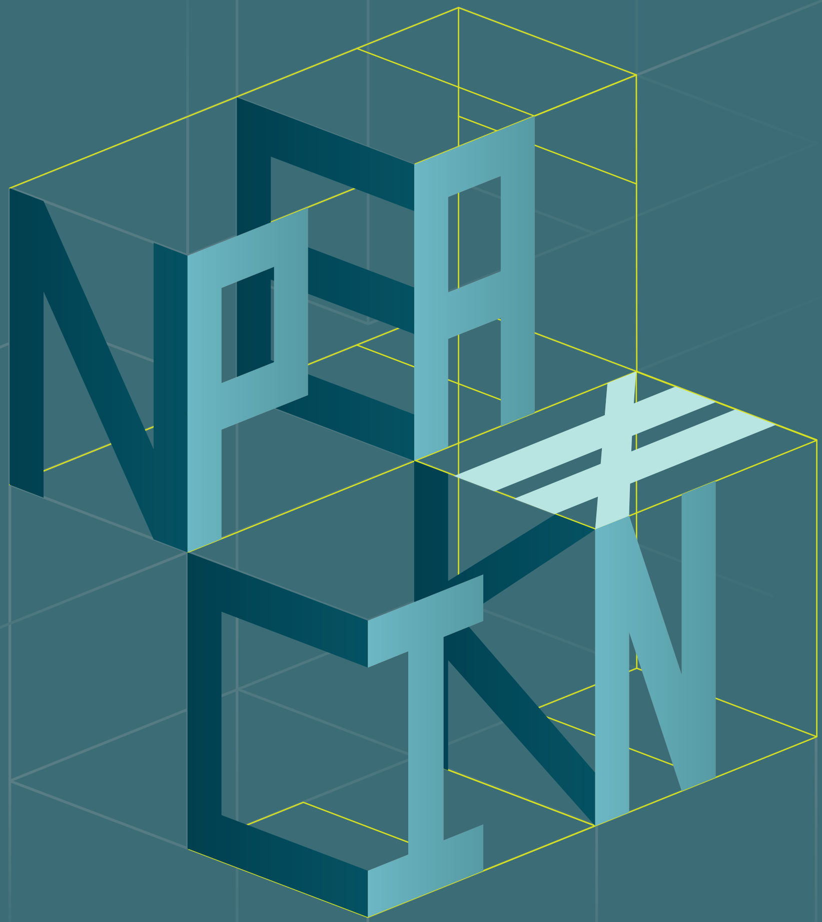

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**VINCENT
DEWITTE**

Thesis submitted in fulfillment of the requirements for the degree of
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Department of Rehabilitation Sciences
Faculty of Medicine and Health Sciences

GHENT UNIVERSITY

FACULTY OF MEDICINE AND HEALTH SCIENCES

Promotor	
Prof. dr. Barbara Cagnie	Ghent University, Ghent, Belgium
Co-Promotor	
Prof. dr. Lieven Danneels	Ghent University, Ghent, Belgium
Supervisory Committee	
Prof. dr. Katie Bouche	Ghent University Hospital, Ghent, Belgium
Prof. dr. Arne Roets	Ghent University, Ghent, Belgium
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aan Sofie, Ella Noa & César

When you reach for the stars you may not quite get one,
but you won't come up with a handful of mud either.
Leo Burnett

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Table of contents

Essentially, all models are wrong
but some are useful.

Prof. George E.P. Box

GENERAL INTRODUCTION

NECK PAIN, A PAIN IN THE NECK

Epidemiology & socio-economic impact

Neck pain is a complex and far-reaching problem that has generated interest and concern for decades. Although neck pain is less common than low back pain (LBP), few people live without ever having experienced neck pain as a result of trauma, surgery, overuse, or repetitive strain.[1-3] In industrialized countries, the annual prevalence of neck pain has been reported to range from 27% to 48%, of which, women are more often affected than men, and prevalence peaks at middle age.[3, 4]

It is commonly accepted that neck pain usually resolves in a few weeks with or without medical attention.[4-8] However, up to 23% of individuals who recover from a neck pain episode develop a subsequent episode.[9] Regrettably, approximately two thirds of people who have an episode of neck pain will suffer persistent, recurrent or fluctuating pain and disability long after resolution of the injury.[4, 9-13]

