NeuroImage: Clinical 20 (2018) 901–912

Contents lists available at ScienceDirect

NeuroImage: Clinical

journal homepage: www.elsevier.com/locate/ynicl

A meta-analytic study of experimental and chronic orofacial pain excluding headache disorders

Lizbeth J. Ayoub[a,d], David A. Seminowicz[b,c], Massieh Moayedi[a,d,e,*]

[a] Faculty of Dentistry, University of Toronto, Toronto, ON, Canada
[b] Department of Neural and Pain Sciences, School of Dentistry, University of Maryland, Baltimore, MD, United States
[c] Center to Advance Chronic Pain Research, University of Maryland Baltimore, Baltimore, MD, United States
[d] Centre for the Study of Pain, University of Toronto, Toronto, ON, Canada
[e] Department of Dentistry, Mount Sinai Hospital, Toronto, ON, Canada

ARTICLE INFO

Keywords:
Pain
VBM
sMRI
MRI
Facial pain
Orofacial pain
Trigeminal
fMRI
Brain
Plasticity
Grey matter volume

ABSTRACT

Chronic orofacial pain (COFP) disorders are prevalent and debilitating pain conditions affecting the head, neck and face areas. Neuroimaging studies have reported functional and grey matter abnormalities, but not all the studies have reported consistent findings. Identifying convergent abnormalities across COFPs provides a basis for future hypothesis-driven research aimed at elucidating common CNS mechanisms. Here, we perform three coordinate-based meta-analyses according to PRISMA guidelines to elucidate the central mechanisms of orofacial pain disorders. Specifically, we investigated consistent patterns of: (1) brain function to experimental orofacial pain in healthy subjects, (2) structural and (3) functional brain abnormalities in COFP. We computed our coordinate-based meta-analyses using GingerALE. The experimental pain meta-analysis revealed increased brain activity in bilateral thalami, posterior mid-cingulate cortices, and secondary somatosensory cortices, the right posterior parietal cortex extending to the orofacial region of the right primary somatosensory cortex and the right insula, and decreased activity in the right somatomotor regions. The structural COFP meta-analysis identified consistent higher grey matter volume/concentration in the right ventral thalamus and posterior putamen of COFP patients compared to healthy controls. The functional COFP meta-analysis identified a consistent increase in brain activity in the left medial and posterior thalamus and lesser activity in the left posterior insula in COFP, compared to healthy controls. Overall, these findings provide evidence of brain abnormalities in pain-related regions, namely the thalamus and insula, across different COFP disorders. The convergence of thalamic abnormalities in both structure and function suggest a key role for this region in COFP pathophysiology.

1. Introduction

Chronic orofacial pain (COFP) disorders involve the head, face, and neck areas, notably the masticatory muscles, temporomandibular joint and associated structures. COFP is an umbrella term that encompasses several debilitating chronic syndromes affecting the orofacial region (Benoliel and Sharav, 2010). To meet these broad classification terms, the painful syndrome must be present for > 12 weeks or persisting beyond expected healing time. As such, there are few epidemiological studies investigating the prevalence of all COFP disorders. It has been estimated that 7–11% of the population report COFPs (Benoliel and Sharav, 2008; Zakrzewska, 2013).

Pain in the orofacial region is psychologically important, as it is implicated in vital biological functions such as eating, drinking, speech and sexual behavior (Vadivelu et al., 2014). From a systems perspective, there are at least two mechanisms by which pain in the trigeminal system can potentially become chronic: (1) increased nociceptive drive along the trigeminal nociceptive pathway and/or (2) dysfunctional or aberrant descending modulation from supraspinal regions (Davis and Moayedi, 2013; Tracey and Bushnell, 2009). Increased nociceptive drive is associated with increased activity in the trigeminal nociceptive pathway's central projections, including the trigeminal brainstem sensory nuclear complex, the ventroposteriormedial (VPM) and mediodorsal (MD) nuclei of the thalamus, and further cortical projections of the trigeminothalamic tract such as the primary somatosensory cortex (S1), the mid-cingulate cortex (MCC), and the dorsoposterior insula (Sessle, 2000). Additionally, increased nociceptive drive is related to grey matter plasticity in healthy subjects (Teutsch et al., 2008). Over extended periods of time, this nociceptive barrage can drive maladaptive plasticity, and engender central sensitization

* Corresponding author at: Faculty of Dentistry – University of Toronto, 124 Edward Street, Room 260B, Toronto, ON M5G 1G6, Canada.
E-mail address: m.moayedi@dentistry.utoronto.ca (M. Moayedi).

https://doi.org/10.1016/j.nicl.2018.09.018
Received 18 April 2018; Received in revised form 17 September 2018; Accepted 21 September 2018
Available online 25 September 2018

