



Psychiatric comorbidities in patients with Atypical Odontalgia

Anna Miura^a, Trang T.H. Tu^{a,*}, Yukiko Shinohara^a, Lou Mikuzuki^a, Kaoru Kawasaki^a, Shiori Sugawara^a, Takayuki Suga^a, Takeshi Watanabe^a, Motoko Watanabe^b, Yojiro Umezaki^c, Tatsuya Yoshikawa^a, Haruhiko Motomura^a, Miho Takenoshita^a, Hidefumi Maeda^d, Akira Toyofuku^a

^a Department of Psychosomatic Dentistry, Graduate school of Medical and Dental Sciences, Tokyo Medical and Dental University, Tokyo, Japan

^b Department of Oral and Maxillofacial Radiology, Tokyo Dental College, Tokyo, Japan

^c Department of Geriatric Dentistry, Fukuoka Dental College, Fukuoka, Japan

^d Department of Endodontology and Operative Dentistry, Faculty of Dental Science, Kyushu University, Fukuoka, Japan.

ARTICLE INFO

Keywords:

Atypical odontalgia
Psychiatric comorbidity
Persistent idiopathic facial pain, orofacial pain
Depression

ABSTRACT

Objective: Atypical Odontalgia (AO) is a condition characterized by tooth pain with no apparent cause. Although psychiatric comorbidity seems to be very common, it has rarely been studied. To clarify the influence of psychiatric comorbidity on the clinical features in patients with AO, we retrospectively evaluated their examination records.

Methods: Clinical features and psychiatric diagnoses of 383 patients with AO were investigated by reviewing patients' medical records and referral letters. Psychiatric diagnoses were categorized according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5). We also analyzed visual analogue scale (VAS), self-rating depression scale (SDS), and the short-form McGill pain questionnaire (SF-MPQ) scores.

Results: Of the 383 patients with AO, 177 (46.2%) had comorbid psychiatric disorders. The most common were depressive disorders (15.4%) and anxiety disorders (10.1%). Serious psychotic disorders such as bipolar disorder (3.0%) and schizophrenia (1.8%) were rare. Dental trigger of AO was reported in 217 (56.7%) patients. There were no significant correlations between psychiatric comorbidities and most of the demographic features. Higher VAS and SDS scores, higher frequency of sleep disturbance, and higher ratings of "Fearful" and "Punishing-cruel" descriptors of the SF-MPQ were found in patients with psychiatric comorbidity.

Conclusions: About half of AO patients had comorbid psychiatric disorders. Dental procedures are not necessarily causative factors of AO. In AO patients with comorbid psychiatric disorders, pain might have a larger emotional component than a sensory one. VAS, SDS, and SF-MPQ scores might aid in the noticing of underlying comorbid psychiatric disorders in AO patients.

1. Introduction

Atypical Odontalgia (AO) is a condition characterized by tooth pain with no apparent cause and hypersensitivity to stimuli in radiographically normal teeth [1,2]. AO is classified as a subtype of atypical facial pain or persistent idiopathic facial pain (PIFP) [3]. Although similar diseases were reported over 200 years ago [4], AO now seems to be considered as a "psychogenic" disorder, because dental procedures often worsen rather than ameliorate symptoms [1,5]. The efficacy of tricyclic antidepressants on AO symptoms was reported approximately 40–50 years ago, and depression was thus regarded as a causative factor [6,7]. Besides depression, latent psychological disturbances (emotional

stress, anxiety or hypochondriac) and somatization have been implicated in orofacial pain, but the detailed etiological mechanisms are still unclear [8,9]. Several pain studies have proposed a new explanation for AO, describing it as a neuropathic syndrome similar to PIFP, which has now become mainstream [1,10,11].

While AO pathophysiology mechanisms are indeed likely to include neuropathic components, the high prevalence of psychiatric comorbidities often makes diagnosis confusing. At the same time, psychiatric comorbidities in patients with AO greatly influence the results of various perceptual examinations and treatments. This represents a significant barrier to the establishment of AO criteria and elucidation of its pathophysiology [8]. Understanding the associated psychological

* Corresponding author at: Department of Psychosomatic Dentistry, Graduate school of Medical and Dental Sciences, Tokyo Medical and Dental University, 1-5-45 Yushima, Bunkyo-ku, Tokyo 113-8510, Japan.

E-mail address: tu.ompm@tmd.ac.jp (T.T.H. Tu).

