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Perspectives on Next Steps in Classification of Orofacial Pain – Part 1: Role of Ontology

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Abstract

The purpose of this paper is to review existing principles of orofacial pain classifications and to specify design recommendations for a new system that would reflect recent insights in biomedical classification systems, terminologies and ontologies. The paper was initiated by a symposium organized by the International RDC/TMD Consortium Network in March 2013, to which the present authors contributed. The following areas are addressed: problems with current classification approaches, status of the ontological basis of pain disorders, insufficient diagnostic aids and biomarkers for pain disorders, exploratory nature of current pain terminology and classification systems, and problems with prevailing classification methods from an ontological perspective. Four recommendations for addressing these problems are: 1) develop a hypothesis-driven classification structure built on principles that ensure to our best understanding an accurate description of the relations among all entities involved in orofacial pain disorders; 2) take into account the physiology and phenomenology of orofacial pain disorders in order to adequately represent both domains including psychosocial entities in a classification system; 3) plan at the beginning for field-testing at strategic development stages; and 4) consider how the classification system will be implemented. Implications in relation to the specific domains of psychosocial factors and biomarkers for inclusion into an orofacial pain classification system are described in two separate papers.

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1 Introduction

It is a widely accepted principle that appropriate treatment of what is called ‘orofacial pain’ requires an accurate diagnosis. However, biomedical science has not yet given us the means to determine what would make such a diagnosis accurate. Because a diagnosis is an assertion *about something*, the minimal requirement for an accurate diagnosis would be a precise determination of that something. When, for example, we make a diagnosis of myofascial pain (MFP), what is that ‘something’ we are talking about? Is it the pain itself or is it what sometimes is called the underlying ‘*disease entity’* which is assumed to cause the pain? If the latter, what kind of entity is then a ‘disease entity’, what is its physical structure? Questions of this sort are questions about the ontology of pain, ‘ontology’ being the study of the type of entities that exist in reality, what these entities consist of, and how they relate to each other. Ontology, ideally, comes thus prior to terminology, which is the discipline of how to give adequate names to entities, in the hope that the relevant audiences can easily understand what the names stand for – i.e. what entities they refer to – and also use the names consistently and univocally.

Unfortunately, the ontology of orofacial pain disorders – and of pain in general – has not yet been sufficiently established which leads, for instance, to diagnostic criteria regarding orofacial pain disorders which vary considerably across publications. This variation between diagnostic criteria can cause misalignment of the diagnostic process and lead to inadequate coverage of the breadth of orofacial pain disorders (1). Indeed, the International Headache Society (IHS), the American Academy of Orofacial Pain (AAOP), and the International RDC/TMD Consortium Network (Consortium) are all constantly monitoring, if not revising, their respective classifications due to the evolving understanding of the respective disorders. The need to revise classification systems also emerges because our classification systems are based on the changing foundations of scientific knowledge and understanding.

Differential diagnosis of painful pathologies in the orofacial region is a challenge, not only because patients present with overlapping signs and symptoms, but also because they often have the added challenge of comorbidities. Since pain diagnoses mainly derive from interpretation of the patients’ histories, it is essential for the clinician to be open-minded and to search for what is hidden behind patients’ words when they describe their pain. Therefore, the derivation of diagnoses from different perspectives warrants further exploration and development. Insights gleaned from these can contribute to a classification for orofacial pain disorders based on reliable diagnostic criteria.

The challenge regarding orofacial pain is similar, though of larger scope, to the one posed by temporomandibular disorders (TMD). Diagnosis and treatment of TMDs have suffered for a long time by the lack of clarity about what should be classified under this term (2). The most commonly used research classification system for TMD has been the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) (3). Table 1 lists major milestones

that have required substantial investment, collaboration, and critique in order to develop criteria for the assessment TMDs. The success of this approach for TMDs is, at present, supported by a number of indicators:

- the extensive amount of research worldwide on TMD over the past 20 years that was stimulated by the publication of the RDC/TMD in 1992;
- the recursive aspect of the RDC/TMD by which it facilitated research on itself;
- early recognition of the RDC/TMD as a model for all chronic pain disorders (4);
- successfully addressing criticisms of the RDC/TMD and subsequent increasing approval of the draft versions of the DC/TMD at scientific meetings (5–9)
- critical analysis by RDC/TMD researchers of the state of the art in applying the RDC/TMD protocol (7, 9–11);
- funding by NIH for the Validation Project (Schiffman, PI), in order to examine the reliability and validity of the RDC/TMD (12);
- funding by NIH, because an operationalized classification system existed (RDC/TMD), for OPPERA (Maixner, PI), in order to identify etiologic factors involved in the disorders (13);
- bridging clinical and research domains via publication in the newest AAOP Guidelines (14), and
- use of the RDC/TMD as the exemplar for development of diagnostic criteria for all chronic pain disorders (15).

The method used to develop diagnostic criteria for TMD suggests that it may be feasible, utilizing similar efforts, to develop research diagnostic criteria for other types of orofacial pain disorders. The above indicators of progress associated with the development of the TMD diagnostic taxonomies demonstrate the widespread adoption and acceptance of the classical clinical approaches to taxonomy development. However, these many successes should not obscure the many questions that continue to surround the classification of pain-related disorders.

The science behind the etiology, pathophysiology and management of pain disorders, including orofacial pain and TMD, is still in an exploratory phase, and one result is that the terminology used in the domain remains in permanent flux. More research is thus required to discover the ontological basis of pain disorders. That is, we must find out what entities exist that are to be named, and find out what names currently in use do, or do not, reflect accurately what these entities actually are, if anything at all. For example, is myofascial pain, as the name suggests, actually related to disorders at the level of muscle and fascia? Or is it actually only pain felt in muscle that is centrally generated? The latter has been suspected for some time (16), but the available diagnostic systems did not appear to have the facility to incorporate this view.

