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Association Between Subjective Tinnitus and Cervical Spine or Temporomandibular Disorders: A Systematic Review

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Abstract

Movements of the neck and jaw may modulate the loudness and pitch of tinnitus. The aim of the present study was to systematically analyze the strength of associations between subjective tinnitus, cervical spine disorders (CSD), and temporomandibular disorders (TMD). A systematic literature search of the *Medline*, *Embase*, and *Pedro* databases was carried out on articles published up to September 2017. This covered studies in which tinnitus and CSD or TMD were studied as a primary or a secondary outcome and in which outcomes were compared with a control group. Included articles were evaluated on nine methodological quality criteria. Associations between tinnitus and CSD or TMD were expressed as odds ratios. In total, 2,139 articles were identified, of which 24 studies met the inclusion criteria. Twice, two studies were based on the same data set; consequently, 22 studies were included in the meta-analysis. Methodological quality was generally limited by a lack of blinding, comparability of groups, and nonvalidated instruments for assessing CSD. Results indicated that patients with tinnitus more frequently reported CSD than subjects without tinnitus. The odds ratio was 2.6 (95% CI [1.1, 6.4]). For TMD, a bidirectional association with tinnitus was found; odds ratios ranged from 2.3 (95%CI [1.5, 3.6]) for arthrogenous TMD to 6.7 (95%CI [2.4, 18.8]) for unspecified TMD. Funnel plots suggested a publication bias. After adjusting for this, the odds ratios decreased, but associations persisted. There is weak evidence for an association between subjective tinnitus and CSD and a bidirectional association between tinnitus and TMD.

Keywords

subjective tinnitus, systematic review, neck pain, temporomandibular disorder

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Introduction

Tinnitus is a sound that is perceived in the absence of an acoustic event occurring external to the listener's body. It is commonly described as the sound of, for example, crickets, winds, falling tap water, grinding steel, escaping steam sound, or as a combination of sounds (Han, Lee, Kim, Lim, & Shin, 2009). Tinnitus can be perceived in one ear, both ears, or more centrally located ''in the head'' (Heller, 2003). In adults of the general population, the prevalence of tinnitus ranges between 10% and 15% (D. Baguley, McFerran, & Hall, 2013). In people older than 60 years of age, the prevalence of tinnitus increases to about 18% (Davis & El Rafaie, 2000).

In a minority of people with tinnitus, the sound is audible to an observer and is therefore called *objective tinnitus*. In most of these patients, it is possible to determine the underlying etiology. However, in the vast majority of tinnitus sufferers, the sound is audible only to the patient and is called *subjective tinnitus* (Ward, Vella, Hoare, & Hall, 2015).

Numerous studies suggest that subjective tinnitus arises in the central auditory system due to neuroplastic adaptations that occur in response to changes in the

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peripheral auditory system (Eggermont & Roberts, 2004; Kaltenbach, 2011; Moller, 2007; Norena & Farley, 2013; Roberts et al., 2010). Animal studies indicate that peripheral damage, for example, noise trauma, results in changes in spontaneous neural activity (Eggermont, 2005). The central auditory system is thought to compensate for the reduced input by upregulating the excitability of the central auditory neurons (Eggermont & Roberts, 2012; Knipper, Van Dijk, Nunes, Ruttiger, & Zimmermann, 2013; Tyler, 1984).

Two thirds of patients may experience modulations to their subjective tinnitus through somatosensory system effects in addition to those associated with central auditory neurons. These patients are able to modulate the loudness and pitch by muscle contractions of the neck, head, or jaw (Bjorne, 2007; Bonaconsa, Mazzoli, Magnano, Milanesi, & Babighian, 2010; Levine, 1999; Pinchoff, Burkard, Salvi, Coad, & Lockwood, 1998; Rocha & Sanchez, 2007; Rubinstein, 1993; Sanchez, Yupanque Guerra, Lorenzi, Brandao, & Bento, 2002; Vernon, Griest, & Press, 1992). To indicate this type of tinnitus, the term *somatosensory tinnitus* has been proposed (Levine, Abel, & Cheng, 2003). Moreover, cervical spine disorders (CSD; e.g., pain, tenderness; Abel & Levine, 2004; Bjorne, 2007; Folmer & Griest, 2003; Michiels, De Hertogh, Truijen, & Van de Heyning, 2015; Oostendorp et al., 2016; Reisshauer et al., 2006; Sahin, Karatas, Ozkaya, Cakmak, & Berker, 2008) or temporomandibular disorders (TMD; Ramirez, Ballesteros, & Sandoval, 2008) are frequently associated with tinnitus. However, in most of these studies, the prevalence data are not compared with a control group, and the strength of the association between tinnitus and CSD or TMD remains unclear.

To the best of our knowledge, a systematic review of studies on the association between subjective tinnitus and CSD or TMD has not yet been carried out. As movements of the neck and jaw may increase or decrease the loudness and pitch of tinnitus, understanding the association between tinnitus and CSD or TMD is important because in the future, treatment of CSD or TMD might be used to reduce tinnitus. The aim of the present study was to systematically analyze the level of evidence for a bidirectional association between subjective tinnitus and symptoms of CSD or TMD.

Methods

Identification and Selection of Studies

A database search was performed in Medline, Embase, and Pedro to identify articles published within the time period of 1966 to September 2017. The following search terms were used: Tinnitus and (Temporomandibular Joint or Jaw or Cervical Vertebrae or Neck Muscles or Facial Muscles or Neck Pain or Masticatory Muscles or Musculoskeletal or Trigger point or ((Head or Jaw or Neck or Shoulder) and (Muscle or Pain or Trauma or injuries))) (Appendix 1: electronic search strategy).

Titles and abstracts were assessed for their relevance by the first author (E. J. B.). In the next round, selected full-text articles were retrieved and their relevance independently assessed by two observers (E. J. B. and P. D.). Interobserver agreements were expressed as Cohen's kappa. Inclusion criteria were a *cross-sectional* or *longitudinal cohort* design in which tinnitus and CSD or TMD were treated as either primary or secondary outcomes and that this group was compared with a control group. Exclusion criteria were reviews, letters to the editor, animal studies, number of patients <10, and articles describing neck or jaw disorders caused by a trauma. The term *trauma* was used as part of the search strategy to avoid missing possibly relevant articles. No language restrictions were applied. In case the authors were not able to understand an article for language reasons, it was translated. References of the studies included were checked for relevant studies that had been missed in the database searches.

