Comorbidity Between Facial Pain, Widespread Pain, and Depressive Symptoms in Young Adults

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Aims: *To assess, firstly, the prevalence of facial pain associated with widespread pain and the prevalence of high levels of depressive symptoms (ie, "depressiveness") among subjects with this pain condition, and secondly, the association between depressiveness and a facial pain condition.* ***Methods:*** *This study forms part of the Northern Finland Birth Cohort study. The original material consisted of all people whose expected birthdate was in 1966 in Northern Finland. Of these, 5,696 participated in a follow-up study at the age of 31. As part of it, data on facial pain, pain in other areas of the body, depressiveness (measured using the Symptom Checklist-25 depression subscale) and sociodemographic background data were gathered using questionnaires. Prevalence proportion ratios were estimated using log-binomial regression models.* ***Results:*** *Facial pain and simultaneous widespread pain were reported by 8.3% of the subjects (6.6% of men and 9.9% of women), and 27.4% of those with widespread pain were depressive. Comorbidity between facial pain, widespread pain, and depressiveness was found to be particularly prevalent among women.* ***Conclusion:*** *Comorbidity should be taken into account in clinical practice. A multidisciplinary approach is needed, especially for patients with complex pain conditions.* J OROFAC PAIN 2006;20:24–30

Key words: facial pain, depression, widespread pain

Facial pain is a common symptom, causing significant discomfort, suffering, and even psychosocial morbidity.[1] The etiology and pathology of facial pain vary and are somewhat controversial.[2,3] Epidemiologic[4,5] and clinical[6,7] studies have shown that facial pain is related to pain conditions in different parts of the body. Earlier, in an epidemiologic study of the Northern Finland Birth Cohort,[8] which consisted of 5,696 31-year-old adults, Rauhala et al found that 12% of men and 18% of women reported experiencing facial pain in the past year, and that this pain was associated with pain in distinct parts of the body (ie, neck and occiput, shoulders, arms or elbows, lower back)[5] as well as with high levels of depressive symptoms (ie, "depressiveness").[9] However, comorbidity between facial pain, widespread pain, and depressiveness was not studied.

It has been shown that chronic pain conditions and depressive disorders have some pathophysiologic characteristics in common.[10] It is therefore understandable that an association has been found between depression and facial pain in several clinical[11–15] and epidemiologic studies.[4,9,16–18] It has been suggested that facial

pain as part of a widespread pain condition in particular is associated with depression,[16,19] which makes diagnosis and treatment of facial pain complicated. In the diagnosis and treatment of facial pain, it is important to recognize comorbidity between facial pain conditions, widespread pain, and depressiveness, as well as to be aware of how prevalent this comorbidity is at the population level. It has been shown that psychological distress and widespread body pain predict persistent facial pain,[20] which may respond more poorly to treatment than localized pain. Because facial pain is prevalent especially among young adults,[21] it is important to define the prevalence of facial pain conditions that are linked with widespread pain among this age group as well as the prevalence of depressiveness in these pain conditions.

The aim of the present study was to assess *(1)* the prevalence of facial pain associated with widespread pain and the prevalence of depressiveness (ie, high levels of depressive symptoms) among subjects with this pain condition, and *(2)* the association between depressiveness and a facial pain condition.

Materials and Methods

This study is part of the Northern Finland Birth Cohort 1966 study. The original sample was collected from a geographically defined area, the 2 northernmost provinces of Finland. It consisted of an unselected, general population-based birth cohort of 12,058 live births, whose expected date of delivery was in 1966, representing 96.3% of all such births.[8] In 1997, the members of the cohort were sent a postal questionnaire (n = 11,541). The number of eligible replies was 8,690, and the response rate was 75.3%. Those who lived in Northern Finland or in the Helsinki area were invited to a clinical examination (n = 8,463). Data were obtained from 5,696 subjects, representing 67.3% of those who were invited to the clinical examination. The subjects answered a computer-aided questionnaire, which included the following topics:

1. Facial pain. Subjects were asked, "Have you had any pain or ache in the face during the last year?" A yes-or-no response was required; those who responded "yes" were asked to describe the frequency of the pain as "now and then," "quite often," or "constantly."
2. Pain in other areas. Subjects were asked, "Have you had any pain or ache during the last year in the following parts of the body: neck/occiput, shoulders, arms/elbows, wrists/hands/fingers, chest, hips, thighs, knees/calves, ankles/feet, lower back?" For each question, the respondent was asked to answer no or yes (now and then/quite often/often or constantly). Wide-spread pain was defined according to screening criteria established by White et al[22] with some modifications. Subjects who reported pain involving at least 1 upper extremity, 1 lower extremity, and either the neck, back, or chest were assessed to be suffering from widespread pain.