At a similar level of importance to developing research diagnostic criteria based on sound ontological principles is research into diagnostic aids and biomarkers for pain disorders.

Whilst diagnostic tests for pain-related common TMDs exhibit sensitivity and specificity > 0.90 (17), the link between the test and underlying pathophysiology of the disorder remains poorly understood. As a potential bridge between clinical tests and underlying pathophysiologic processes related to the disorder, biomarkers deserve investigation. Although the presence of certain psychosocial entities has been demonstrated to impact on the prognosis of pain patients, more research is also required to assess the effect of psychosocial factors as moderators or mediators for each of disease progression and treatment outcome. Moreover, the relationship between moderating or mediating variables and biomarkers, such as for psychosocial factors or pain mechanisms, warrants attention. Collectively, these domains point to areas where the present approach to classification needs to be carefully evaluated and revised as additional knowledge accumulates.

The authors of this paper were invited to review the state of the art with respect to formal development of diagnostic criteria for orofacial pain disorders with the goal to examine the arguments in favour of or against the development of Research Diagnostic Criteria for Orofacial Pain (RDC/OFP) and to assess methods and techniques that most likely would lead to success. Their findings were presented and discussed during a symposium organized at the 2013 IADR General Session in Seattle and sponsored by the International RDC/TMD Consortium Network. The domains and perspectives represented by the authors are: orofacial pain disorders, qualitative research, behavioural medicine, medical classification and related statistical methods, and realism-based ontology. The selection of these specific domains and perspectives was not intended to be a comprehensive list of domains relevant for classification; rather, they represent a particular direction of interest to this group.

Questions for which answers were sought included 1) whether traditional and conservative approaches to medical classification are sufficient or whether they need to be complemented by recent developments in the application of ontological realism (described below), 2) whether psychosocial constructs identified for TMD are useful for orofacial pain, 3) whether qualitative research methods could provide significant insights into orofacial pain which would potentially affect how we identify entities as well as axes or dimensions, and 4) how biomarkers might be incorporated into an emerging classification system. In this paper, we outline some major issues associated with the first question concerning classical approaches to medical classification. We also offer suggestions for avoiding problems that may result from not dealing with them appropriately, and we provide some overall recommendations for developing an RDC/OFP. The ontological literature is, in general, difficult for the non-specialist to enter; we are not aware of any other ontology papers with the goal of serving as a tutorial for the field of pain. We try to provide an introduction, but this paper may be difficult to understand at times, given that the language is that of ontology and is necessarily one of precision. The two other papers in this series (18, 19) address the remaining three questions and include applications of what we develop in this paper to the respective domains of incorporating psychosocial entities and incorporating biomarker entities into a classification system.

2 What is ontological realism, and how does it relate to pain disorders?

Ontology, is devoted to the study of what entities exist in reality and how these entities relate to each other. Applied to pain, an ontological account of pain is thus one in which researchers try to determine what type of entity – or types of entities in case the word 'pain' would be used in multiple senses – pain is, and what other types of entities must exist for pain to exist. To compound the difficulty, the use of 'pain' in multiple senses (or meanings) might not even be recognized. This situation can be readily illustrated with a historical medical example: for nearly 50 years everyone accepted the assumption that what used to be termed 'diabetes type 1' and 'diabetes type 2' were two subtypes of a single disorder, 'diabetes'. We now know that there is no 'diabetes' at all and that 'diabetes type 1' and 'diabetes type 2' are two distinct and unrelated diseases. Therefore, experts no longer formally use the term 'diabetes', yet non-experts and patients still use that term due to not knowing that diabetes does not exist. Simultaneously, two other types of entity exist of which they are unaware.

Ontological Realism has been developed as a specific philosophical theory that offers a principled methodology to (1) analyse domains of interest and (2) build representational artefacts called 'ontologies' that mimic the structure of reality in accordance with our best scientific understanding (20). Ontological Realism is based on three axioms. The *first axiom* is that there is only one reality, and that one reality is objectively the way it is, i.e. organized in only one specific way.

The *second axiom* is that this reality is accessible to us – we can smell, hear, see, feel, etc, parts of it – and as a consequence, thanks to the anatomy and physiology of our brains, we are able to build cognitive representations of that reality and engage in scientific research.

The *third axiom* is that these cognitive representations are not necessarily immediately and fully accessible, and therefore we need ways of communication through one or other form of language. Terminologies, classification systems, and ontologies, when properly designed and corresponding closely to reality, contribute to better communications linking our representations to the underlying reality.

The jaw stretch reflex is an example of the accurate application of these three axioms: (1) it exists, at least according to our best scientific understanding; (2) its existence has been discovered; and (3) a name has been given which adequately encodes what this reflex is all about. This name also reflects the ontology of the part of reality in which jaw stretch reflexes exist since (1) other sorts of stretch reflexes were discovered and (2) the jaw stretch reflex was correctly recognized as being a specific kind of stretch reflex related to the jaw.

Adherence to Ontological Realism allows authors of ontologies, when sufficiently trained, to describe unambiguously and reproducibly what is generic in their domain of interest in line with relevant scientific theories, and to classify discovered entities. Here, 'entity' is anything existing such as, for example, *processes*, *objects*, *qualities*, *dispositions*, and so forth. Most importantly, Ontological Realism distinguishes between *particulars* and *types*. Particulars are entities that carry identity such as this paper, the first author of this paper, and the headache he suffered from while writing this paper. *Types* are generic entities which we

refer to by using unqualified terms such as ‘paper’, ‘human being’, and ‘pain’ thereby not referring to any specific paper (such as the one you are reading right now), human being or pain. Particulars are said to be ‘instances’ of types and all particulars that are instances of the same type form a *class*.