Assessment of Characteristics of Studies

The methodological quality of the studies included was independently judged by two observers (E.J. B. and E. A. K.) according to nine criteria of a modified version of *Quality Assessment of Case-Control Studies* (2014). The criteria were (1) "Was the research question or objective in this article clearly stated and appropriate?" (2) "Was the study population clearly specified and defined?" (3) "Were controls selected or recruited from the same or similar population that gave rise to the patients (including the same timeframe)?" (4) "Were the definitions and inclusion and exclusion criteria used to identify or select patients and controls valid, reliable, and implemented consistently across all study participants?" (5) "Were the patients clearly defined and differentiated from controls?" (6) "Were the patients and controls randomly selected?" (7) "Were controls matched to patients on one or more attributes?" (8) "Were the measures of exposure clearly defined, valid, reliable, and implemented consistently across all study participants?" and (9) "Were the assessors blinded to the patient or control status of participants?" Criteria were scored: [+] = Yes, [–] = No, [?] = Cannot be determined/unclear/ not reported. Each quality item addresses a different source of potential bias and can impact study results disproportionately. If, for example, only one quality item is not fulfilled, it does not mean that the study has a better quality than a study with two quality items not fulfilled. Therefore, the results of methodological quality assessment will be described per item, without summing across items (see Table 2).

Data Synthesis and Analysis

Data were entered in the program Comprehensive Meta-Analysis V3 (Biostat, Englewood, NJ, USA). If odds ratios were provided in the original article, then they were entered into the database. When odds ratios were not reported, the data were entered into the database as they were reported in the article (Borenstein, Hedges, Higgins, & Rothstein, 2009). Meta-analyses were performed assuming a random-effects model. The summary statistic of the association between tinnitus and CSD or TMD was expressed as odds ratios. To explore publication bias for each association, funnel plots were made. To adjust for potential publication bias, Duval and Tweedie's (2000) nonparametric trim-and-fill approach to impute theoretical missing studies was applied.

Results

Search Strategy and Study Selection

A total of 2,139 records were found: in PubMed, 1,069; in Embase, 1,053; and in Pedro, 17. After removing duplicates, 1,581 articles remained. In 1,517 of these, the association between tinnitus and CSD or TMD had not been studied. Two observers assessed the full text of 64 articles, of which 24 met the inclusion criteria. Interobserver agreement expressed as Cohen's kappa was 0.70 (absolute agreement: 86%). Two of these articles, Saldanha, Hilgenberg, Pinto, and Conti (2012) and Chole and Parker (1992) were based on the same data set as Hilgenberg, Saldanha, Cunha, Rubo, and Conti (2012) and Parker and Chole (1995), respectively. Only the latter articles were included, as they contained the most relevant information for this review. Consequently, a total of 22 independent articles were included in this study (Akhter et al., 2013; Bernhardt et al., 2004; Bonaconsa et al., 2010; Buergers, Kleinjung, Behr, & Vielsmeier, 2014; Camparis, Formigoni, Teixeira, & De Siqueira, 2005; De Felicio, Melchior, Ferreira, & Rodrigues Da Silva, 2008; de-Pedro-Herraez, Mesa-Jimenez, Fernandez-de-Las-Penas, & de-la-Hoz-Aizpurua, 2016; Effat, 2016; Fernandes, de Godoi Goncalves, de Siqueira, & Camparis, 2013; Hilgenberg et al., 2012; Khedr et al., 2010; Kuttila, Kuttila, Le Bell, Alanen, & Suonpaa, 2005; Lee et al., 2016; Park & Moon, 2014; Parker & Chole, 1995; Pekkan, Aksoy, Hekimoglu, & Oghan, 2010; Peroz, 2003; Pezzoli et al., 2015; Ren & Isberg, 1995; Rocha & Sanchez, 2007; Rubinstein, Osterberg, Rosenhall, & Johansson, 1993; Tuz, Onder, & Kisnisci, 2003). No additional articles were identified from the reference lists of the articles (Figure 1). No articles surfaced in our search strategy that needed translation.

Data Extraction and Quality Assessment

Study characteristics. Almost all studies were cross-sectional ($n = 20$) in design. Data of two longitudinal studies were extracted from baseline measurements (Table 1; Bonaconsa et al., 2010; Lee et al., 2016). Twelve studies investigated the presence of CSD or TMD in patients with and without tinnitus. Ten studies examined the presence of tinnitus in patients with and without TMD only. No studies were found in which tinnitus was explored in patients with and without CSD. Of the studies investigating the association between tinnitus and TMD, three studies examined patients with and without tinnitus, wherein both groups also complained about bruxism (Camparis et al., 2005), disc displacements of the temporomandibular joint (TMJ; Ren & Isberg, 1995), or headache or facial pain (Pezzoli et al., 2015). Most patients were recruited from general or specialized hospitals/ENT departments. Almost all studies included adult patients and controls of all ages. However, in one study, patients and controls were students less than 21 years old (Akhter et al., 2013), and in another study, patients and controls were exactly 70 or 76 years old (Rubinstein et al., 1993). In four studies, patients and controls were recruited from a community database (Table 1; Khedr et al., 2010; Kuttila et al., 2005; Park & Moon, 2014; Rubinstein et al., 1993).

Several studies also reported TMD symptoms of arthrogenous (TMDa) or myogenous origin (TMDm). If, in addition to an overall outcome for TMD, a TMDa or TMDm symptom was also reported, then these specified outcomes instead of TMD (not specified) were used in the meta-analyses. The following strategy was applied to decide whether TMDa was investigated in a study: (a) the authors of the study reported it; (b) if it was not reported, then data regarding disc derangement were used; (c) if these were not reported, then data regarding *pain in temporomandibular joint* were used; and (d) if these were missing, then data regarding joint sounds were used. For TMDm, (a) data regarding myofascial pain (dysfunction) were used; (b) if this was not reported, then Diagnosis Group I.a and I.b of the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) were used (Dworkin & LeResche, 1992); (c) if these were not reported, then data regarding pain/tenderness on palpation of masticatory muscles were used; and (d) if these were not reported, then data regarding pain in the lower lateral face were used.

Studies were grouped into one of five categories: (a) The association between tinnitus and CSD was analyzed in five studies (Khedr et al., 2010; Kuttila et al., 2005;