<https://doi.org/10.1016/j.jpsychores.2017.11.001>

Received 30 August 2017; Received in revised form 24 October 2017; Accepted 3 November 2017

0022-3999/ © 2017 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

factors of AO may thus improve treatment approaches. For example, anti-depressants cannot be prescribed for pain control without psychiatric assessment, especially in bipolar disorder or schizophrenia patients. Nevertheless, there is surprisingly little evidence on the psychiatric comorbidities in patients with AO.

In our daily practice, we receive many AO patients who had psychiatric comorbidities and require psychosomatic pain management. Considering this, combined with the lack of knowledge on psychiatric comorbidities in patients with AO, we performed a retrospective study in our clinic to examine the psychiatric comorbidities of AO and its influences on the clinical manifestations of AO.

2. Methods

2.1. Subjects

We retrospectively analyzed data from 383 patients with localized pain of teeth and/or gingiva and who had been diagnosed with AO according to the PIFP criteria in the International Classification of Headache Disorders (ICHD)-3 beta. The definitive diagnosis was confirmed by the Chief Professor of our clinic. All patients had first been referred to the Psychosomatic Dentistry Clinic in Tokyo Medical and Dental University Hospital, Tokyo, Japan, between January 2013 and August 2016. Inclusion criteria for patients with AO were as follows: over 18 years old, tooth pain for more than six months, or persistent pain after tooth extraction with no abnormal findings of pathology in the clinical or radiographic examination [2,9,10,12,13]. Exclusion criteria were as follows: any topical or systemic causes for the pain, such as odontogenic pain, cluster headache and trigeminal neuralgia [13].

2.2. Ethics approval

All patients agreed to participate in this study and signed a written informed consent. The study protocol was approved by the Ethical Committee of Tokyo Medical and Dental University (D2013-005).

2.3. Clinical characteristics

Clinical characteristics were obtained from the patients' medical charts, including demographic information (sex, age, duration of illness), history of headache, onset event (especially dental treatment), and other comorbid oral psychosomatic disorders. The examiners in this study were all experienced trained clinicians and researchers in psychosomatic dentistry.

2.4. Comorbid psychiatric disorders

Comorbid psychiatric disorders were examined by reviewing referral letters from patients' psychiatrists. All the patients were required to submit referral forms if they had experienced any history of psychiatric disorders. None of the patients had been newly referred to a psychiatrist after confirmative diagnosis of AO. The psychiatric diagnoses in the referral forms were categorized according to The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) [14]. Specifically, patients presenting with any of a few mood/depressive disorders (e.g., major depressive disorder, dysthymic disorder) were categorized as having a "depressive disorders", those with any of a few anxiety disorders (e.g., generalized anxiety disorder, panic disorder) were categorized as having an "anxiety disorders", and those with any of a few bipolar disorders (e.g., bipolar I disorder, bipolar II disorder) were categorized as having a "bipolar and related disorders". Instead of basing diagnoses on structured clinical interview results, we adopted the diagnosis given by the attending psychiatrist who had examined the patient because information that relied only on patient's memories may be lacking in accuracy.

2.5. Depression scale

Depression was clinically accessed using Zung's self-rating depression scale (SDS) [15]. This form contains 20 items (10 symptomatically negative items and 10 symptomatically positive items), each of which is scored from 0 to 4. Patients completed the SDS by themselves and their depressive state was reviewed at the initial examination. Zung's SDS scores are interpreted as follows: < 50, within normal range; 50–59, a tendency for minimal to mild depression; 60–69, a tendency for moderate to severe depression; > 70, a trend towards severe depression [16].

2.6. Sleep disturbance

We evaluated sleep disturbance using our semi-structured interview. Our questionnaire assessed the following: trouble falling asleep or staying asleep, frequently waking up at night several times, and waking up too early in the morning for at least two weeks. We also recorded the use of sleep medicine and patients' sleep history if available. In the present study, instead of recording the patients' sleep disorders in detail, we only focused on determining whether the patients experienced sleep disturbance.

2.7. Pain scale

The characteristics of pain were examined using the short-form McGill pain questionnaire (SF-MPQ) at the initial visit [17]. The SF-MPQ contains 15 descriptors (11 sensory and 4 affective). The 11 sensory descriptors are as follows: throbbing, shooting, stabbing, sharp, cramping, gnawing, hot-burning, aching, heavy, tender, and splitting. The 4 affective are as follows: tiring-exhausting, sickening, fearful, and punishing-cruel. These descriptors are rated on an intensity scale as follows: 0 = none, 1 = mild, 2 = moderate, or 3 = severe.