The method proposed by Ontological Realism resulted, for example, in the Ontology of General Medical Science (OGMS). This system provides a collection of carefully defined representational units that allow biomedical researchers to describe and classify what they observe in terms of, for instance, *disorders*, *diseases*, *diagnoses*, *clinical pictures*, and so forth. In addition, OGMS allows biomedical researchers to identify where terminology as currently used goes astray (21). This methodology allowed us, for example, to distinguish six types of pain-related phenomena implicitly present in the IASP definition for ‘pain’ (22). This methodology also allowed us to provide an ontologically adequate description of what is called ‘persistent dento-alveolar pain disorder’ (PDAPD) (23). PDAPD is an ontologically adequate description because it leaves no room for misinterpretation as to what each term used in that description corresponds to in reality. For example the pain that patients with PDAPD suffer from is persistent, is constant over time, occurs in the dentoalveolar tissues, and, surely, is a pain. The use of the word disorder at the end of PDAPD is important because it expresses that when the term is used as a diagnosis relative to some patient, it does not refer to that patient’s pain, but to the disorder which forms the physical basis for that pain.

The ontological basis for describing some portion of reality – for example the parts of reality involved in causing, feeling and treating pain – is considered to be established when scientists have been able to identify the types of entities that are part of it, and how instances of these types relate to each other. Despite tremendous advancement in the field of pain research in recent years, for example in the neurophysiology of pain, researchers have not yet been able to obtain a complete picture of the ontological basis of pain disorders. They also cannot answer the question of whether the class of ‘pain disorders’ constitutes a group of entities or is just the result of a temporary delineation inspired by lack of deeper insight. Evidence for the latter are: (1) the unavailability of sufficient diagnostic aids and biomarkers, (2) the shifts in terminology, and (3) the rather haphazard way in which current pain classifications are designed, all signs of a science being in an exploratory rather than explanatory phase. Answering the question will be simpler when pain researchers are offered the methods and tools to communicate about their findings in ways which are consistent with a given ontology. In case no agreement for one specific ontology of choice can yet be reached, they will need to communicate about how and in which parts competing ontologies differ from each other.

3 Problems with current approaches to classification

Diagnostic classifications, when adequately designed, are important for many reasons. Initially, disease-related classifications aimed to achieve nothing more than documenting cause of death (epidemiology of mortality) (24, 25). Diagnoses based on accurate diagnostic classifications usually dictate therapeutic options and indicate a prognosis. Diagnostic labels offer a form of common language researchers can communicate in, for instance to classify

for research purposes patients who exhibit certain similarities in groups that distinguish them from patients classified in other groups. Moreover, high quality diagnostic classifications are the foundation of reliable health statistics and, in turn, these significantly affect health care policies. Accurate and unambiguous classification of relevant clinical syndromes also ensures proper reimbursement of health care providers for their services (26).

However, at least three requirements have to be satisfied to maximize these benefits. The *first* one is that the content of a classification should reflect exactly what exists in reality. If it is the case that diseases truly exist in various types, then an ideal classification of diseases should contain precisely one representational unit for each distinct type of disease that exists. In this manner each particular disease from which a patient is suffering can be asserted to belong to the class formed by all instances of that disease type. Note that what commonly – nonetheless wrongly – would be called '*a definition for disease*' need not exist for diseases to exist. For example, human beings clearly existed a long time before there was an attempt to 'define' human being (first axiom of Ontological Realism). What requires definitions are not the types of entities we discovered to exist through scientific research, but rather the representational units – such as terms – that we select to denote these types so that when we use these terms in communication, our audiences do not understand them differently than intended.

The *second* requirement is that the structure of the classification reflects how the corresponding part of reality is organized. If, for example, a diagnostic classification has *as its purpose* to provide *the most effective treatment*, then the classification must be derived from an ontology which includes representational units for the entity types *diagnosis*, *treatment* and *outcome* as well as for all subtypes thereof. The required level of detail – in ontological terms: the level of *granularity* – for these subtypes must be such that any further detail in, for example, some specific subtype of diagnosis would not lead to a different outcome for any of the treatments already associated with that specific subtype. If the goal of the diagnostic classification is to provide *the most cost-effective treatment*, then the underlying ontology needs to contain additional representational units for the entity *cost* and its relevant subtypes up to a level of granularity satisfying the same requirement explained. This may result in a diagnostic classification which is differently structured than the one designed for optimal care. Different does not, however, mean contradictory: there will be more detail in certain areas of the first ontology and in other areas of the second one, but, when both are correctly designed, the two ontologies could be fused into one without causing any inconsistencies.

The *third* requirement relates to what the classification has to offer in terms of assisting its users in classifying cases correctly, for instance by using appropriate terminology, maintaining clear definitions for terms, providing criteria for class membership, and so forth. For example, although an ontologically accurate definition for the term 'human being' would be one stating that the term refers to entities whose parents are human beings (it is ontologically accurate since it is indeed the case today that *all and only* human beings have other human beings as parents), it does not help an alien from outer space to successfully identify whether one or more of the various life forms an explorer ship collected are

instances of human beings unless that alien knows already what human beings are, how they look like, etc.

Clearly, these requirements are currently not met by diagnostic classifications existing today, and for sure they are definitely not met in the domain of diseases which manifest themselves through the primary symptom of pain, for example, headache and orofacial pain. The current goal of pain classifications is rather to gain scientific insight into what is the case in reality: we are still using classifications to *discover* rather than *represent* what is the case, testing them as models which we know will need to be refined in the hope that at some point we will get it right. For this strategy to work, we need to ensure that our classifications are built so they do not lead to a distorted view of what we actually believe to exist or that prevent us to see all and only those portions of reality we want to include for the specific purposes the classification is designed. Thus we need instruments to guide us toward what there is to discover (content) and instruments to represent relevant discoveries appropriately through classifications and criteria (form).

