQ-VAS (0-100)	−1.57 (−10.73, 7.59)	.737	−2.51 (−11.11, 6.08)	.566	**−11.81 (−19.01, −4.60)**	**.001**
Pain behaviours						
PCS (0-52)	1.11 (−5.65, 7.75)	.724	1.71 (−4.37, 7.61)	.550	4.03 (−1.58, 9.66)	.160
PSEQ (0-60)	−0.04 (−7.37, 7.30)	.992	−0.51 (−7.38, 6.34)	.883	**−6.77 (−12.79, −0.76)**	**.027**

Note: n values for questionnaires are variable due to a small number of patients not completing all measures; Unstandardized beta values (B) and associated 95% confidence intervals (CI) and *P* values were calculated using generalized linear models (GLM) with presence of neuropathic, musculoskeletal and neurovascular symptoms entered in as independent variables; VAS Pain = pain severity rating at consultation; PHQ-9 = Patient Health Questionnaire – 9; GAD-7 = Generalized Anxiety Disorder - 7; OHIP-14 = Oral Health Impact Profile-14; EQ-Health = EQ-5D-5L health state evaluation; EQ-VAS = current overall health rating; PCS = Pain Catastrophizing Scale; PSEQ = Pain Self-Efficacy Questionnaire; significant effects of symptom type are highlighted in bold.

and multiple symptom types for VAS pain (*P* = .894). A significant interaction between neurovascular pain and multiple OFP symptom types for EQ-VAS was observed (B=−23.95, CI=−44.42,-3.47, *P* = .022); however, reflecting worse reported health for patients with neurovascular pain and (comorbid) neuropathic/musculoskeletal OFP compared with patients with only neurovascular symptoms. Interestingly, after accounting for the presence of TMD pain on (presence of) comorbid body pain (which was highly significant (OR=3 .39, CI =1.68,6.87, *P* = .001)), there was no main effect of multiple OFP symptoms on comorbid body pain nor any significant interaction between TMD and multiple symptom type (for both, *P* > .515).

4 | DISCUSSION

The present study systematically measured HRQoL, psychological function and pain experience in a large sample of patients with (co-existing) musculoskeletal, neuropathic and/or neurovascular OFP. Overall, the study demonstrated a substantial patient burden resulting from OFP. The findings indicate that patients with neurovascular symptoms presented with higher pain levels, had lower health ratings and less pain self-efficacy, while patients with neuropathic pain experienced greater functional, social and psychological oral health disability.

A high proportion of patients attending the clinic presenting with headache disorders had comorbid musculoskeletal OFP, and less frequently, comorbid neuropathic OFP, consistent with the observed interrelations between these disorders. The comorbidity of headache disorders with TMD is particularly well established, a likely consequence of overlapping nociceptive systems, peripheral and central sensitization processes in the trigeminal system common to both, and/or shared genetic risk.[9,11] The relationship between neuropathic OFP and neurovascular symptoms is less well understood, although common pathophysiological mechanisms bridging relevant conditions, such as deregulation of myelination and axonal abnormalities of the trigeminal nerve in TN and migraine, have been proposed.[12]

In line with well-established findings that chronic headache disorders have a substantial impact on mood and HRQoL[3] and previous studies of OFP populations indicating that patients presenting with headache disorders are particularly vulnerable to anxiety and depressive disorders and a high degree of disability,[9,14] we observed a profound impact of neurovascular pain on patient well-being. Interestingly, previous OFP studies have focussed on the differential impact of comorbid TMD and neurovascular pain, reporting significantly greater pain intensity and psychosocial and health impairments than with singular disturbances.[14,15,28] In this study, the presence of neurovascular symptoms in OFP patients was associated with significantly greater pain levels, poorer VAS health ratings and lower self-efficacy to cope with pain relative to TMD or neuropathic pathology—that is, patients with chronic headache disorders had poorer function irrespective of whether they were also diagnosed with TMD or a neuropathic OFP condition. On a clinical level, this highlights the critical relevance of neurovascular pain to the health and functioning of patients presenting in OFP clinics, and, more generally, the importance of specialist neurologists' input in

assessment, diagnosis and management of patients attending OFP clinics as part of a multidisciplinary approach.[8]

Despite clear differences in sensory aspects of their pain, patients with musculoskeletal OFP experienced levels of psychological (dys)function and impaired HRQoL comparable to those with neuropathic OFP, consistent with previous studies.[4,5] A number of oral health domains were more affected by the presence of neuropathic symptoms than by TMD (or neurovascular pain), however, reflecting that aspects of oral HRQoL critically involved with social interactions, such as speech, eating and drinking, are particularly problematic for patients with neuropathic OFP.[13]

Surprisingly, multiple OFP symptoms were a poor predictor of psychosocial function, at least once the presence of neurovascular pain was accounted for. Nevertheless, we found reported health was worse in patients with neurovascular disorders who had comorbid TMD or neuropathic symptoms than those without. It is possible, at least for patients with musculoskeletal pain, that this finding merely reflects the increased severity of (comorbid) disorders as both severity and frequency of headache have been linked with TMD symptoms.[16] However, pain severity at consultation did not differ between neurovascular disorder patients with and without comorbid (musculoskeletal) symptoms and the presence of headache in TMD patients has been shown to dramatically increase the associated risk of depression and high disability even after controlling for severity of TMD,[15] suggesting headache combined with other types of OFP may pose an increased risk of poor health and disability.