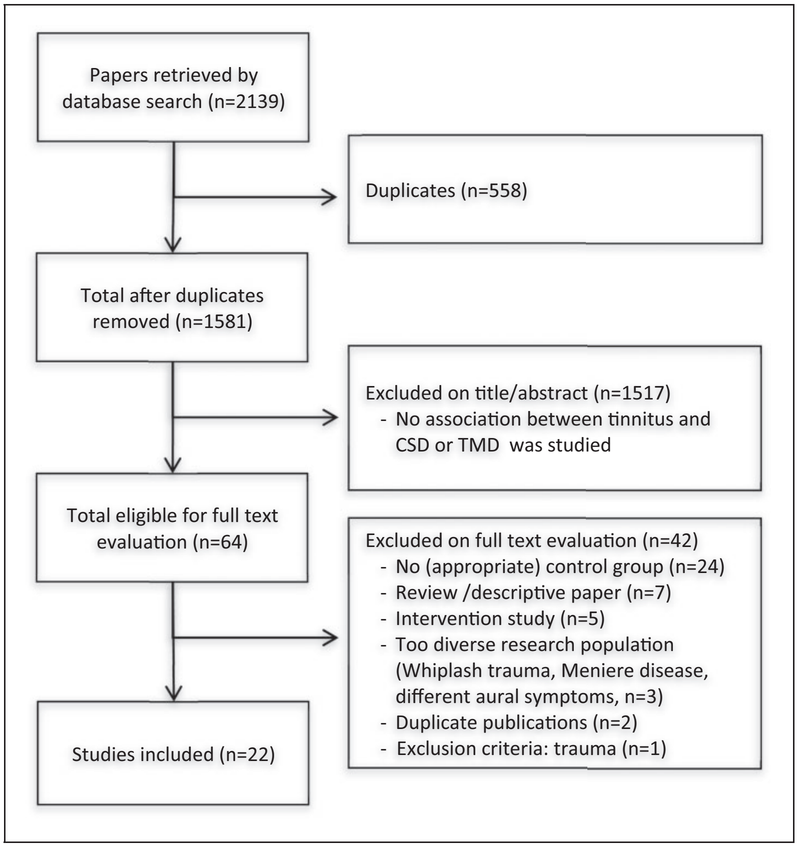

Figure 1. Flow chart of study selection.
CSD = cervical spine disorders; TMD = temporomandibular disorders.

Pezzoli et al., 2015; Ren & Isberg, 1995; Rubinstein et al., 1993); (b) the association between tinnitus and disorders in both neck and jaw (CSD plus TMD) in three studies (Bonaconsa et al., 2010; Peroz, 2003; Rocha & Sanchez, 2007); (c) the association between tinnitus and TMD (not specified) in six studies (Buergers et al., 2014; De Felicio et al., 2008; Effat, 2016; Fernandes et al., 2013; Park & Moon, 2014; Pekkan et al., 2010); (d) the association between tinnitus and TMDa in 11 studies (Akhter et al., 2013; Bernhardt et al., 2004; Camparis et al., 2005; Hilgenberg et al., 2012; Khedr et al., 2010; Kuttila et al., 2005; Parker & Chole, 1995; Peroz, 2003; Pezzoli et al., 2015; Rubinstein et al., 1993; Tuz et al., 2003); and (e) the association between tinnitus and TMDm in seven studies (Bernhardt et al., 2004; Camparis et al., 2005; Hilgenberg et al., 2012; Peroz, 2003; Pezzoli et al., 2015; Ren & Isberg, 1995; Tuz et al., 2003). Some studies considered multiple associations and, as a consequence, belonged to more than one category (Table 1).

Quality assessment. The number of quality criteria met by the studies ranged from 1 to 7 (Table 2). The interobserver agreement expressed as Cohen's kappa was 0.33 (absolute agreement: 64%). Criteria for study objective, population, and group discrimination were fulfilled in 21 studies. Random selection of patients and controls was applied in three studies. In five studies, participants were matched for gender and age. In two studies, assessors were blinded. Patients and controls were recruited from the same population in 16 studies.

Instruments to assess tinnitus, CSD, or TMD were well described in eight studies. In all eight studies, the RDC/TMD (Dworkin & LeResche, 1992) was applied (Buergers et al., 2014; Camparis et al., 2005; De Felicio et al., 2008; de-Pedro-Herraez et al., 2016; Fernandes et al., 2013; Hilgenberg et al., 2012; Pekkan et al., 2010; Tuz et al., 2003). Tinnitus was assessed with a single question in most of the studies ($n = 16$). In six studies, this question was part of the RDC/TMD (Buergers et al., 2014; Camparis et al., 2005; De Felicio et al., 2008; Fernandes et al., 2013; Pekkan et al., 2010; Tuz et al., 2003). In all other studies ($n = 10$), tinnitus was assessed by a single question as part of author-designed questionnaires (nonvalidated). In six studies, a physician assessed tinnitus. No information about severity of tinnitus was reported.

Participants were asked to report the presence of pain in the jaw, neck, and shoulder region by means of author-designed (nonvalidated) questionnaires in five studies (Khedr et al., 2010; Kuttila et al., 2005; Peroz,

Table 1. Overview of Studies Analysing the Association Between Tinnitus and Complaints of Neck, Shoulders, or Temporomandibular Joint in Patients and Controls.

Author	Patients[a]	Patients recruited[b]	Patients N (♀)	Patients age M (SD)	Controls[a]	Controls recruited[b]	Controls N (♀)	Controls age M (SD)	Recruitment method[c]	Assessment method[d]	Outcome[a,e]	Case[f]	Control
Association between tinnitus and CSD													
Tinnitus vs. no tinnitus													
Rubinstein et al., 1993[g]	Tinnitus	Community database	166 (–)	–	No tinnitus	Community database	592 (–)	–	Quest/Phys	Quest/Phys	MP in neck	24%	–
Ren and Isberg, 1995	Tinnitus + DD ipsilateral	Specialized	53 (70%)	–	No tinnitus + DD ipsilateral	Specialized	82 (60%)	–	Quest	Quest	MP in neck	55%	24%
Kuttila et al., 2005	Tinnitus (>1/month)	Community database	126 (–)	–	Tinnitus (<1/month)	Community database	132 (–)	–	Quest	Quest	MP in neck	52%	5%
Khedr et al., 2010	Tinnitus	Community database	439 (46%)	–	No tinnitus	Community database	96 (–)	–	Quest	Quest	MP in neck	37%	33%
Pezzoli et al., 2015	Tinnitus + headache or facial pain	Specialized	334 (84%)	42 (16)	No tinnitus + headache or facial pain	Specialized	917 (85%)	48 (16)	Quest	Palpation	MP in neck	–	–
CSD vs. No CSD													
No studies included													
Association between tinnitus and CSD + TMD													
Tinnitus vs. no tinnitus													
Peroz, 2003	Tinnitus	Specialized	40 (53%)	52 (14)	No tinnitus	Specialized	35 (60%)	50 (15)	Phys	Quest	Muscle hypertonia in head, neck or shoulders	67%	22%
Rocha and Sanchez, 2007	Tinnitus	Specialized	94 (58%)	53 (–)	No tinnitus	Peer accompanying cases	94 (58%)	53 (–)	Phys	Palpation	MP in head, jaw, neck, or shoulders	72%	36%
Bonaconsa et al., 2010	Tinnitus	Specialized	40 (25%)	48 (–)	No tinnitus	Specialized	40 (73%)	43 (–)	Quest	Palpation	MP in head, jaw, neck, or shoulders	83%	45%
CSD + TMD vs. No CSD + TMD													
No studies included													
Association between tinnitus and TMD													
Tinnitus vs. no tinnitus													
Hilgenberg et al., 2012[g]	Tinnitus	Specialized	100 (84%)	39 (12)	No tinnitus	Specialized	100 (65%)	34 (10)	Phys	Phys (RDC/TMD)	TMD	85%	55%
Park and Moon, 2014	Tinnitus	Community database	2,149 (60%)	50 (16)[h]	No tinnitus	Community database	10,061 (57%)	50 (16)[h]	Quest	Quest	TMD	?[i]	?[i]
TMD vs. No TMD													
Tuz et al., 2003[g]	TMD	Specialized	200 (83%)	30 (–)	No TMD	Specialized	50 (54%)	37 (–)	Phys (RDC/TMD)	Quest (RDC/TMD)	Tinnitus	46%	26%
De Felicio et al., 2008	TMD	Specialized	20 (100%)	31 (–)[h]	No TMD	–	8 (100%)	31 (–)[h]	Phys (RDC/TMD)	Quest (RDC/TMD)	Tinnitus	60%	25%
Pekkan et al., 2010	TMD	Specialized	25 (16%)	28 (–)	No TMD	Specialized	20 (15%)	28 (–)	Phys/Quest (RDC/TMD)	Phys/Quest (RDC/TMD)	Tinnitus	52%	0%
Akhter et al., 2013[g]	TMD	Students <22 years	543 (28%)	19 (2)[h]	No TMD	Students <22 years	1,387 (72%)	19 (2)[h]	Quest	Quest	Tinnitus	39%	6%
Fernandes et al., 2013	Painful TMD	Specialized	162 (–%)	38 (13)[h]	No TMD nor painful TMD	Specialized	62 (–%)	38 (13)[h]	Quest (RDC/TMD)	Quest (RDC/TMD)	Tinnitus	88%	12%