The current headache and TMD classification systems are, among pain disorders, the most well-developed at this time. The lack of an ontological basis for either of these major diagnostic systems is reflected both in the terminology and the structure which should be improved to be more precise and unambiguous than they have been thus far. For example, in the ICHD-2, the criteria for chronic tension-type headache and for migraine without aura overlap, allowing a person to be diagnosed with both types of headache for a single headache. This overlap was corrected in ICHD-3 but other overlaps continue such as in trigeminal neuralgia and short lasting unilateral neuralgiform headache attacks with autonomic features. For TMD, while the common disorders exhibit criterion validity (17), the uncommon disorders (27) reflect only face and content validity at this time. The standard path forward is one of multi-site research in order to obtain data from enough individuals with these relatively rare conditions that empirical analysis can be conducted.

4 Adequate diagnostic aids and biomarkers for pain disorders are lacking

Diagnosis should not be confused with disease or disorder (‘disease’ and ‘disorder’ being terms which in medical prose are used almost interchangeably (21)): diseases are inside the patient, diagnoses are essentially created by the clinician and exist in his understanding.

Furthermore, we often use diagnoses that are defined without knowledge about underlying disease processes. As we elucidate the exact processes underlying the disorder, diagnosis approaches aetiology and ultimately the ‘true disease’ (28). This is common in all areas of medicine. Consider migraine that was not too long ago considered to be a ‘vascular’ headache. Following investigation we now appreciate the complexity of the underlying central nervous system events leading to a migraine, and the vascular changes are now understood as only epiphenomena (e.g. see (29)).

Health-care providers have become increasingly dependent on a wide array of laboratory and imaging studies to diagnose and subsequently manage their patients’ diseases (30). Over the years research has enriched medical practice with specific diagnostic biomarkers that aid in diagnosis and enable assessment of disease control or severity. Unfortunately, these

laboratory and imaging studies are largely unavailable in the field of orofacial pain (OFP) (31–33) and headache (HA) (34–37). Ongoing research (e.g., (38, 39)) may change the situation but currently the predictive value of available biomarkers in primary OFP or HA diagnosis is very low (19).

We must, however, appreciate the limitation of diagnostic tests in any clinical setting but particularly so in the diagnosis of OFP and HA. In the absence of adequate biomarkers, the diagnosis of OFP and HA is based on the clinician's ability to recognize a particular combination of signs and symptoms in his or her patient. Diagnosis, however, remains heavily reliant on the patient's 'story' as the proxy for the full symptom profile of the phenotype, the way it is related, and how the clinician interprets these. In many ways the diagnosis of OFP and HA is as much an art form as a science.

5 Current pain terminology reflects the exploratory nature of research in pain disorders

The discipline of giving diseases *names* is commonly termed – depending on the principles applied – 'nomenclature' or 'terminology'. Historically, many diseases have been given the names of the scientist who initially described them (e.g., Charcot Disease) or of a patient who suffered from it (eponyms; e.g., Lou Gehrig's Disease). As knowledge accumulates however, the common consequence is the re-definition of a disease and eventually its name (e.g., ALS: amyotrophic lateral sclerosis, as the rename of Charcot Disease and of Lou Gehrig's Disease). In the field of TMDs, for instance, the recognition and classification of separate joint and muscle disorders in the late 1980's and early 1990's (3, 40) opened an opportunity to revise old and irrelevant terminology. Much of this work has been admirably completed in regards to joint disorders but we are still lacking in regards to muscle pain, particularly chronic masticatory muscle pain. This is often termed 'regional myofascial pain disorder' or 'masticatory muscle myofascial pain' (MMP) (41); both terms are still based on an unsupported premise that the muscle and surrounding fascia are the origins of the underlying nociception. More recently 'persistent orofacial muscle pain' (POMP) was suggested as an alternative to MMP (42). In this manner, tension type headache which was classically thought to present with pericranial muscle tension and hence tenderness is now recognized as being able to present with and without muscle tenderness (43). Similarly MMP was described as accompanied by limitation in the jaw's range of motion, with initial classifications of MMP with and without limitation of range of motion (3). The absence of empirical data demonstrating any utility in making that distinction has now, however, led to it being discarded in the revised TMD taxonomy (17). Clearly until the aetiology of a complaint is determined and until the phenotype is clearly identified, medical terminology is by necessity imprecise (44) in the sense that the names do not adequately reflect the nature of that what is named.

Not withstanding these inherent limitations, clinicians, researchers and the international literature usually adopt strict criteria embedded within universally accepted names of diseases. This ensures a common "medical language" but establishes a potential fiction whereby the disorder name reifies the constellation of stated characteristics as a construct that is widely accepted but for which a unique physical basis may not actually exist. The

development, however, of a common medical language, even if flawed, may nevertheless serve a useful stage-specific purpose whereby data and observation can accrue under the rubric of the “common name” such that evidence can support discarding the term. This situation occurred in the evolution of the RDC/TMD to the DC/TMD (17). One goal of the present paper is to describe methods whereby this process can be improved, shortening the development time of useful classification systems. That several of the present paper’s authors have published research literature and/or monographs that perpetuate this problem by the presentation of disorders with ’accepted’ names is certainly reason to advocate a more critical approach using better principles for identifying a ’disorder’.