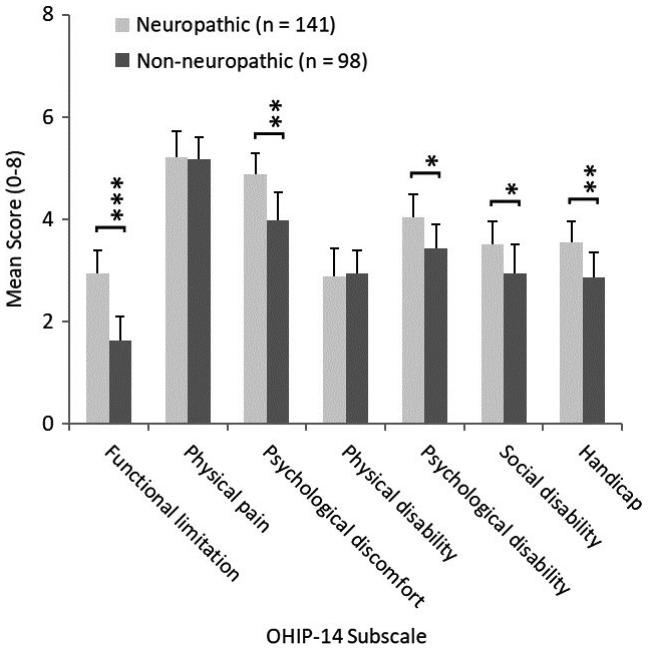

FIGURE 2 Mean scores on OHIP-14 domains for patients with and without neuropathic orofacial symptoms. Error bars represent 95% confidence intervals; n values for subscales are slightly variable due to missing responses on some OHIP-14 items; *Indicates significant differences between groups after controlling for VAS pain severity (*$P < .05$; **$P < .01$; ***$P < .001$)

There was a significant risk of OFP patients with TMD symptoms reporting comorbid chronic body pain. This is consistent with reports that TMD symptoms exhibit significant statistical overlap with other chronic pain conditions.[10] Interestingly, while research has suggested headache in TMD patients is associated with a greater number of bodily pain conditions compared to TMD without headache,[28] we observed no effect of multiple OFP symptoms on body pain in TMD patients. Rather, the presence of (chronic) body pain was more likely in TMD patients irrespective of whether or not they also experienced neurovascular pain, consistent with evidence of dysregulation in central pain pathways in some patients with TMD.[29]

There were some important study limitations. First, while included patients had all been subject to clinical examination and received formal OFP diagnoses, and we did consider pain severity at consultation, we did not consider other indications of severity of symptoms for specific conditions, such as headache frequency/combinations in those with neurovascular pain, which are likely to influence patient-reported outcomes. Second, patients were grouped together by broad symptom-based classifications, each encompassing several conditions with different aetiologies, and within-group differences in measured constructs are likely. For example, differences in HRQoL or psychological distress have been observed between TMD patients with and without combination headaches[16] and between patients with TN and PTTN.[13] Third, the cross-sectional design does not allow causal relationships between OFP disorders and patients' present functioning to be established—this is important considering that psychological dysfunction can increase the risk of OFP,[30] suggesting

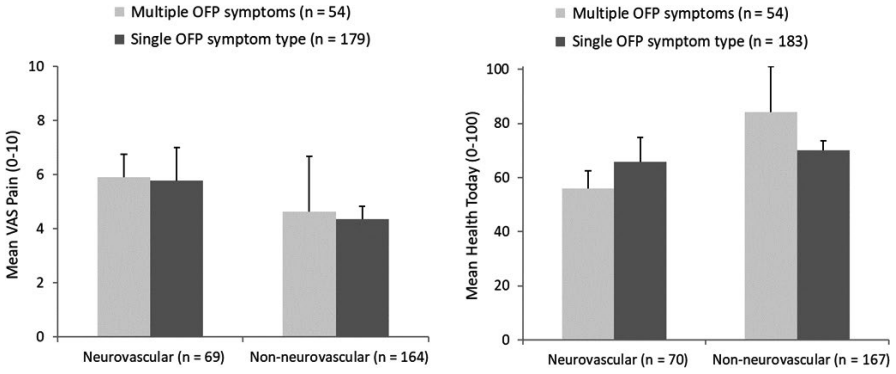

FIGURE 3 Mean VAS pain and EQ-VAS ("health today") scores for patients with and without neurovascular pain according to whether or not they have multiple orofacial symptoms. Error bars represent 95% confidence intervals

a reciprocal relationship. Finally, the sample is unlikely to be reflective of the typical OFP population given the over-representation of patients with neuropathic pain conditions (clinic speciality) and that those individuals seeking treatment are more likely to exhibit psychological dysfunction and greater disability.

In conclusion, this study suggests a substantial burden of chronic OFP in patients attending a tertiary OFP clinic, the extent to which differs according to the presenting class of symptoms, with neurovascular pain the most impactful on pain severity and overall health, and neuropathic symptoms more closely linked with oral health-related functional and psychological impairments. Future prospective studies may establish the extent to which OFP symptom types relate to long-term outcomes of patients, particularly in individuals with complex symptom presentations.

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CONFLICT OF INTEREST

The authors state no conflict of interest.

AUTHOR CONTRIBUTIONS

Tara Renton, **Jared G. Smith** and **Aalia Karamat**: Design of the study. **Aalia Karamat**, **Lydia N. Melek** and **Simone Jayakumar** (IMPARTS): Collection and input of the study data. **Jared G. Smith**: Performing all analyses and writing of the manuscript. Jared G. Smith and **Aalia Karamat**: Data analysis strategy. **Tara Renton**, **Aalia Karamat**, **Lydia N. Melek** and **Simone Jayakumar**: Interpretation of results and write-up of the manuscript. All authors commented on earlier iterations of the manuscript and read and approved the final manuscript.

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