(continued)

Table 1. Continued

Author	Patients[a]	Patients recruited[b]	Patients N (♀)	Patients age M (SD)	Controls[a]	Controls recruited[b]	Controls N (♀)	Controls age M (SD)	Recruitment method[c]	Assessment method[d]	Outcome[a,e]	Case[f]	Control
Buergers et al., 2014	TMD	Specialized	82 (68%)	54 (17)[h]	No TMD	Specialized	869 (49%)	54 (17)[h]	Phys (RDC/TMD)	Phys	Tinnitus	37%	4%
Lee et al., 2016[g]	TMD	Insurance	7,585 (66%)	45 (16)	No TMD	General/ Specialized	30.340 (66%)	45 (16)	Phys	Phys	Tinnitus	?[j]	?[j]
Effat, 2016	TMD	Specialized	104 (81%)	35 (12)	No TMD	General	110 (60%)	31 (8)	Phys	Quest	Tinnitus	52%	12%
Association between tinnitus and TMDa													
Tinnitus vs. no tinnitus													
Rubinstein et al., 1993	Tinnitus	Community database	166 (–)	–	No tinnitus	Community database	592 (–)	–	Quest/Phys	Quest/Phys	Noises in TMJ[k]	11%	–
Peroz, 2003	Tinnitus	Specialized	40 (53%)	52 (14)	No tinnitus	Specialized	35 (60%)	50 (15)	Phys	Phys	Noises in TMJ[k]	23%	1%
Bernhardt et al., 2004	Tinnitus	Specialized	30 (43%)	41 (–)	No tinnitus	Community database	1,907 (52%)	49 (–)	Quest	Palpation	Pain in TMJ	34%	5%
										Phys	Noises in TMJ[k]	37%	28%
Camparis et al., 2005	Tinnitus + bruxism	Specialized	54 (83%)	38 (–)	No tinnitus + bruxism	Specialized	46 (76%)	34 (–)	Quest (RDC/TMD)	Phys (RDC/TMD)	Pain in TMJ	70%	39%
											DD	20%	17%
Kuttila et al., 2005	Tinnitus (>1/month)	Community database	126 (–%)	–	Tinnitus (<1/month)	Community database	132 (–%)	–	Quest	Quest	Pain in TMJ	48%	5%
Khedr et al., 2010	Tinnitus	Community database	439 (46%)	–	No tinnitus	Community database	96 (–)	–	Quest	Quest	Pain in TMJ	21%	12%
Hilgenberg et al., 2012	Tinnitus	Specialized	100 (84%)	39 (12)	No tinnitus	Specialized	100 (65%)	34 (10)	Phys	Phys (RDC/TMD)	Pain in TMJ	53%	24%
											DD + Clicking[k]	43%	30%
											DD + No Clicking + LMO	0%	1%
											DD + No Clicking[k]	6%	4%
											Arthritis	3%	0%
											Arthrosis	1%	1%
Pezzoli et al., 2015	Tinnitus + headache or facial pain	Specialized	334 (84%)	42 (16)	No tinnitus + headache or facial pain	Specialized	917 (85%)	48 (16)	Quest	Phys	DD	?[j]	?[j]
TMD vs. No TMD													
Parker and Chole, 1995	Pain in TMJ + DD	Specialized	200 (87%)	–	No TMD nor pain in TMJ + DD	General	649 (61%)	–	Phys	Quest	Tinnitus	59%	24%
Tuz et al., 2003	*MP in jaw + DD*	Specialized	200 (83%)	30 (–)	No TMD	Specialized	50 (54%)	37 (–)	Phys (RDC/TMD)	Quest (RDC/TMD)	Tinnitus	42%	26%
	DD											44%	26%
Akhter et al., 2013	*Pain in TMJ*	Students <22 years	543 (28%)	19 (2)[h]	No TMD	Students <22 years	1,387 (72%)	19 (2)[h]	Quest	Quest	Tinnitus	48%	6%
	DD											6%	6%
	DD + Pain in TMJ											55%	6%
	DD + LMO											4%	6%
	Pain in TMJ + LMO											9%	6%
	DD + Pain in TMJ + LMO											4%	6%

(continued)

Table 1. Continued

Author	Patients[a]	Patients recruited[b]	Patients N (♀)	Patients age M (SD)	Controls[a]	Controls recruited[b]	Controls N (♀)	Controls age M (SD)	Recruitment method[c]	Assessment method[d]	Outcome[a,e]	Case[f]	Control
Association between tinnitus and TMDm													
Tinnitus vs. No tinnitus													
Ren and Isberg, 1995[g]	Tinnitus + DD ipsilateral	General	53 (70%)	–	No tinnitus + DD ipsilateral	General	82 (60%)	–	Quest		MP lower lateral face	79%	56%
Peroz, 2003	Tinnitus	Specialized	40 (53%)	52 (14)	No tinnitus	Specialized	35 (60%)	50 (15)	Phys	Palpation	MP in jaw	93%	71%
Bernhardt et al., 2004	Tinnitus	Specialized	30 (43%)	41 (–)	No tinnitus	Community database	1,907 (52%)	49 (–)	Quest	Palpation	MP in jaw	50%	16%
Camparis et al., 2005	Tinnitus + bruxism	Specialized	54 (83%)	38 (–)	No tinnitus + bruxism	Specialized	46 (76%)	34 (–)	Quest (RDC/TMD)	Phys (RDC/TMD)	MP in jaw	85%	48%
Hilgenberg et al., 2012	Tinnitus	Specialized	100 (84%)	39 (12)	No tinnitus	Specialized	100 (65%)	34 (10)	Phys	Phys (RDC/TMD)	MP in jaw	32%	22%
											MP in jaw + LMO	39%	16%
Pezzoli et al., 2015	Tinnitus + headache or facial pain	Specialized	334 (84%)	42 (16)	No tinnitus + headache or facial pain	Specialized	917 (85%)	48 (16)	Quest	Phys	MP in facial or masticatory muscles	?[i]	?[i]
TMD vs No TMD													
Tuz et al., 2003	*MP in jaw*	Specialized	200 (83%)	30 (–)	No TMD	Specialized	50 (54%)	37 (–)	Phys (RDC/TMD)	Quest (RDC/TMD)	Tinnitus	59%	26%
de-Pedro-Herraez et al., 2016	MP in jaw	Specialized	31 (100%)	39 (–)	No MP in jaw	Specialized	31 (100%)	41 (–)	Quest (RDC/TMD)	Quest	Tinnitus	52%	10%