Contributing further to such reification are society’s beliefs regarding what constitutes health versus what constitutes disease. As human diseases affect people of varied attitudes, expectations and cultures, the very concept of disease is heterogeneous, yet current taxonomic systems do not generally make that distinction. For example, the ICHD-2 has included low levels of headache as a disorder, whereas headache specialists may regard such low levels of headache as a normal characteristic of life (for example, within the range of normal allostasis) and not a formal disorder. Since the basic idea of disease hinges on deviation from health, the two are intimately related. Whether people believe themselves to be subsequently “ill” varies with class, gender and ethnic group. These are critical issues that must be confronted when constructing a disease taxonomy, regardless of whether using ontological methods or other approaches. Further elaboration is, however, beyond the scope of this paper and is, in part, addressed in Durham et al (18); moreover, we hope that others will pursue this issue with regard to orofacial pain taxonomic development.

6 The exploratory nature of pain research and management is also reflected in pain disorder classifications

6.1 Prevailing design philosophies

Classification, in general, aims to organize a group of entities into a logical and applicable system that typically possesses a number of characteristics. A classification is based on a plan or “schema” (a formal description of its structure) that depends on its purpose and that embeds or reflects the view and underlying reasoning of its designers (usually a committee) in terms of how they believe the corresponding domain to be structured. Since a domain can be perceived from many different perspectives, there are many ways to organize differentiating characteristics in a classification.

The most prevalent approach for the classification of pain has been the definition of individual disorders based on the specific combination of clinical signs and symptoms. The International Association for the Study of Pain [IASP] (45), the International Headache Society [IHS] (43), the International RDC/TMD Consortium Network [Consortium] (3, 17, 27), and the American Academy of Orofacial Pain [AAOP] (14, 46) all base their classifications on this approach. To validate that a specific combination of signs and symptoms that define the disorder is reliable, advanced statistical methods are applied (47–51). Many classification systems find their initial application in the research setting (52), for example the RDC/TMD (3). The RDC/TMD classifies a number of painful and non-painful

disorders of the temporomandibular joint and muscles of mastication. As discussed previously, the extensive use of the RDC/TMD in the research setting has led to a need to simplify, expand and refine this system (11, 53, 54).

While some classifications are designed towards one purpose, more advanced classifications may be versatile enough to cover a number of different purposes. For example the classification of the IHS is a hierarchical system that allows increasingly detailed levels of diagnosis, each level suiting a specific purpose. So as to be a user-friendly and efficient classification, the diagnoses (objects) should be in as few groups as consistent with its purpose. A classification that aims to record the epidemiology of 'headache' may only need to record the major classifications of these as presented in the major divisions (level 1) of the IHS's classification (43). In contrast clinical research on the social impact of migraine headaches will require more detailed levels of classification (level 2 or 3). It is interesting to note that there are "off-shoots" of these classifications based on specific characteristics. Thus "chronic facial pain" (55) or "chronic daily headache" (56) have appeared as 'temporal', and "indomethacin responsive headaches" (57) as 'therapeutic' sub-classifications. The former is probably most useful in epidemiologic and disease burden studies whilst the latter allows a treatment-dependent diagnostic challenge. However, neither approach offers much advantage in guiding clinical diagnosis and therapy (55).

Beyond these requirements, different groups may adopt different grouping philosophies. "Lumpers" will tend to prefer classifications with major definitions that include larger patient populations whilst "splitters" tend to subclassify (52). At the extreme, a "splitter's" philosophy may lead to the conclusion that there are no diseases, only patients (52)! Of course, we need both approaches. Regardless of the chosen "schema" and the number of groups, the classification must include and define (accommodate) all of the diagnoses in its predefined set of diseases.

It is common to see that classifications have one or more categories termed "other" or "wastebasket" diagnoses (categories). Indeed we all have patients with chronic OFP whose diagnosis remains elusive (47, 58, 59). The signs and symptoms do not neatly "pigeon hole" into established diagnoses. Many of these share temporal features: pain for most or all of the day, which is long standing or chronic (defined here as > 6 months) (60). Past attempts at terminology have left us with diagnoses of 'diseases' such as atypical odontalgia, atypical facial pain, and persistent idiopathic facial pain; these are inadequate as they tend to lump a number of underlying diagnostic entities that may present with similar, but subtly different, clinical phenotypes (61, 62). An alternative method whereby (based on findings) diagnostic hypotheses are tested enabled us to define novel entities such as 'neurovascular orofacial pain' (47, 63, 64) and 'painful traumatic trigeminal neuropathies' (65, 66).

Multi-axial systems recognize the biopsychosocial model of pain with the inherent complexity of the pain experience and the clear relationship between onset, treatment response and psychosocial issues (67–69). For example the RDC/TMD includes a separate axis for the classification of psychosocial dysfunction/suffering. It would clearly be an advantage to have integrated classifications of OFP and of HA that take into account psychosocial factors. These factors may represent mechanisms that shape the expression of

the phenotype at the diagnostic level (e.g., whether the threshold for reporting of ‘pain’ in response to palpation is above or below the diagnostic test stimulus level) or affect comorbidity, prognosis, and/or response to treatment. While the development of multi-axial systems represents a positive development in disease conceptualization via the application of the biopsychosocial model to pain disorders, such systems are not without problems as discussed in the next section.

6.2 Issues with prevailing classification methods from a clinical perspective

For a number of reasons current classifications are not always accurate or adequate. Often syndromes overlap in their clinical phenotype. For example, tension type headache (TTH) may be extremely difficult to differentiate from a mild migraine without aura because of overlap in the appearance of ostensibly ‘diagnostic’ features. Mild nausea and photo- and phonophobia may also form part of the TTH phenotype (43), TTH may be aggravated by exercise (70), regional muscle tenderness is equally prevalent in both types of headache (71–73), and even headache precipitants are identical between migraine and TTH (74). Interestingly “TTH” co-existing in migraine sufferers responds to sumatriptan, a migraine-specific drug, whilst in non-migraine patients ‘TTH” does not respond (75). This suggests that the responsive “TTH” may be a form of mild migraine headache and supports their phenotypic overlap. Does one headache type have variable features, between individuals or perhaps within the same individual across time, or do these characteristics support two different headache types? Field-testing of classifications often reveal novel subtypes of the same diagnosis or new diagnoses hidden within previous ones. Thus cluster headache (CH) was extracted from “migraines”, and subsequently paroxysmal hemicrania was sub-classified from CH.