Information about depressiveness and sociodemographic background (marital status, educational level, and self-rated general health) were obtained through the postal questionnaire. Depressiveness was measured using the Symptom Checklist-25 (SCL-25),[23] which is a 25-item shortened version of a 90-item questionnaire designed by Derogatis et al.[24] The SCL-25 has also been used in the Nordic countries in a large population study.[25] A depression subscale containing 13 questions was used in this study. Subjects recorded their own estimates of the severity of their symptoms on a scale of 1 (not at all) to 4 (very much). The responses were summed and divided by the number of answers. A score of 1.75 or more indicated depressiveness.[26,27] For the analyses, marital status was dichotomized as single or married/cohabiting. Self-rated general health was dichotomized as good (very good/good/moderate) or poor (poor/very poor). Education was classified into 4 categories: education in university or in institutions of higher education, vocational education, comprehensive school only, and other.

Statistical Analyses

Since both marital status and education were significantly associated with depressiveness, they were included in the multivariate models as covariates. Because this was a cross-sectional study, the prevalence proportion ratio (PPR), which is the ratio of 2 proportions at the time of the study, was used. Interpretation is similar to relative risk, ie, PPR > 1 indicates increased "risk"; PPR < 1, decreased "risk." Prevalence proportion ratios with 95% confidence intervals (CI) were estimated by applying a generalized linear model where the distribution of the outcome variable was binomial and the link function was a log (log-binomial model).[28] The statistical analyses were performed using the SAS GENMOD procedure, version 8.02.[29]

Table 1 Factors Related to Reported Facial Pain Calculated with PPR and 95% CI

		Prevalence of facial pain*			
	n	n	%	PPR	95% CI
Gender					
Male†	2,681	326	12.2	1.00	
Female	2,962	531	17.9	1.47	1.30–1.68
Depressiveness					
No†	4,850	655	13.5	1.00	
Yes	764	200	26.2	1.94	1.68–2.22
Widespread pain					
No†	3,800	387	10.2	1.00	
Yes	1,837	469	25.5	2.51	2.22–2.83
Self-reported health					
Good†	5,438	808	14.9	1.00	
Poor	168	45	26.8	1.81	1.37–2.30
Marital status					
Married/cohabiting†	4,064	588	14.5	1.00	
Single	1,548	267	17.3	1.19	1.04–1.36
Education					
Tertiary education	2,505	354	14.1	1.00	0.86–1.16
Secondary education	648	114	17.6	1.23	1.00–1.51
Vocational education†	1,708	242	14.2	1.00	
Other	730	140	19.2	1.35	1.12–1.63

* The total number varies between different variables because of missing data.
† Reference category.

Results

Factors associated with reported facial pain are presented in Table 1. Almost one third of the cohort members had widespread pain. Facial pain and simultaneous widespread pain was reported by 8.3% of the subjects (6.6% of men and 9.9% of women) (Table 2). Patients with widespread pain accounted for 55% of all facial pain cases (54% among men, 55% among women).

As measured with the SCL-25 depression subscale, 23.4% of all subjects with facial pain and 27.4% of all subjects with facial pain and simultaneously widespread pain were depressive. The prevalence of depressiveness among those with facial pain was higher among women than among men. Overall, 17.3% of men with facial pain and 18.9% of men with facial pain and comorbid widespread pain were depressive. The corresponding figures for women were 27.1% and 32.4%, respectively (Table 3).

A multivariate analysis was performed to control for the effects of potential confounders. After adjustment for education and marital status, depressiveness was associated with facial pain (PPR 1.51, 95% CI 1.31–1.74) and with widespread pain (PPR 2.37, 95% CI 2.09–2.69). Among women with widespread pain, depressiveness was associated with facial pain (PPR 1.48, 95% CI 1.21–1.80). Among men with widespread pain, depressiveness was not significantly associated with facial pain.