Note. CSD = cervical spine disorders; TMJ = temporomandibular joint.
[a]TMD = temporomandibular disorder not specified; DD = temporomandibular disc displacements; LMO = limited mouth opening.
[b]Recruitment setting: General = general hospital/ENT department; Specialized = specialized tinnitus or TMD clinic/department.
[c]Recruitment method: Quest = by questionnaire; Phys = by a physician.
[d]Assessment method: RDC/TMD = research diagnostic criteria for temporomandibular disorders (Dworkin & LeResche, 1992).
[e]Assessment outcome: MP = myofascial pain.
[f]TMDa = TMD arthrogenous; TMDm = TMD myogenous. Peroz (2003) reported "Verspannungen im hals-, schulter- und oberarm bereich und kaumuskeln" (we grouped this under "hypertonia in head, neck, and shoulder muscles").
[g]Not included in meta-analysis as explained in methods and results.
[h]Value = overall mean age cases + controls.
[i]Unknown percentage, odds ratios as a result of multivariable logistic regression analyses were presented.
[j]Incidence study: In the TMD group ($n = 7{,}585$), 362 developed tinnitus, and in the control group ($n = 30{,}340$), 530 developed tinnitus; Parker and Chole (1995) analyzed two control groups. We combined the groups.
[k]Regarding "Noises in TMJ" and clicking, we assume that the subjects heard subjective tinnitus in addition to sound that the jaw joint might produce, as the authors distinguish between these two percepts in their discussion; [–] not reported (Dehmel et al., 2008).

Table 2. Quality Assessment of the Studies.

Author	Year	Quality criteria 1	2	3	4	5	6	7	8	9
Rubinstein	1993	+	+	+	+	+	+	–	–	?
Parker and Chole	1995	+	–	–	?	?	?	–	–	?
Ren and Isberg	1995	+	+	+	+	+	–	–	–	?
Peroz	2003	+	+	–	+	+	?	–	–	?
Tuz et al.	2003	+	+	+	+	+	–	–	+	?
Bernhardt et al.	2004	+	+	+	–	+	–	–	+	?
Camparis et al.	2005	+	+	+	+	+	?	–	+	?
Kuttila et al.	2005	+	+	+	+	+	+	–	–	?
Rocha and Sanchez	2007	+	+	+	+	+	–	+	+	–
De Felicio et al.	2008	+	+	?	+	+	?	–	+	?
Bonaconsa et al.	2010	–	+	?	+	+	?	+	+	–
Khedr et al.	2010	+	+	+	+	+	–	+	+	?
Pekkan et al.	2010	+	+	–	+	+	?	–	+	?
Hilgenberg et al.	2012	+	+	+	+	+	?	–	+	+
Akhter et al.	2013	+	+	+	+	+	–	–	–	?
Fernandes et al.	2013	+	+	+	+	+	–	–	+	+
Buergers et al.	2014	+	+	+	–	+	–	–	+	?
Park and Moon	2014	+	+	+	+	+	–	–	+	?
Lee et al.	2016	+	+	+	+	+	+	+	?	?
Pezzoli et al.	2015	+	+	+	+	+	–	–	+	?
de-Pedro-Herraez et al.	2016	+	+	+	+	+	–	+	?	?
Effat	2016	+	+	–	+	+	–	–	–	?

Note. 1. Was the research question or objective in this article clearly stated and appropriate? 2. Was the study population clearly specified and defined? 3. Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same timeframe)? 4. Were the definitions, inclusion, and exclusion criteria used to identify or select cases and controls valid, reliable, and implemented consistently across all study participants? 5. Were the cases clearly defined and differentiated from controls? 6. Were the cases and controls randomly selected? 7. Were controls matched to cases on one or more attributes? 8. Were the measures of exposure clearly defined, valid, reliable, and implemented consistently across all study participants? 9. Were the assessors blinded to the case or control status of participants? [+] Yes, [–] No, [?] cannot be determined/unclear/not reported (modified version of Quality Assessment of Case-Control Studies, 2014).

2003; Ren & Isberg, 1995; Rubinstein et al., 1993) or RDC/TMD (Buergers et al., 2014; Camparis et al., 2005; De Felicio et al., 2008; Fernandes et al., 2013; Hilgenberg et al., 2012; Pekkan et al., 2010; Tuz et al., 2003). In the other studies, participants were asked to report pain provoked during physical examination of that region, such as assessment of myofascial trigger points (TrPs; Simons, Travell, & Simons, 1999). In one study, a physician was trained to deliver a standardized finger pressure for evaluating TrPs (Bernhardt et al., 2004). In another study, an algometer was used for assessment of TrPs (Hilgenberg et al., 2012).

Meta-analysis. The results of Lee et al. (2016) were reported as hazard ratios (tinnitus with and without TMD, Crude HR = 2.73, $p < .001$) instead of odds ratios and were not included in the meta-analysis. Rubinstein et al. (1993) reported not only significant differences in TMD between patients with and without tinnitus but also about CSD. Because no data of CSD were reported in the controls, these data were also not included in the meta-analysis.

Tinnitus and CSD. One study (Khedr et al., 2010) did not and three studies did find a significant association between myofascial pain in the neck region and tinnitus. All studies investigated CSD in patients with and without tinnitus. The study-size weighted odds ratios ranged from 1.2 to 10.9, with an overall odds ratio of 2.6 (95% CI [1.1, 6.4]; Figure 2).

Tinnitus and CSD plus TMD. All three studies analyzing the association between tinnitus and CSD plus TMD found a significant association between myofascial complaints in head, jaw, neck, or shoulders. All studies investigated CSD plus TMD in patients with and without tinnitus. All patients were recruited from specialized hospitals. Of these patients, 67% to 83% perceived tinnitus.