The SF-MPQ also included the visual analogue scale (VAS) and Present Pain Intensity (PPI) test. The severity of pain was evaluated with the VAS, on which 0 represents no pain and 100 represents the worst pain ever experienced, by asking patients to mark where on the VAS they considered their pain to be. The PPI score measures six degrees of pain intensity using a 1–5 intensity scale, whereby 0 = no pain, 1 = mild, 2 = discomforting, 3 = distressing, 4 = horrible, and 5 = excruciating. (Range: 0–5).

2.8. Pain regions

Pain regions were examined by reviewing patients' medical charts. The oral cavity was divided into eight regions in this study, and included the maxillary posterior tooth, maxillary anterior tooth, mandibular posterior tooth, and mandibular anterior tooth (right and left sides for all regions). When pain regions overlapped, we marked this as pain present in both regions. All eight regions were marked as pain regions in patients that complained of entire intraoral pain.

2.9. Statistical analysis

Data were analyzed using Mann-Whitney *U* tests and Chi-square tests using PASW for Windows version 17.0. (SPSS, Inc., Chicago, IL). Results are expressed as the mean (\pm standard deviation, SD) or the number of patients (%). A *p* value of < 0.05 was considered as statistically significant.

3. Results

3.1. Clinical characteristics of patients with AO

In total, 383 patients with AO were recruited (325 female and 58 male; age range of 18 to 86 years, Table 1). The mean age of AO onset

Table 1
Clinical manifestations of Atypical Odontalgia (AO)

Variables		n = 383	
Sex (male/female)		58/325	
Age, mean(SD), in years		53.62 (13.81)	
Duration of AO, median (interquartile range), in months		24 (3–360)	
SDS ^a , mean(SD)		45.40 (10.35)	
VAS ^b , mean(SD)		53.08 (29.61)	
A history of headache	Absent	168 (43.9)	
	Present	215 (56.1)	
AO triggered by dental procedures	Absent	166 (43.3)	
	Present	217 (56.7)	
	Root canal treatment	55 (14.4)	
	Extraction	47 (12.3)	
	Prosthesis treatment	46 (12.0)	
	Resin filling/Inlay	24 (6.3)	
	Receiving dental implant	19 (4.9)	
	Occlusal adjustment	8 (2.1)	
	Periodontal treatment	7 (1.8)	
	Orthodontic treatment	6 (1.6)	
	Tooth whitening	3 (0.8)	
	Hypersensitivity treatment	1 (0.2)	
	Osteoplasty	1 (0.2)	
Comorbid oral psychosomatic disorders (%)	Absent	272 (71.0)	
	Present	111 (29.0)	
	(multiple answers included)	83 (21.7)	
	Burning mouth syndrome	20 (5.2)	
	Phantom bite syndrome	18 (4.7)	
	Temporomandibular joint disorder	3 (0.8)	
	Halitophobia	2 (0.7)	
Comorbid psychiatric disorders (%)	Absent	206 (53.8)	
	Present	177 (46.2)	
	(multiple answers included)		Hospitalization experiences
	Depressive disorders	59 (15.4)	8 (2.1)
	Anxiety disorders	39 (10.1)	0 (0)
	Somatic symptom and related disorders	17 (4.5)	0 (0)
	Bipolar and related disorders	12 (3)	5 (1.3)
	Insomnia disorder	11 (2.8)	0 (0)
	Schizophrenia	7 (1.8)	1 (0.2)
	Obsessive-compulsive and related disorders	4 (1.0)	1 (0.2) ^c
	Eating disorder	2 (0.5)	1 (0.2) ^c
	Borderline Personality Disorder	2 (0.5)	0 (0)
	Trauma and Stressor-Related Disorders	1 (0.2)	0 (0)
	Diagnosis is unspecified	32 (8.4)	0 (0)

Values are presented as frequency (%) unless specified.

^a Zung Self-rating Depression Scale.

^b Visual Analog Scale.

^c Overlapped.

was 53.62 ± 13.81 years. The median duration of AO was 24.0 months (interquartile range 3–360).