Discussion

The sample, which consisted of an unselected general population-based birth cohort, made it possible to estimate the prevalence of depressiveness and self-reported facial pain without selection bias related to care-seeking behavior. The response rate for computer-aided questionnaire was acceptable. The study population comprised about half of he original cohort. This is due to the fact that only those living in Northern Finland or in the Helsinki area were invited to the medical examination which included the questionnaire. The sample was homogenous concerning age and place of residence. Further, the gender distribution of the respondents (47.5% men/52.5% women) approximated that of persons who were sent the postal questionnaire (50.7% men/49.3% women). No

Table 2 Prevalence of Facial Pain and Widespread Pain Conditions in Subjects with or without Depression

	All subjects		Depression*			
			No		Yes	
	n	%	n	%	n	%
Prevalence of facial pain						
All	857	15.2	655	13.5	200	26.2
Men	326	12.2	268	11.3	56	19.6
Women	531	17.9	387	15.7	144	30.1
Prevalence of widespread pain						
All	1,841	32.6	357	46.8	1,477	30.4
Men	882	32.9	129	45.3	750	31.5
Women	959	32.4	228	47.7	727	29.4
Prevalence of facial pain with widespread pain						
All	469	8.3	340	7.0	128	16.8
Men	176	6.6	142	6.0	33	11.6
Women	293	9.9	198	8.0	95	19.9
Prevalence of facial pain without widespread pain						
All	387	6.9	315	6.5	71	9.3
Men	150	5.6	126	5.3	23	8.1
Women	237	8.0	189	7.7	48	10.0

* The total number varies between different variables because of missing data.

Table 3 Prevalence of Depressiveness in Subjects with or without Widespread Pain

	All subjects		Widespread pain*			
			No		Yes	
	n	%	n	%	n	%
Total cohort						
All	764	13.6	406	10.7	357	19.5
Men	285	10.7	156	8.7	129	14.7
Women	479	16.3	250	12.5	228	23.9
Subjects with facial pain						
All	200	23.4	71	18.4	128	27.4
Men	56	17.3	23	15.4	33	18.9
Women	144	27.1	48	20.3	95	32.4
Subjects without facial pain						
All	564	11.9	335	9.9	229	16.8
Men	229	9.8	133	8.1	96	13.7
Women	335	13.9	202	11.5	133	20.2

* The total number varies between different variables because of missing data.

other demographic data were available for comparing responders and nonresponders. Thus it is possible that the sample is not representative of the original cohort, and this represents a limitation of the study. One strength of this study of a large sample is the opportunity to study both somatic and psychological problems simultaneously.

An important finding of this study was that more than half of the subjects with facial pain also experienced comorbid widespread pain. These findings support an earlier study in which single associations of facial pain were found with pain in other areas as well as with depressiveness.[5,9] The results of the present study are in agreement with previous clinical studies that show an overlap between different facial pain conditions and widespread pain. Hagberg et al,[6] using a questionnaire, found that female patients with TMD had an increased risk for musculoskeletal pain in various parts of the body, such as the neck, shoulders, thoracic back, wrists/hands, and knees, compared with women in a population sample. Similarly, Turp et al,[7] found that 66% of female facial pain patients also reported pain extending outside of the head and face.

Another finding was that the prevalence of depressiveness was about 30% among subjects with facial pain and simultaneous widespread pain. The prevalences of depression and pain in the present study are in line with results from other large population studies. It should be kept in mind that prevalences based on questionnaires are usually clearly higher than those obtained by interviews or clinical examination. The corresponding levels of depressiveness, measured with the SCL-25 depression subscale, are in the same range as those found in a large Nordic multicenter investigation.[23]