Study Name	Group by Diagnose	Odds ratio observed	Odds ratio adjusted	Lower limit	Upper limit	p-Value
Ren and Isberg, 1995	CSD	3.8		1.8	7.9	0.00
Kuttila et al., 2005	CSD	7.6		5.3	10.9	0.00
Khedret al., 2010	CSD	1.2		0.7	1.9	*0.51*
Pezzoli et al., 2015	CSD	1.5		1.4	1.7	0.00
	CSD	**2.6**	**2.6**	**1.1**	**6.4**	**0.03**
Peroz, 2003	CSD+TMD	7.0		2.5	19.6	0.00
Rocha and Sanchez, 2007	CSD+TMD	4.9		2.5	9.5	0.00
Bonaconsa et al., 2010	CSD+TMD	5.8		2.1	16.1	0.00
	CSD+TMD	**5.5**	**4.9**	**3.4**	**9.0**	**0.00**
De Felicio et al., 2008	TMD	4.5		0.7	28.2	*0.11*
Pekkan et al., 2010	TMD	44.3		2.4	812.0	0.01
Femandes et al., 2013	TMD	7.4		3.8	14.6	0.00
Buergers et al., 2014	TMD	12.6		7.3	22.0	0.00
Park & Moon, 2014	TMD	1.7		1.4	2.0	0.00
Effat, 2016	TMD	8.1		4.0	16.2	0.00
	TMD	**6.7**	**4.5**	**2.4**	**18.8**	**0.00**
Rubinstein et al., 1993	TMDa	2.2		1.2	4.0	0.01
Parker & Chole, 1995	TMDa	4.6		3.3	6.4	0.00
Peroz, 2003	TMDa	9.9		1.2	82.5	0.03
Tuz et al., 2003	TMDa	2.3		1.1	4.6	0.03
Bemhardt et al., 2004	TMDa	1.5		0.7	3.2	*0.28*
Camparis et al., 2005	TMDa	1.2		0.4	3.3	*0.71*
Kuttila et al., 2005	TMDa	6.9		4.8	9.9	0.00
Khedr et al., 2010	TMDa	2.1		1.1	4.1	0.03
Hilgenberg et al., 2012	TMDa	1.8		1.0	3.2	0.05
Akhter et al ., 2013	TMDa	1.7		1.2	2.4	0.01
Pezzoli et al., 2015	TMDa	1.2		0.9	1.6	*0.29*
	TMDa	**2.3**	**2.5**	**1.5**	**3.6**	**0.00**
Peroz, 2003	TMDm	4.9		1.2	19.7	0.02
Tuz et al., 2003	TMDm	4.1		1.4	11.9	0.01
Bemhardt et al., 2004	TMDm	5.4		2.6	11.1	0.00
Camparis et al., 2005	TMDm	6.3		2.4	16.2	0.00
Hilgenberg et al., 2012	TMDm	4.0		2.2	7.2	0.00
Pezzoli et al., 2015	TMDm	1.3		1.0	1.7	0.03
de-Pedro-Herraez et al., 2016	TMDm	10.0		2.5	39.7	0.00
	TMDm	**4.1**	**3.3**	**2.1**	**8.1**	**0.00**

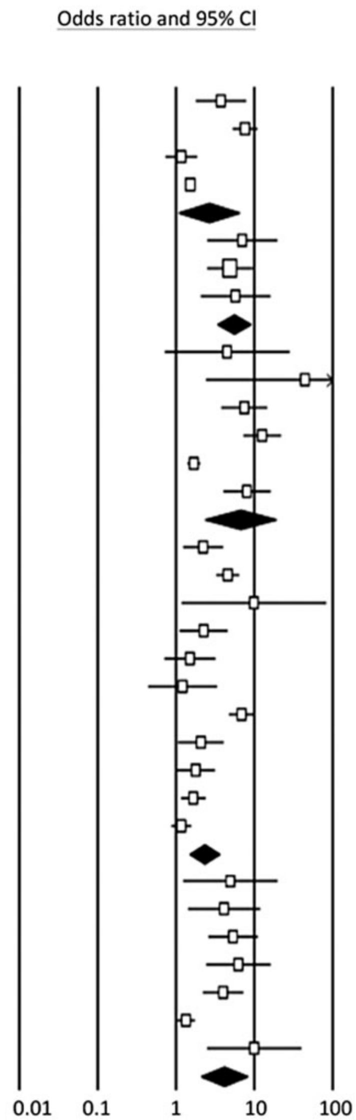

Figure 2. Forest plot of the association between tinnitus and CSD or TMD differentiated into five categories.
Adjusted odds ratios: To adjust for potential publication bias, Duval and Tweedie's (2000) nonparametric trim-and-fill approach to impute theoretical missing studies was applied.
CSD = cervical spine disorders; TMD = temporomandibular disorders; TMDa = TMD arthrogenous; TMDm = TMD myogenous.

The study-size weighted odds ratios ranged from 4.9 to 7.0, with an overall odds ratio 5.5 (95% CI [3.4, 9.0]).

Tinnitus and TMD (not specified). All studies but one (De Felicio et al., 2008) found an association between tinnitus and TMD (not specified). One study investigated TMD in patients with and without tinnitus (Park & Moon, 2014). Conversely, five studies investigated tinnitus in patients with and without TMD (Buergers et al., 2014; De Felicio, De Oliveira, Nunes, Jeronymo, & Ferreira-Jeronymo, 1999; De Felicio et al., 2008; Effat, 2016; Fernandes et al., 2013). Overall, 37% to 88% of patients with TMD who were recruited from specialized TMD clinics perceived tinnitus. The study-size weighted odds ratios ranged from 1.7 to 44.3, with an overall odds ratio of 6.7 (95% CI [2.4, 18.8]).

Tinnitus and TMDa. Eight out of 11 studies found a significant association between tinnitus and TMDa. Of the patients who were recruited from specialized TMD clinics, 20% to 59% perceived tinnitus; when recruited elsewhere, 21% to 48% perceived tinnitus. Eight studies investigated TMDa in patients with and without tinnitus (Bernhardt et al., 2004; Camparis et al., 2005; Hilgenberg et al., 2012; Khedr et al., 2010; Kuttila et al., 2005; Peroz, 2003; Pezzoli et al., 2015; Rubinstein, 1993). Conversely, three studies examined tinnitus in patients with and without TMDa (Akhter et al., 2013; Parker & Chole, 1995; Tuz et al., 2003). Temporomandibular disc displacements was investigated in four studies (Akhter et al., 2013; Camparis et al., 2005; Hilgenberg et al., 2012; Pezzoli et al., 2015), while pain or noises in the TMJ were studied in the other studies. The study-size weighted odds ratios ranged from 1.2 to 9.9, with an overall odds ratio 2.3 (95% CI [1.5, 3.6]).