Regarding the pain and depression assessments, the average SDS score and VAS score at the initial visit was 45.40 ± 10.35 and 53.08 ± 29.61, respectively. Of the 383 patients with AO, 244 (63.7%) were within the normal SDS score range. A history of headache was observed in 215 (56.1%) patients. Dental trigger of AO was reported in 217 (56.7%) patients; 55 patients (14.4%) developed AO after root canal treatment, 47 (12.3%) after tooth extraction, and 46 (12.0%) after prosthesis treatment. In addition, 111 (29.0%) patients complained of oral psychosomatic disorders other than AO, the most common of which was Burning Mouth Syndrome (BMS) (83/383; 21.7%).

The classification of psychiatric comorbidities in patients with AO is shown in Table 1. Psychiatric disorders comorbidities were present in 177 (46.2%) patients. Of these, the most common psychiatric disorders were depression in 59 patients (15.4%), anxiety disorders in 39 (10.1%), somatic symptom disorders in 17 (4.5%), and insomnia

disorders in 11 (2.8%). Obsessive-compulsive disorders were observed in 4 patients (1.0%), eating disorders in 2 (0.5%), and trauma and stressor-related disorder in 1 (0.2%). Two (0.5%) patients were diagnosed with borderline personality disorder. Diagnosis was unspecified in 32 patients (8.4%). Psychotic disorders such as bipolar disorder (12 patients, 3%) and schizophrenia (7 patients, 1.8%) were rare. Fifteen patients (3.9%) had experienced hospitalization.

Of 177 patients with psychiatric comorbidities, 8 patients (4.5%) had multiple psychiatric diagnosis. In addition to major depressive disorder, generalized anxiety disorder were observed in 4 patients, somatic symptom disorder in 1 and schizophrenia in 1. One patients had both obsessive-compulsive disorder and anorexia nervosa. We also observed one patient had depressive disorder, generalized anxiety disorder and somatic symptom disorder. It should be noted that, at the initial visit, some patients might have had an undiagnosed or untreated mental illness. However, during the subsequent assessment and follow-up period, we did not detect new disorders that required referral to a psychiatrist in any of the patients.

Table 2
Distribution of pain location in Atypical Odontalgia patients.

Maxillary right		Maxillary left	
Molars	139(36.2) ^a	Anterior teeth	92(24.0)
	137(35.7)		62(16.1)
Molars		Anterior teeth	
			155(40.5)
			Molars
Mandibular right		Mandibular left	

^a Values are presented as frequency (%). Include overlapped.

3.2. Pain regions

Based on the reported complaints of patients with AO, we counted the incidence and number of painful regions. Localized pain was observed in 167 patients (43.6%), and 216 (56.4%) had pain in multiple regions. It is noteworthy that 30 patients (7.8%) had pain in the entire intraoral region. A total of 95 patients (24.8%) had pain on the right side, 137 (35.8%) had pain on the left side, and 151 (39.4%) had bilateral pain. Pain was more frequent in the molars than in the anterior teeth, but was more poorly localized and was often spread among several teeth or to other areas of the oral cavity (Table 2).

We also investigated the relationship between the treated regions and the painful regions (Table 3). Of the 217 patients with AO triggered by dental procedures, 132 patients (60.8%) had painful regions that matched with treated regions, 63 (29.0%) had pain matched with both treated regions and other areas, and 22 (10.2%) had pain at entirely different places from treated regions.

Furthermore, we compared the rate of consistency between painful regions and treated regions between patients with and without psychiatric comorbidities (Table 3). Ninety-two (42.4%) patients with dental-triggered AO had comorbid psychiatric disorders, and 125 (57.6%) patients with dental-triggered AO without comorbid psychiatric disorders. Psychiatric comorbidity was observed without significant difference regardless of matching between the pain regions and treated regions.

3.3. Associations between AO patients with and without psychiatric comorbidities, patient characteristics, and SF-MPQ results

As shown in Table 4, we compared clinical characteristics and SF-MPQ scores between patients with psychiatric comorbidities (n = 177) and without psychiatric comorbidities (n = 206). The mean SDS score and incidence of sleep disturbance in patients with psychiatric comorbidities were significantly higher than that in patients without psychiatric comorbidities (both, $p < 0.001$).

Similarly, comparing SF-MPQ scores between these two groups revealed that mean scores of “Fearful” and “Punishing-cruel” items and the VAS results were significantly higher in those with psychiatric comorbidities than in those without psychiatric comorbidities ($p = 0.004$, 0.005, and 0.045, respectively). Both “Fearful” and “Punishing-cruel”

were classified as affective descriptors; there were no between-group differences in the mean scores of sensory descriptors.