In some cases, classifications may be limited in their scope and clinicians need to use more than one. For example the IHS classification is lacking in its approach to OFP, and to attain reasonable diagnostic levels the AAOP and RDC/TMD classifications have both been needed (47); one recent advance has been the reconciliation between the clinical (AAOP) and research (RDC/TMD) systems with the publication of the DC/TMD (17) that is also incorporated in the newest edition of the AAOP guidelines (14). Problems occur even with specifically tailored classifications; recent validity studies on the RDC/TMD conclude that the specified clinical tests as independent diagnostic criteria would be unacceptably susceptible to diagnostic misclassification. Moreover, while the more common diagnoses had good examiner reliability, some lack of agreement was clearly present, even when well-trained examiners perform these procedures (76).

Finally, a primary challenge for multi-axial systems is synthesis by the clinician of the many fragments of information and answering the question: which axis (if any) best defines the disease for this individual? For example, a patient with recurrent headache temporally linked to recurring stressful life events could be diagnosed according to the type of headache or could be diagnosed as a stress disorder (where the headache is just another symptom of the stress). At present, negotiating this type of direction in a diagnosis is clearly part of the art of medicine; while we in no way wish to diminish the significance of the phenomenology associated with a clinical phenotype – that is, the role of a patient’s narrative of disease, we

do believe that such circumstances in diagnosis (headache vs stress as the “real” disorder) could surely be better reflected in our disease concepts rather than left to the art or whims of a given provider.

7 Problems with prevailing classification methods from an ontological perspective

Even when clinicians and biomedical researchers are experts in their domain, there is no guarantee that they are also experts in designing terminologies or classifications for use in their domain. That the publication of a (new version of a) classification is based on consensus is also not a guarantee for quality. Moreover, quality is usually measured or expressed in different ways. One aspect of quality is the degree to which users are able to classify cases in the same way. Another aspect is whether all cases can be classified, and an altogether too easy solution to guarantee full inclusiveness is the introduction of ‘other’ or ‘not elsewhere classified’ type of classes. Consistency of classification can be increased by using criteria for class membership. But then these criteria need to be defined in such a way that following the criteria does not lead to cases being classifiable in more than one class such that, in the event of a diagnostic classification, a specific patient may be diagnosed as having two disorders at the same time while in reality that patient has only one disorder.

Quality from an Ontological Realism perspective is more demanding. It means for classifications that the definitions for classes must follow certain principles, and that these classes correspond to the ontological categories that follow the principles of Ontological Realism. If the classification is designed for the medical domain, then the classes should be based on OGMS. The main goal for these additional quality criteria is to ensure that ontology-based classifications cannot only be reliably used by humans, but also that datasets collected in their terms can be fully integrated. The principles can also be used to demonstrate how, for example, pain classifications fall short of good ontological and even terminological design in many respects. This will be illustrated by listing some important guidelines and demonstrating how these are inconsistently adhered to in the International Classification of Headache Disorders (ICHD-3) (http://ihs-classification.org/en/), specifically in the newly revised Chapter 13; this is followed by examples from the DC/TMD. These example taxonomies were chosen because the complexity of headache and facial pain readily lends itself to exhibiting violations of the ontological principles.

7.1 P1: Be explicit whether assertions are about particulars or types

Assertions should be construed in such a way that the terms used therein are unambiguous, including whether types or particulars are intended. The description in ICHD-3 for ‘*13.11 Persistent idiopathic facial pain (PIFP)*’ which reads ‘*persistent facial pain with varying presentations and without clinical neurological deficit*’ violates this principle. The term ‘*persistent facial pain*’ in the latter is ambiguous as it can be interpreted as denoting either a particular or a type. Interpreted as denoting some particular, it means that for a specific patient to have such a pain, that pain – i.e. that very same patient’s pain and not some other patient’s pain – should present itself in various ways, for instance dull now, throbbing then, and so forth to qualify for being an instance of the type PIFP. Interpreted as denoting a type,

instances would be themselves invariant, thus some instances being dull, others throbbing, and so forth.

7.2 P2: Be precise about the sort of particulars to be classified using the classification

The ICHD-3 and its documentation do not present a coherent view of what might be the most generic type of which all particulars to be classified should be instances of. In the preface we are first told it is *disorders* and later *patients*, while some of the definitions indicate that it is *pains*. The recently revised Chapter 13 has as title '*Painful cranial neuropathies and other facial pains*', thus indicating that it is both *pains* and *disorders* that are classified therein. Inspection of the hierarchy adds other types to the mix such as, for example, *palsies* and *syndromes*. Although certain instances of patients, pains, palsies, syndromes and disorders are related to each other, most of these instances cannot be instance of more than one of these types. It makes therefore no sense to classify all these entities in a mono-axial system.

7.3 P3: Particulars that correctly can be classified at a certain class level, and thus are instances of the corresponding type, should also be instance of all the types that correspond with higher-level classes

The newly revised Chapter 13 exhibits several violations of this principle. It lists, for example, the class '*13.1.2 Painful Trigeminal Neuropathy*' as a subclass of '*13.1. Trigeminal Neuralgia*'. While '*Neuralgia'* is defined as being pain in the distribution of nerve(s) and pain as a sensory and emotional experience, a '*Neuropathy'* is defined as a disturbance of function or pathological change in a nerve. There is no way that one can be a special kind of the other as emotional experiences do not happen in the distribution of a nerve. Of course, when a neuropathy is painful, there is an emotional experience *involved*, i.e. *related* to the neuropathy, but that does not mean that the neuropathy itself *is* an emotional experience.