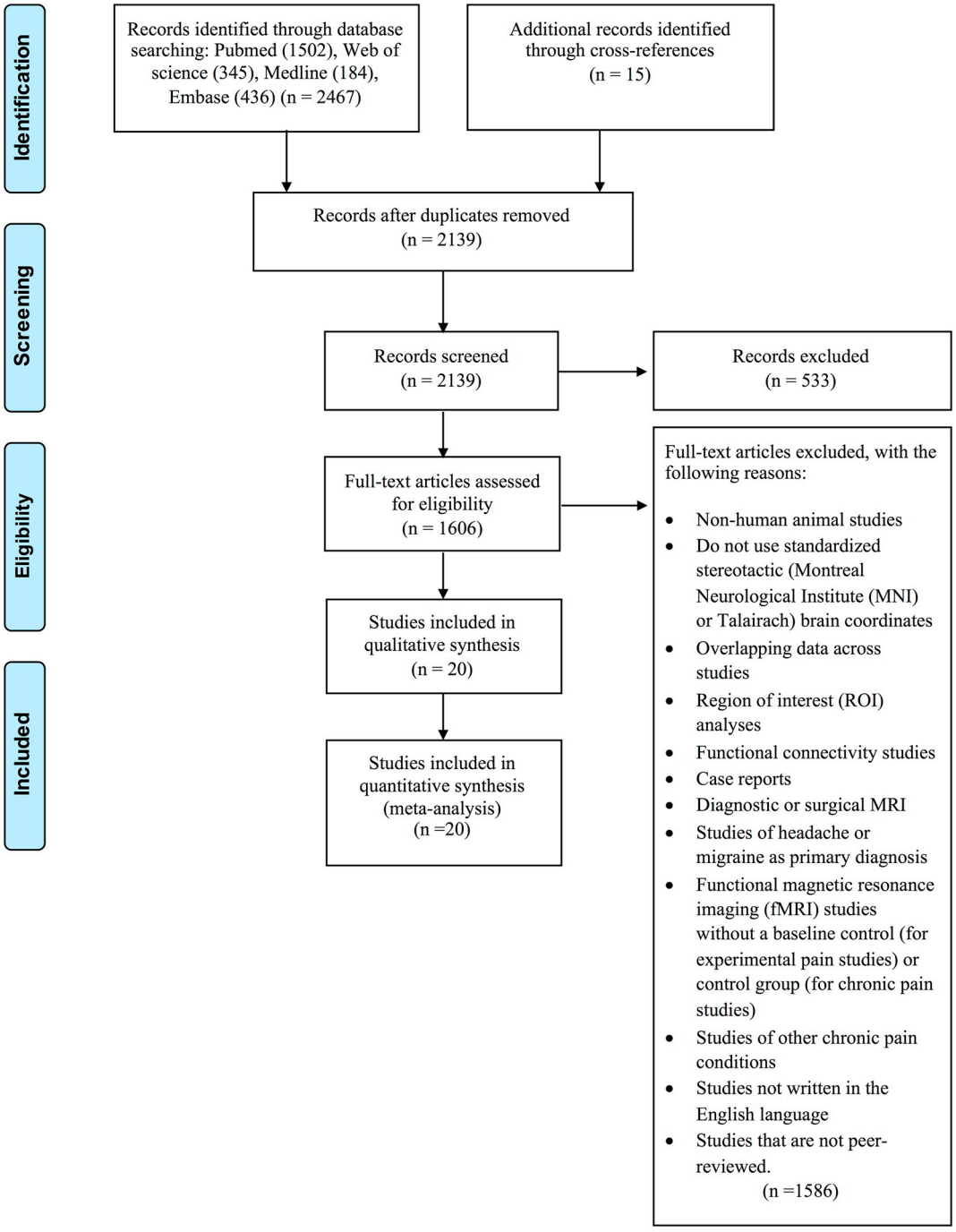

Fig. 1. Article selection for functional studies. Flow diagram according to PRISMA guidelines for functional MRI article selection procedures.

(Kuner and Flor, 2016). These processes lead to a disruption of function, and a diseased state.

Descending modulation of pain involves cortical and subcortical brain structures, typically described as including dorsolateral and medial prefrontal cortices (dlPFC, mPFC), anterior cingulate cortex (ACC), anterior insula, amygdala, and brainstem regions including the periaqueductal grey (PAG), and rostroventromedial medulla (RVM) (Bushnell et al., 2013). Involvement of these descending modulatory circuits has been reported in functional magnetic resonance imaging (fMRI) studies of placebo analgesia (Colloca et al., 2016) and conditioned pain modulation (Bogdanov et al., 2015; Youssef et al., 2016). In the diseased state, it is thought that the pain modulatory circuits become dysfunctional, where endogenous analgesic brainstem changes occur (Mills et al., 2018) and maladaptive pain remains (Sharav and Benoliel, 2015).

Here, we provide a quantitative meta-analysis of orofacial pain in health and in disease. COFPs investigated are non-odontogenic in origin and include musculoskeletal pain disorders (e.g., temporomandibular disorders (TMD)) and neuropathic orofacial pain disorders (e.g., trigeminal neuropathic pain (TNP), burning mouth syndrome (BMS)), as well as a number of other orofacial syndromes. A meta-analysis of experimental pain in healthy subjects can provide an understanding of spatially consistent brain activations in response to acute nociceptive stimulation in the orofacial region. Furthermore, separate meta-analyses of COFP structure and function may highlight consistent structural and functional abnormalities, respectively, in chronic pain. A recent meta-analysis of experimental dental pain found consistent activation in the dlPFC (Lin et al., 2014). Another meta-analysis investigating