4. Discussion

This was an extensive retrospective study of patients with AO. Clinical characteristics of patients AO were fairly consistent with previous studies, in which female patients were found comprise the overwhelming majority [18]. Our findings help clarify the characteristics of AO and comorbid psychiatric disorders, as well as what measures may be useful for confirming these comorbidities. First, we found that 46.2% of patients with AO had a comorbid psychiatric disorder, of which the most common were depression and anxiety disorders. Very few patients had more serious mental illness such as bipolar disorder and schizophrenia. Second, patients with comorbid psychiatric disorders had higher self-rated depression, physical pain, sleep disturbance, and higher affective descriptors (fearful and punishing-cruel). Third, there were no differences between the patients with and without comorbid psychiatric disorders in terms of age, duration of AO, sex, history of headache, and the coincidence rate between the treated regions and painful regions in this study. The treated regions did not always match with the painful regions, regardless of psychiatric history.

4.1. Psychiatric comorbidities in Patients with AO

AO is classified as a subtype of PIFP [3], and has been widely referred to as “phantom toothache” [1,10,11]. Because of lack of knowledge of etiological and pathophysiological mechanisms, many researchers have debated the taxonomy of PIFP and related disorders such as trigeminal neuralgia, temporomandibular joint disorder, BMS, and AO [19–21]. Some studies have suggested that PIFP is closely associated with psychiatric disorders [21–23]. A background of depressive illness was observed in the majority of PIFP patients [6] and the facial pain in patients with somatoform pain disorder was regarded as atypical facial pain [23]. Although changes in psychological functioning are common in AO and PIFP, there is insufficient evidence to support the claim that psychological factors are the primary cause [24]. However, it is increasingly evident that chronic medical conditions are associated with higher rates of psychiatric disorders [25,26].

It remains difficult to diagnose psychiatric disorders because of the

Table 3
Consistency of painful and treated regions in Atypical Odontalgia patients.

Treated regions	Maxillary right				Maxillary left			
	Molars		Anterior teeth		Molars		Anterior teeth	
	Total	Psychiatric comorbidity	Total	Psychiatric comorbidity	Total	Psychiatric comorbidity	Total	Psychiatric comorbidity
Matched (%)	43(19.8)	14(6.4)	25(11.5)	12(5.5)	31(14.2)	16(7.3)	60(27.6)	21(9.6)
Unmatched (%)	28(12.9)	15(6.9)	25(11.5)	8(3.6)	20(9.2)	7(3.2)	32(14.7)	17(7.8)
Matched (%)	46(21.1)	18(8.2)	11(5.0)	4(1.8)	15(6.9)	5(2.3)	56(25.8)	18(8.2)
Unmatched (%)	21(9.6)	11(5.0)	7(3.2)	2(0.9)	11(5.0)	4(1.8)	29(13.3)	10(4.6)
	Mandibular right				Mandibular left			
	Molars		Anterior teeth		Molars		Anterior teeth	

lack of any established biological marker. Taiminen et al. [27] precisely observed the associations between idiopathic oral pain and psychiatric disorders; their study used semi-structured interviews (Structured Clinical Interview for DSM IV - SCID). In contrast, we adopted the diagnosis made by a psychiatrist who had previously examined the patient, which may be a limitation of the present study.

In our study, 46.2% of AO patients had comorbid psychiatric disorders. This prevalence rate is lower than that reported by Takenoshita et al. [18], who found that only 33.3% of AO patients had no specific psychiatric diagnoses. However, they only recruited patients who had an official referral form from a psychiatrist, which is different from the recruitment procedure in the current study. Additionally, there were fewer AO patients with serious comorbid psychiatric disorders such as schizophrenia (1.8%), bipolar disorder (3.0%), and borderline personality disorder (0.5%), compared to those with depressive disorders (15.4%) and anxiety disorders (10.1%). Considering that tricyclic antidepressants cannot be used in patients with schizophrenia or bipolar disorder, these findings are very important for us to provide more sufficient medications for AO patients [28].