7.4 P4: Keep knowledge separate from what the knowledge is about

Several ICHD-3 classes have labels of the form '*X attributed to Y*', as in '*13.1.2.4 Painful Trigeminal neuropathy attributed to MS plaque*' which is then further described as '*Trigeminal neuropathy* ***induced*** *by MS plaque*' (note that '*attributed to'* is not consistent with '*induced by'*, an issue dealt with in P5). '*Attributed'* means, in this case, that it is somebody's opinion that the neuropathy is caused by MS plaque, leaving open the possibility that the neuropathy is not caused by a co-existing MS plaque at all. The problem here is that a feature on the side of the clinician – his or her believing, probably with some degree of confidence – is presented as if it were a feature of the neuropathy, which is of course absurd. Each instance of neuropathy either is, or is not, induced by MS plaque. It is true that this sort of classes is pervasive in classification systems but they nevertheless rest on a mistake: a confusion of ontology with epistemology (77).

7.5 P5: Class descriptions should be consistent with class labels

There are several instances where the descriptions contain conflicting (see example in P4), inaccurate or incomplete (e.g., '*13.1.2.4 Painful Trigeminal neuropathy attributed to MS*

plaque' leaves the pain out in the description) information compared to the class label. Sometimes it is additional information. It would make sense to be more consistent in the use of what is called '*description*'.

7.6 P6: Use Aristotelian definitions

Classes should have – in addition to a label and a description – a definition that provides the necessary and sufficient conditions for an instance to be a member of the corresponding class. These definitions should be in Aristotelian form, which means that they are roughly of the form: an X is a Y which Z, where Y is the immediate less specific class above X. An example would be: *a Painful Post Traumatic Trigeminal Neuropathy is a Painful Trigeminal Neuropathy which occurs after trauma* (or is caused by trauma, whatever the domain experts feel appropriate). Definitions of this form are helpful in avoiding odd shifts to happen such as between '*13.3.2. Secondary Nervus Intermedius Neuropathy attributed to Herpes Zoster*' and '*13.3 Nervus Intermedius (Facial Nerve) Neuralgia*' which would lead to the rather odd Aristotelian definition (shortened) of 'a … Neuropathy … is a … Neuralgia … which is attributed to Herpes Zoster'"; no neuropathy can *be* a pain.

7.7 P7: Clinical criteria do not replace Aristotelian definitions

Whereas definitions should describe what the entities that fall under a class ***are***, clinical criteria help in ***recognizing*** whether a particular entity might fall under the class. Such criteria are typically more restrictive than definitions should be. '*13.1.1.1 Classical trigeminal neuralgia, purely paroxysmal*', for example, exhibits the criterion '*at least three attacks of facial pain fulfilling criteria B–E*'. This criterion should not be interpreted to mean that patients who had only two such attacks do not have this form of neuralgia. They might indeed have the disorder, but the criterion does not allow a clinician to make the – perhaps correct – diagnosis. This line of thinking applies to all time-related criteria, an often encountered one being the criterion for chronic pain as pain that is present for longer than six months: if a patient does suddenly have a pain for the first time in his life, it might very well be a chronic pain, but we have no way to tell at that point in time whether that is the case unless we wait six months (78). If so, it would also be wrong to state that the patient's pain *became* chronic after six months since, again, it was chronic all the time, but we didn't know. This issue of how chronic pain defined by the past rather than the prediction of how it will unfold in the future from this point in time has been critically addressed elsewhere as well (78), also indicating the need for more sophisticated approaches to classification in order to capture "the potential for" such 'change' over time: does this represent a different disorder at the outset, or does this represent an attribute residing on a separate axis?

7.8 Examples from DC/TMD taxonomy

Examples of non-adherence can even be found in the DC/TMD and its documentation (whose authorship includes several of the present authors, hence our interest in including examples based on the DC/TMD in addition to the ICHD-3), not the least in the proposed extended taxonomy (see table 4 of (17)). Almost all labels in the taxonomy are under-specified with respect to what they stand for (P5): 'neoplasm' and 'subluxation', for example, are not intended to include any neoplasm or any subluxation, but only those

involving the TMJ. Worse, where everything represented in that table is a temporomandibular joint disorder as made clear by the highest level term (I.), there is a lower level term (I.2.) which groups what is called ‘joint disorders’. What is the difference? And if there is a difference, why assign the same term to different types of entities? The same kind of mistake is made by introducing ‘I.1.A. – Arthralgia’ as a subtype of ‘I.1. – pain’: does ‘arthralgia’ not mean ‘joint pain’? While this table represents an advancement for the field of orofacial pain, as described well in (27), its limitations were known by the authors simultaneous with the recognition that this is a work in progress.

Using Aristotelian definitions (P6/P7) might have prevented the misclassification – or, alternatively, the inadequate definition - of ‘I.5. – Congenital/developmental disorders’ directly under ‘I. – Temporomandibular joint disorders’, rather than under ‘I.2. – Joint disorders’ (if an argument for the existence of I.2. can be made at all).