Tinnitus and TMDm. All seven studies found a significant association between tinnitus and TMDm. These studies examined myofascial pain in the jaw region. Five studies investigated TMDm in patients with and without tinnitus (Bernhardt et al., 2004; Camparis et al., 2005; Hilgenberg et al., 2012; Leher, Dietrich, & Peroz, 2003; Pezzoli et al., 2015). One study investigated tinnitus in patients with and without TMDm (Tuz et al., 2003). Patients were recruited from specialized TMD clinics. The study-size weighted odds ratios ranged from 1.3 to 10.0, with an overall odds ratio of 4.1 (95% CI [2.1, 8.1]).

Finally, three studies investigated laterality between unilateral tinnitus and unilateral TMD (Buergers et al., 2014; Ren & Isberg, 1995; Rocha & Sanchez, 2007). In two studies, all the participants had both conditions on the same side (Buergers et al., 2014; Ren & Isberg, 1995), while the contralateral TMJ region was asymptomatic in 94% (Ren & Isberg, 1995). The third study found an association of laterality in 56.5% ($p > .001$) of the patients between the tinnitus side (or the side with the worst tinnitus) and the side of the body with most TrPs (Rocha & Sanchez, 2007).

Publication bias. Based on the funnel plots (Figure 3(a) to (e)), publication bias was suggested regarding the association between tinnitus and CSD/TMD, TMD (not specified), and TMDm. The overall odds ratio reduced after *trim and fill* from 5.5 to 4.9 for the association with CSD/TMD, from 6.7 to 4.5 for the association with TMD (not specified), and from 4.1 to 3.3 for the association with TMDm (Duval & Tweedie, 2000).

Discussion

Summary of Main Results

In the majority of the studies, a significant association between tinnitus and TMD was identified. This relationship is bidirectional meaning that, patients with tinnitus more frequently experienced TMD than subjects without tinnitus, and, vice versa, patients with TMD experienced tinnitus more frequently compared with subjects without TMD. For CSD, the results only revealed a unidirectional relationship. Thus, patients with tinnitus more frequently reported CSD. None of the included studies reported on the reverse relation, that is, whether patients with CSD have an increased probability to experience tinnitus. Meta-analysis showed that patients with tinnitus have an average of 2.6 and 6.7 times greater risk of reporting CSD or TMD, respectively.

Bias and Quality Assessment

Almost all studies reported a significant association between tinnitus and CSD or TMD, which may suggest a risk of publication bias. This bias seems to be confirmed by the absence of data points on the left side of the funnel plots in Figure 3(b), (c), and (e). When theoretical missing studies were imputed, the adjusted odds ratios for these items reduced, but an association persisted. In Figure 3(d), one theoretical missing study is imputed in the right side of the funnel plot causing a minimum increment of the adjusted odds ratio. This might be caused by a systematic difference between the studies of higher precision and the only study of lower precision. In the analysis, one outlier was found with an odds ratio of 44.3 (Pekkan et al., 2010). Quality assessment could not sufficiently explain this outlier, except that the sample size was small.

The methodological quality assessment showed that only in a few studies were the assessors blinded (2/22) and the patients and controls randomly selected (3/22) or matched for gender and age (5/22; Table 2). Despite this shortcoming, no studies found a significant difference regarding distribution of gender or mean age between comparison groups. Further, in some studies, patients and controls were not recruited from the same population. For instance, patients visiting a specialized TMD clinic were compared with controls visiting a dentist for minimal dental care. Consequently, recruitment from different populations may result in differences between groups that influence outcomes. To analyze effects of quality, we initially intended to perform a meta-regression to explore associations between quality criteria of studies and their outcomes. After reviewing the results, however, we decided to refrain from meta-regression because quality criteria were either met in the vast majority of studies or not met, resulting in a skewed distribution between studies.

Instead of a validated questionnaire such as the *Tinnitus Handicap Inventory* (Newman, Jacobson, & Spitzer, 1996), tinnitus was often assessed by means of a single question as part of the RDC/TMD or other