Comorbidity between facial pain, widespread pain, and depressiveness was more prevalent among women than men. The role of depressiveness in facial pain conditions as part of widespread pain has been noted in several studies with patient samples. Differences between studies exist, partly caused by the criteria used to define widespread pain. Raphael and colleagues[19] found that women with myofascial face pain and a history of widespread pain were more likely to have a history of major depression compared with women with myofascial face pain but no widespread pain. Using an interview, they found that nearly one fourth of myofascial pain patients also indicated a history of fibromyalgia. In a study by Yap et al,[30] 16% of the 202 TMD patients studied responded positively to more than 3 pain items. They observed significant correlations between the number of pain items endorsed and depression (measured using the SCL-90). The percentage of subjects who reported 3 or more pain items in the Yap et al study was approximately 1.8 times higher than that observed in a study by Dworkin et al[16] (9.2%). Based on the depression score scale, 39% of the patients were moderately or severely depressed. In a study by Velly et al,[31] a cluster analysis was used to classify 162 subjects with TMD into subgroups of localized and generalized disorder; the latter disorder was found to relate to depression.

An epidemiologic study found multiple chronic pain symptoms to be associated with depression.[16] The overlap between chronic pain symptoms and depression may reflect a shared underlying pathophysiologic basis. Depressive disorders are chronic conditions that produce both emotional and physical symptoms. Increasing evidence suggests that a neurodegenerative process may occur in some patients with depressive disorders. Serotonin and norepinephrine neurotransmitter systems influence neuroplasticity in the brain,[32] and a dysfunction in these systems can affect both the ascending and descending pathways, resulting in symptoms of depression but also in painful physical symptoms.[33] Additionally, a possible explanation is disregulation of the main hormone system, the hypothalamic-pituitary-adrenal (HPA) axis, which has a wide range of central and peripheral functions.[34,35] High levels of cortisol, indicating HPA hyperactivity, have been noted in cases of depression and facial pain[35,36] as well as fibromyalgia.[37,38] Thus, individuals who have an underlying abnormality of the stress hormone response resulting in high cortisol levels may be prone to overlapping symptoms of facial pain, generalized pain, and depression.[35] Furthermore, it has been noted that individual differences in responses to psychologic and environmental challenges may be related to genetic polymorphisms.[39,40] These findings may also explain the observed comorbidity.

In this study, the proportion of facial pain subjects with widespread pain was about the same among men and women (54% versus 55%). These results are not in line with studies that have shown more prominent gender differences. In an epidemiologic study by Bassols et al[41] of 1,964 subjects, women reported pain in more locations than did men (a mean of 3.4 in women versus 2.7 in men). The gender differences are even more prominent in patient samples compared to population samples.[6] In studies with patient samples, the gender differences may be, at least partly, due to differences in care-seeking behavior. In the present study, the

prevalence of depressiveness was 2 times higher in subjects with facial pain with comorbid widespread pain compared to the total cohort. Comorbidity between widespread pain conditions and depressiveness among women could be explained by biological mechanisms. It has been demonstrated in both animal and human studies of the pathophysiology of pain and depression[42] that females are more susceptible than males to stress-induced HPA axis disregulation.

The limitations of the present study included the cross-sectional study design, which does not allow for causal inferences concerning the relationship between depression and pain. Additional research is needed to address this issue. Further, the data on pain and depressiveness were based on questionnaires. It should be noted that information given by this method, used for practical reasons because of the large sample size, is not as reliable as data from in-person interviews or clinical examinations.

Facial pain is not a manifestation of 1 particular disorder but rather a symptom related to different disorders. Despite the multifactorial etiology of facial pain, the earlier epidemiologic study with the same subjects[5] as well as the clinical study performed with a subsample of this cohort[43] stress the importance of TMD symptoms in the background of the facial pain. In Sipilä et al's earlier case-control study[43] with 52 facial pain cases and 52 pain-free controls assessed clinically, 71% of the facial pain cases and 29% of the controls had moderate or severe TMD. The association between TMD and facial pain was significant. Confounding due to other pain conditions, such as those of dental origin, could be an alternative explanation to the findings. Unfortunately, in the present study, it was not possible to differentiate facial pain according to its origin, which is a limitation of the study. It is likely that diagnostic misclassification may have attenuated the association between facial pain symptoms and widespread pain.

The present study showed that half of facial pain conditions among young adults were part of a more widespread pain. More than one quarter of the subjects with facial pain and widespread pain were also depressive. In clinical practice, a multidisciplinary approach is needed, especially for patients with complex pain conditions.

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