The short version of the diagnostic criteria (Table 2 of (17)) contains, for certain criteria, logical ambiguities as to what would count for a positive or negative finding. While the ambiguity is in principle resolved in the examiners’ protocol (79), a separate level of concern remains with the criteria as presented for both research and clinical usage. Specifically, part of the exam for arthralgia states the following requirement: ‘2. Report of familiar pain in the TMJ with at least one of the following provocation tests: a) palpation of the lateral pole or around the lateral pole; OR b) maximum unassisted or assisted opening, right or left lateral, or protrusive movement(s)’. This leaves open the question of whether the ‘OR’ involves doing the test, or the results of the test. From the perspective of clinical efficiency, it might be sufficient that one may pick whatever test first and then ignore the 2nd one when the 1st one turns out to be positive; this would satisfy the criteria as stated. A structured exam has, as its intent, the systematic gathering of clinical data such that one has a fixed pool of findings from which to build deeper understanding of the clinical phenomena (in addition to constructing a diagnosis) – perhaps, for example, of value for a differential diagnosis related to an auxiliary clinical hypothesis. Consequently, discarding the 2nd test, because the 1st test was positive and only one finding need be obtained, negates some of the intent and value of a systematic process. Which goal does the DC/TMD have for the clinician: efficiency, or systematic evaluation?

8 Recommendations

In general, our comments indicate that the development of a classification system should be hypothesis driven; relying on only observed data does not shine the light where the keys might be found again in the future. Our comments and examples also highlight the need for ontological rigor in hierarchical classification systems to ensure that the relations expressed among classes correspond to what is the case in reality and are formulated in a way that is logical and useful. Of course, any classification system, regardless of the principles underlying its conceptual structure, must be empirically tested. Yet, a positive outcome of empirical testing is no guarantee that the principles described in section 7 are adhered to.

Consequently, our **first recommendation** for the development of an orofacial pain classification system is to create a template that carefully defines what needs to be included,

is based on hypotheses about the disorders, and guides the development of a set of principles for how the classification system will be structured. We point to the ontologies that have been developed for such purposes, and we naturally recommend that those ontologies be used, but intermediate steps in how structure is imposed into a classification system are always part of the process (15). The arrow must travel across intermediate space before it reaches its target, and of course that space can be dissected into yet smaller and smaller bits albeit at the cost of obscuring the goal.

Our **second recommendation** is that future orofacial pain classifications should also contain representations for various types of psychosocial entities, as we describe in Durham et al (18), and for relevant entities involved in the physiology and phenomenology of pain disorders. Psychosocial entities are important for the prognosis of pain disorders and are core components of emerging concepts of chronicity (78). Both quantitative and qualitative researches are of great value here. While quantitative research has identified a number of psychosocial entities for incorporation into an orofacial pain classification, qualitative research is useful for verification and explanation (80). Inclusion of representations of phenomenological entities requires still more insight into illness phenomenology. Comprehensive representation of the full scope of the respective entities requires, at this time, the incorporation of at least proxies, in the form of biomarkers, for the physiology associated with the disorders; here, “physiology” can also refer to that which underlies what might be observed as the phenomenology – the lived experience – of the entities as well. We elaborate further in this volume on both themes in Ceusters et al (19) and in Durham et al (18), respectively. In any case, this second recommendation necessitates the integration of multiple axes into one hierarchical system which is a challenging task, yet is indeed motivated following research findings that relate psychological issues with a biomarker and pain onset (e.g. (81)). With the two-axis system of the RDC/TMD and, now, DC/TMD being already challenged with a 5-axis system specifically targeting the chronic form of pain disorders (15), the challenge becomes yet greater. Such “multi-faceted” pain classifications will therefore have to include integrated criteria for sign/symptom complexes, measures of psychosocial comorbidity, etiology, consequences, and biomarkers. Their integration will ensure that all measures are used early in diagnosis, in establishing the treatment and prognosis, and in assessing outcome (82). It is here that the ontological approach can contribute a lot through application of the important ontology-based principles for building classifications as outlined above.

Our **third recommendation** is that field-testing during strategic stages of development could include qualitative research, not only of the patients but perhaps more so of the providers, in order to explore how a draft multi-axial classification system built on, for example, strong ontological principles could be better implemented in the clinical setting.

Our **fourth**, and final, **recommendation** is that requirements for implementation of a classification system should be considered as part of the overall development. The RDC/TMD was, to these experienced and perhaps biased authors, appropriate not only for research but also clinical use at the outset, in that approximately 85% of individuals with TMD-like complaints could be readily classified with the RDC/TMD (Ohrbach and Dworkin, unpublished data); we would regard that as excellent, given that those 85% of

individuals would be more reliably classified. Critiques of the RDC/TMD, however, included: the system was not comprehensive – did not classify everyone; too time-consuming; and concern that population-based parameters could be inappropriate for individual patients. Consequently, the RDC/TMD was not embraced in most clinical settings. While it was not intended for use in clinical settings, it was in fact better than most clinical diagnostic systems in that it was reliable, based on more data, and epidemiologically sound. Our fourth recommendation is aimed at trying to minimize a research-clinic split in the potential use of any developing taxonomy for orofacial pain disorders.

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Table 1

Major milestones and relevance for evolution of the diagnostic criteria for TMDs.

Year	Milestone	Relevance
1992	RDC/TMD published	Research community successful in promoting critical discussion about TMD diagnosis through use of the RDC/TMD
1999	International RDC/TMD Consortium Network established	Facilitate better collaboration among researchers
2001	RDC/TMD Validation Project initiated	Examine the reliability and validity of RDC/TMD diagnoses and Axis II
2008	Symposium sponsored by Consortium Network, held at IADR/Toronto	Researchers not associated with Validation Project invited to provide critical commentary in response to data-based presentations by Validation Project investigators
2009	Closed workshop sponsored by Consortium Network and IASP OFP SIG, held at IADR/Miami	Establish new diagnostic criteria for TMD and revise Axis II
2011	Closed workshop sponsored by Consortium Network and IASP OFP SIG, held at IADR/San Diego	Expand classification of TMD to include less common but clinically relevant TMDs, evaluate Axis II and pain interviews, and create third axis for additional measures
2014	Publication of DC/TMD and publication of revised Guidelines for Orofacial Pain by AAOP	Guidelines incorporated, for the first time, research-based diagnostic criteria