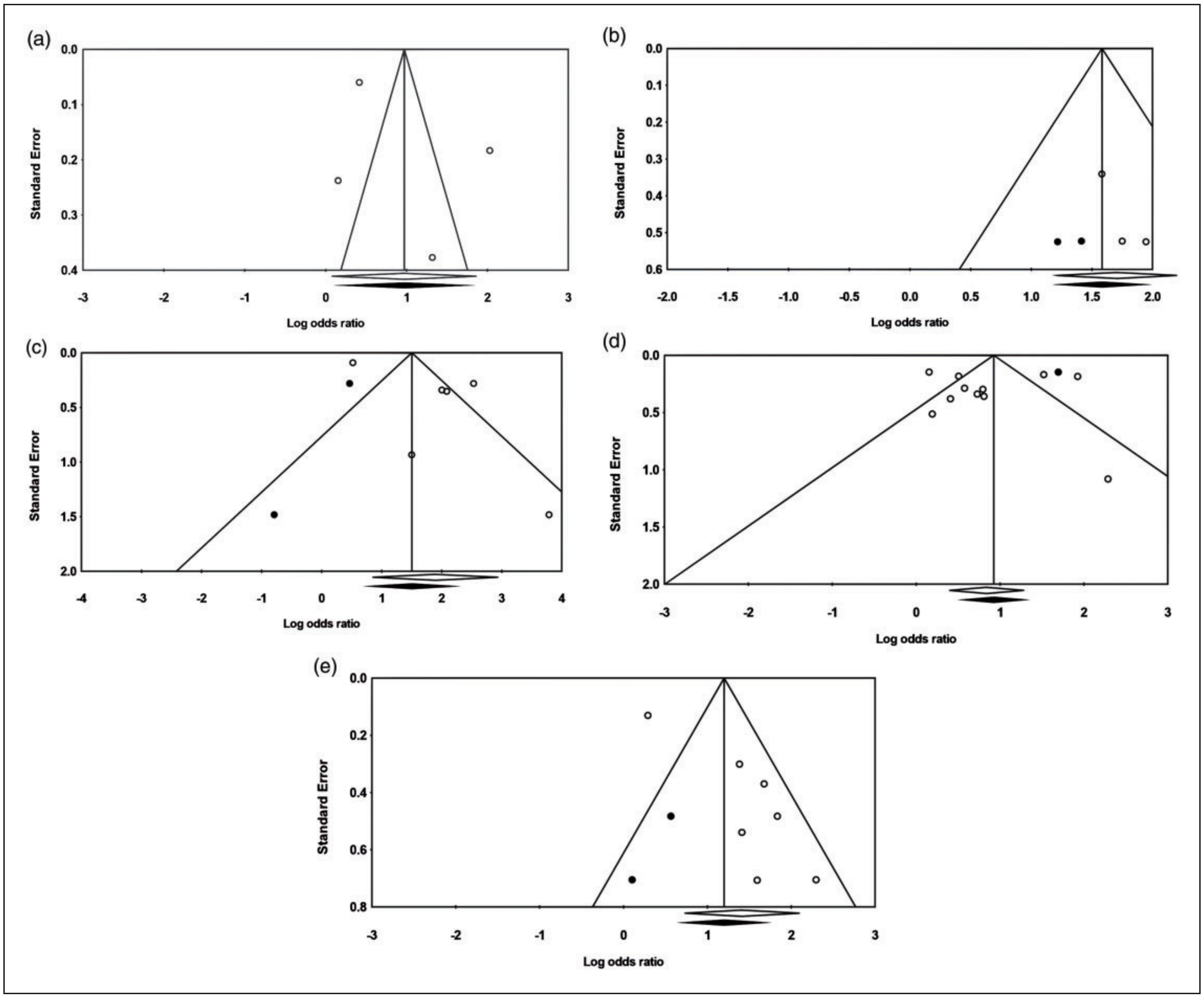

Figure 3. Funnel plots of studies regarding association between tinnitus and CSD or TMD. (a) Association between tinnitus and CSD; (b) association between tinnitus and CSD and TMD; (c) association between tinnitus and TMD (not specified); (d) association between tinnitus and TMD (arthrogenous); (e) association between tinnitus and TMD (myogenous).
[o] = Studies included.
[•] = Imputed studies to adjust a summary odds ratio in light of these "missing" studies, compensating for the risk of publication bias (Duval & Tweedie, 2000).
Open and closed rhombuses represent the mean log odds ratios before and after study imputation, respectively (Duval & Tweedie, 2000).
CSD = cervical spine disorders; TMD = temporomandibular disorders.

questionnaire. Thus, only information on the presence, and not about the severity, of tinnitus was provided. It is therefore unclear whether severity of tinnitus affected the associations.

As only one author screened abstracts, titles, and selected full texts, studies may have been missed. To reduce the chance of missing studies, references of the included studies were checked.

We used a modified version of *Quality Assessment of Case-Control Studies* for methodological quality assessment of case-control, cross-sectional, and cohort studies. A negative feature of this tool was that the quality criteria were widely interpretable, which resulted in a low kappa value, but with an acceptable absolute agreement. After discussion, however, consensus was reached on all topics. Classifying studies according to their risk of bias was considered, but it was impossible to state at which level and in which direction the individual quality items contributed to a study's risk of bias. Therefore, the results of methodological quality assessment are described.

In exploring the association between tinnitus and TMD, we combined studies recruiting patients with tinnitus in a TMD clinic and studies recruiting patients with TMD in a tinnitus clinic. This might have induced selection bias, but as the association was bidirectional, this analysis did not appear to influence results.

The majority of the studies exploring the association between TMD and tinnitus are of acceptable quality, and almost all found an association between TMD and tinnitus. However, we found no high-quality studies, as each study had at least one critical unfilled individual quality criterion, such as lack of blinding or comparability of the groups, which could have contributed to a study's risk of bias. Based on the Grading of Recommendations Assessment, Development and Evaluation level of evidence scale, we qualified the overall level of evidence for this association as low (Grading of Recommendations Assessment, Development and Evaluation, 2017).

In addition, we found no high-quality studies exploring the association between CDS and tinnitus. In contrast to the good clinometric properties of the instrument assessing TMD, CSD was assessed only by means of author-designed questionnaires or by examination for tenderness or TrPs. The latter was almost always performed by means of palpation and only once by means of pressure algometry. Therefore, we also qualified the overall level of evidence for this association as low.

Explanatory Models

A frequently described explanation for subjective somatosensory tinnitus is that a TMJ disorder (e.g., disc displacement) or hypertonia of the masticatory muscles might influence middle ear muscle tension or ventilation through an anatomical connection (e.g., the tensor veli palatini, the eustachian tube, or several ligaments). These influences would generate afferent signals that would—via the cochlear nerve—influence the auditory pathways (for review, see Ramirez et al., 2008). However, as tinnitus and its somatosensory modulation can persist after cutting the system off at the auditory nerve (D. M. Baguley, Axon, Winter, & Moffat, 2002; House & Brackmann, 1981), these peripheral explanations cannot provide the sole explanation. Recently, studies have shown anatomical and functional connections between the trigeminal and dorsal column systems of the somatosensory system and the cochlear nucleus (CN) of the auditory system in the medulla oblongata (Shore & Zhou, 2006). The spinal trigeminal nucleus receives nociceptive and proprioceptive input from the head, face, oral structures, TMJ, and cervical spine (C1–C3) and projects to the CN (Shore, 2011). A possible functional role of the auditory-somatosensory interactions involves the differentiation between external auditory signals and those generated by the body itself (Shore, 2005). This functional connection in the brainstem between the auditory and somatosensory system might mediate an association between subjective tinnitus and CSD and TMD (Dehmel, Cui, & Shore, 2008). In addition, in case of cochlear damage, this connection is upregulated, as over a time interval of days after reduced auditory nerve input, responses to somatosensory stimulation are heightened (Shore, Roberts, & Langguth, 2016). The interaction between both systems might explain why tinnitus sufferers can modulate the loudness and pitch of their tinnitus (Ralli et al., 2016; Shore et al., 2016). It is also conceivable that based on stochastic resonance, the somatosensory input may lead to the development of subjective tinnitus, as it may lift subthreshold auditory nerve input to the CN above detection threshold (Krauss et al., 2016).

The association between tinnitus and CSD or TMD is mostly ipsilateral (Buergers et al., 2014; Ren & Isberg, 1995; Rocha & Sanchez, 2007). This suggests that neural interactions between CSD or TMD and tinnitus are based on neural circuits that are sensitive to (mostly) ipsilateral stimuli. This is consistent with the functional connections between the spinal trigeminal nucleus and the CN, which are both located peripheral to major neural decussations in the brainstem (Gelfand, 2009; Somayaji & Rao, 2014). Thus, the possible ipsilateral association between tinnitus and CSD or TMD is consistent with a cross-modal mechanism between the trigeminal systems and the CN.

To better understand a possible underlying mechanism, further exploration of the association between tinnitus and CSD or TMD is needed. This could include not only the relationship of CSD or TMD to unilateral tinnitus but also the different symptoms of TMD, such as disc derangement and pain, in relation to tinnitus.

Clinical Implications

This review implies that physical examination of the TMJ and the neck region may help explain some phenomena described by patients with tinnitus. However, our study does not provide information on possible effects of treatment of CSD or TMD on tinnitus. Nevertheless, explaining the existence of a possible association to the patient might support the patient's ability to understand and cope with tinnitus.

Recommendations

Future studies investigating the association of tinnitus with CSD or TMD should focus on improving methodological quality, such as blinding and ensuring comparability of groups, and using validated instruments for diagnosing tinnitus and symptoms of CSD. CSD and TMD should also be evaluated on the side corresponding to the lateralization of the perceived tinnitus.

Conclusion

There is weak evidence for an association between subjective tinnitus and CSD and a bidirectional association between subjective tinnitus and TMD. However, the association between subjective tinnitus and CSD/TMD, TMD (not specified), and TMDm may be overestimated due to publication bias in the available studies.

Declaration of Conflicting Interests

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Supplemental Material

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