4.2. Notice underlying psychiatric comorbidities

In our study, the patients with psychiatric comorbidities showed a higher proportion of sleep disturbance, higher self-rated depression, and higher self-reported affective descriptors (fearful and punishing-cruel). While there were no significant differences between AO patients with/without psychiatric disorders in sensory descriptors of the SF-MPQ, scores for the affective descriptors “Fearful” and “Punishing-cruel” were significantly higher in patients with comorbid psychiatric disorders. This suggests that, in AO patients with comorbid psychiatric disorders, pain might have a larger emotional component than a sensory one.

Additionally, the mean VAS score was also significantly higher in patients with psychiatric disorders, which indicates a greater self-reported pain severity, but there was no significant difference in self-reported pain intensity (PPI scores). While the reason behind these seemingly conflicting results is hard to explain, patients may find it easier to express the degree of pain on visual measure than via linguistic expression.

These above results suggest that the SDS, VAS, sleep disturbance, and rating of affective descriptors of the SF-MPQ may be helpful in noticing comorbid psychiatric disorders. These findings may help

Table 4
Clinical characteristics and Short Form –McGill Pain Questionnaires (SF-MPQ) scores of Atypical Odontalgia (AO) patients with and without psychiatric comorbidities.

	With psychiatric comorbidity (n = 177)	Without psychiatric comorbidity (n = 206)	p value
Age, mean(SD), in years	53.52(13.90)	53.71(13.77)	0.84
Duration of illness, median (interquartile range), in months	26.0(3-360)	24.0(3-360)	0.38
SDS, mean(SD)	47.78(9.85)	43.6(10.99)	< 0.01
Sex (female)	151	174	0.81
A history of headache	102	113	0.58
Sleep disturbance	118	70	< 0.01
AO triggered by dental treatment	92	125	0.087
Pain located in the treated regions	56	76	
Pain in the treated area and another regions	25	38	0.69
Pain area different from the treated regions	11	11	
SF-MPQ descriptors			
Sensory			
Throbbing, mean(SD)	0.99(1.07)	0.96(1.08)	0.72
Shooting, mean(SD)	0.46(0.82)	0.41(0.77)	0.47
Stabbing, mean(SD)	0.54(0.90)	0.54(0.92)	0.79
Sharp, mean(SD)	0.83(1.10)	0.64(0.97)	0.098
Cramping, mean(SD)	0.97(1.13)	0.87(1.05)	0.49
Gnawing, mean(SD)	0.66(0.98)	0.58(0.93)	0.48
Hot-burning, mean(SD)	0.47(0.94)	0.42(0.84)	0.97
Aching, mean(SD)	1.28(1.03)	1.12(1.09)	0.098
Heavy, mean(SD)	1.15(1.14)	1.07(1.03)	0.62
Tender, mean(SD)	0.9(1.03)	0.84(1.02)	0.54
Splitting, mean(SD)	0.23(0.67)	0.25(0.72)	0.92
Affective			
Tiring-exhausting, mean(SD)	1.5(1.20)	1.32(1.13)	0.15
Sickening, mean(SD)	1.17(1.12)	0.98(1.08)	0.088
Fearful, mean(SD)	0.74(1.07)	0.46(0.89)	0.004
Punishing-cruel, mean(SD)	0.93(1.18)	0.62(1.04)	0.005
VAS, mean(SD)	56.5(31.34)	49.85(27.59)	0.045
PPI, mean(SD)	2.56(1.34)	2.50(1.26)	0.67

SD: Standard Deviation.

clinicians provide the appropriate care required by AO patients with comorbid psychiatric disorders. About half of the patients in this study had psychiatric comorbidities suggests that psychological therapy may be beneficial in patients with AO. The optimum treatment strategy for patients thus might require a combination of medication and psychological therapy.

One of the most interesting findings of our study was the distribution of pain regions. One previous study reported that 13% of PIFP patients had bilateral pain [29]. The author concluded that the high prevalence of bilateral pain indicated that PIFP was distinct from trigeminal neuralgia, as neurovascular compression was not associated with PIFP. In our study, however, 95 patients (24.8%) had pain on the right side, 137 (35.8%) had pain on the left side, and 151 (39.4%) had bilateral pain, bilateral pain was more common than reported in previous study. This result suggests that a difference of pathophysiology might exist between AO and PIFP. Further, psychiatric comorbidities may have some influence on AO; this suggests that there might be a difference in pain mechanisms between AO and PIFP.

Dental procedures are still considered to be triggers of AO now, and nerve damage such as that induced by endodontic treatments or tooth extraction has been associated with the onset of permanent neuropathic facial pain [30]. Dental interventions such as tooth extraction or root canal treatments are common invasive procedures that may pose the risk of neuropathy secondary to direct or indirect neuronal trauma [31–33]. However, our results indicated that dental procedures are not necessarily causative factors of AO (root canal treatments 14.4% and tooth extraction 12.3%), regardless of psychiatric comorbidities.

There were several limitations to this study that should be noted. First, sample data were collected at a single particular facility, which might be different from a general dental setting. Second, we included only AO patients and so were unable to directly compare results to patients with pain other than AO. Future research might find more useful clinical results when by comparing AO with “typical” tooth pain, such as pulpitis. Third, the psychiatric diagnoses might have varied among the attending psychiatrists, and in some patients with multiple disorders, only the primary psychiatric diagnosis (or the present one) was reported in the referral letter. Indeed, every psychiatric assessment has its own weakness.

In conclusion, about half of the patients with AO had a comorbid psychiatric disorder in our study. However, only 5% of the patients had serious psychiatric disorders. Clinicians should pay attention to the VAS, SDS, and SF-MPQ scores, as these might contain information about underlying comorbid psychiatric disorders in patients with AO. Future research should aim to investigate other comorbid oral psychosomatic disorders, treatment responses, and objective indicators such as brain functional imaging in patients with AO, especially as a function of psychopathology.

Conflicts of interest

The authors declare no conflicts of interest.

Acknowledgments

This study was supported in part by Japan Society for the Promotion of Science (JSPS) KAKENHI, Grant Number 16K11881.

References

- [1] M. Melis, S.L. Lobo, C. Ceneviz, K. Zawawi, E. AL-Badawi, G. Maloney, N. Mehta, Atypical Odontalgia: a review of the literature, *Headache* 43 (10) (2003) 1060–1074.
- [2] L. Baad-Hansen, Atypical odontalgia - pathophysiology and clinical management, *J. Oral Rehabil.* 35 (1) (2008) 1–11.
- [3] Headache Classification Committee of the International Headache Society (IHS), The international classification of headache disorders, *Cephalalgia*, 3rd Edition, 33(9) 2013, pp. 629–808 (beta version).
- [4] Hunter J, Comb W. The Natural History of the Human Teeth, 2nd ed. J Johnson 1778; p.370–377.
- [5] D.C. Wilson, Atypical facial neuralgia, *JAMA* 99 (10) (1932) 813–817.
- [6] R.G. Lascelles, Atypical facial pain and depression, *Br. J. Psychiatry* 112 (1966) 651–659.
- [7] J.J. Gayford, The aetiology of atypical facial pain and its relation to prognosis and treatment, *Br. J. Oral Surg.* 7 (1970) 202–207.
- [8] M. Harris, Psychogenic aspects of facial pain, *Br. Dent. J.* 136 (5) (1974) 199–202.
- [9] T. List, G. Leijon, M. Helkimo, A. Oster, S.F. Dworkin, P. Svensson, Clinical findings and psychosocial factors in patients with atypical odontalgia: a case-control study, *J. Orofac. Pain* 21 (2) (2007) 89–98.
- [10] L. Baad-Hansen, T. List, H. Kaube, T.S. Jensen, P. Svensson, Blink reflexes in patients with atypical odontalgia and matched healthy controls, *Exp. Brain Res.* 172 (2006) 498–506.
- [11] E.R. Vickers, M.J. Cousins, Neuropathic orofacial pain part 1: prevalence and pathophysiology, *Aust. Endod. J.* 26 (1) (2000) 19–26.
- [12] M. Melis, S. Secchi, Diagnosis and treatment of atypical odontalgia: a review of the literature and two case reports, *J. Contemp. Dent. Pract.* 8 (3) (2007) 81–89.
- [13] L. Baad-Hansen, M. Pigg, S.E. Ivanovic, H. Faris, T. List, M. Drangsholt, P. Svensson, Intraoral somatosensory abnormalities in patients with atypical odontalgia—a controlled multicenter quantitative sensory testing study, *Pain* 154 (8) (2013) 1287–1294.
- [14] Diagnostic and Statistical Manual of Mental Disorders, 5th Edition, DSM–5. American Psychiatric Association 2013;31–715.
- [15] W.K.A. Zung, Self-rating depression scale, *Arch. Gen. Psychiatry* 12 (1) (1965) 63–70.
- [16] K. Fukuda, S. Kobayashi, A study on a self-rating depression scale, *Seishin Shinkeigaku Zasshi (Article in Japanese)* 75 (10) (1973) 673–679.
- [17] R. Melzack, The short-form McGill pain questionnaire, *Pain* 30 (1987) 191–197.
- [18] M. Takenoshita, T. Sato, Y. Kato, A. Katagiri, T. Yoshikawa, Y. Sato, E. Matsushima, Y. Sasaki, A. Toyofuku, Psychiatric diagnoses in patients with burning mouth syndrome and atypical odontalgia referred from psychiatric to dental facilities, *Neuropsychiatr. Dis. Treat.* 6 (2010) 699–705.
- [19] H. Forsell, S.K. Jaaskelainen, T. List, P. Svensson, L. Baad-Hansen, An update on pathophysiological mechanisms related to idiopathic orofacial pain conditions with implications for management, *Oral Rehabil.* 42 (2015) 300–322.
- [20] A. Woda, S. Tubert-Jeannin, D. Bouhassira, N. Attal, B. Fleiter, J.P. Goulet, C. Gremau-Richard, M.L. Navez, P. Picard, P. Pionchon, E. Albuissou, Towards a new taxonomy of idiopathic orofacial pain, *Pain* 116 (2005) 396–406.
- [21] H. Merskey, N. Bogduk, Classification of Chronic Pain, Descriptions of Chronic Pain Syndromes and Definitions of Pain Terms, IASP Press, 1994, pp. 59–60.
- [22] C. Feinmann, M. Harris, R. Cawley, Psychogenic facial pain: presentation and treatment, *Br. Med. J.* 288 (1984) 436–438.
- [23] K.J. Burchiel, A new classification for facial pain, *Neurosurgery* 53 (5) (2003) 1164–1166.
- [24] S.B. Graff-Radford, W.K. Solberg, Is atypical odontalgia a psychological problem? *Oral Surg. Oral Med. Oral Pathol.* 75 (5) (1993) 579–582.
- [25] B. Wells, Psychiatric disorder in a sample of the general population with and without chronic medical conditions, *Am. J. Psychiatry* 145 (1988) 976–981.
- [26] S.F. Lerman, Z. Rundich, S. Brill, H. Shalev, G. Shahar, Longitudinal associations between depression, anxiety, pain, and pain-related disability in chronic pain patients, *Psychosom. Med.* 77 (3) (2015) 333–341.
- [27] T. Taiminen, L. Kuusalo, L. Lehtinen, H. Forsell, N. Hagelberg, O. Tenovu, S. Luutonen, A. Pertovaara, S. Jaaskelainen, Psychiatric (axis I) and personality (axis II) disorders in patients with burning mouth syndrome or atypical facial pain, *Scand J Pain* 2 (4) (2011) 155–160.
- [28] K. Oshima, T. Ishii, Y. Ogura, Y. Aoyama, I. katsumi, Clinical investigation of patients who develop neuropathic tooth pain after endodontic procedures, *J. Endod.* 35 (7) (2009) 958–961.
- [29] S. Maarbjerg, F. Wolfram, T.B. Heinskou, P. Roach, A. Gozalov, J. Brennum, J. Olesen, L. Bendtsen, Persistent idiopathic facial pain – a prospective systematic study of clinical characteristics and neuroanatomical findings at 3.0 tesla MRI, *Cephalalgia* 0 (0) (2016) 1–10.
- [30] M.E. Lynch, A.K. Elgeneidy, The role of sympathetic activity in neuropathic orofacial pain, *J. Orofac. Pain* 10 (4) (1996) 297–305.
- [31] W.K. Lobb, K.L. Zakariassen, P.J. McGrath, Endodontic treatment outcomes: do patients perceive problems? *J. Am. Dent. Assoc.* 127 (1996) 597–600.
- [32] D.R. Nixdorf, A.S. Law, K. Lindquist, G.J. Reams, E. Cole, K. Kanter, R.H. Nguyen, D.R. Harris, Frequency, impact, and predictors of persistent pain after root canal treatment: a national dental PBRN study, *Pain* 157 (2016) 159–165.
- [33] N. Polycarpou, Y.L. Ng, D. Canavan, D.R. Moles, K. Gulabivala, Prevalence of persistent pain after endodontic treatment and factors affecting its occurrence in cases with complete radiographic healing, *Int. Endod. J.* 38 (3) (2005) 169–178.