Beyond the suffering and discomfort associated with neck pain, the financial and other costs originating from spinal disorders are enormous.[12] Due to medical care expenses, costs related to absenteeism, and diminished quality and productivity in patients' work and personal lives, the burden on society only seems to increase.[2, 4, 12, 14, 15]

Owing to its devastating impact, spinal disorders remain some of the most controversial and difficult conditions for patients, clinicians, and policymakers to manage.[12] Yet, neck pain is a frequent reason to consult general practitioners, medical specialists, and musculoskeletal physiotherapists, amongst other health care professionals.[16, 17] Regarding physiotherapy, patients with a primary complaint of neck pain account for nearly 20-25% of all patients seen in outpatient physiotherapy.[18, 19]

From the above, the magnitude of the condition has become clear. Neck pain, heterogeneous in nature, comprises multiple possible causes.[7, 20, 21] At the moment, however, it rather seems to be a common symptom that a substantial amount of people share.

NECK PAIN ≠ NECK PAIN

Definition, assessment & management of neck & spinal pain

Neck pain is defined as pain perceived in the anatomic region of the neck between the superior nuchal line and the line connecting both spines of the scapulae, as outlined in **Figure 1**, with or without radiation to the head, trunk, or upper limbs.[22] This definition does not presuppose, nor does it imply, that the cause of pain lies within this area. It defines neck pain simply by where the patient feels the pain.[7]

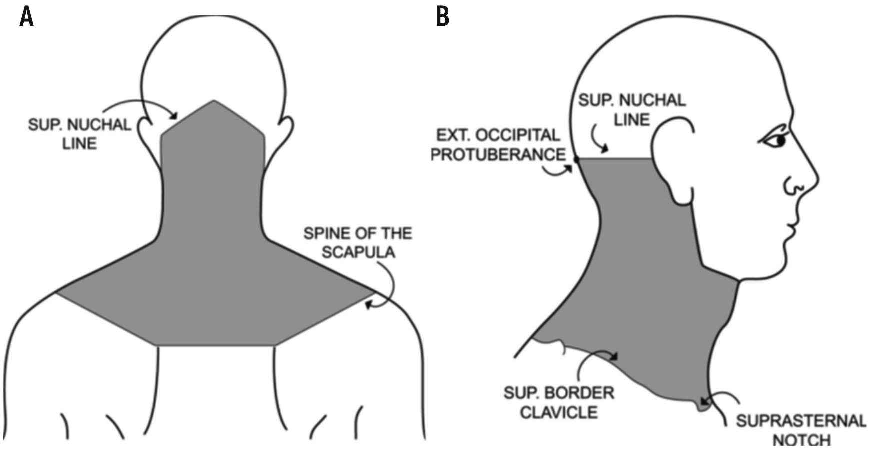

FIGURE 1 The anatomic region of the neck from the back (**A**) and the side (**B**) as defined by 'The Bone and Joint Decade 20002010 Task Force on Neck Pain and Its Associated Disorders'.

Adapted from Guzman et al.[22]

The objective of clinicians is to determine the reason and cause of this pain, and then to administer effective actions to stop and/or control it. Yet, for the majority of patients with neck pain, no single pathologic entity can be ascribed to their condition and is therefore diagnosed as nonspecific neck pain (NSNP).[20, 22-24]

Specific neck pain

From a diagnostic perspective, it is important to make distinction between specific and NSNP. For most patients that present themselves with neck pain, their complaints can be dismissed as normal, age-related symptoms.[7, 18, 24, 25] But, there is a treacherous catch. For a minority of patients there is an actual threat: a diagnosis that cannot be missed, a treatment that needs timely start-up and strict follow-up to avoid permanent damage.[26] For that reason, correct triage is of utmost importance.

A number of serious pathological neck conditions may mimic the presence of mechanical neck pain.[23] **Table 1** presents a non-exhaustive list of serious local pathologies or systemic diseases associated with specific neck pain, adopted from the available literature.[7, 8, 26-29]

Although serious, most conditions are rare, and isolated neck pain is hardly ever the sole presenting feature.[7, 29, 30] Accordingly, the practitioner should estimate the extent to which the obtained signs and symptoms pose a threat to worsen the patient's recovery or place the patient at risk for serious medical consequences. This is typically referred to as 'red flag' screening.[27, 30, 31] When clusters of findings indicate the occurrence of severe pathology underlying a patient's

TABLE 1 Red flags for neck pain associated with serious local pathology or systemic disease amended from the available literature[7, 8, 26-29]

Red flag	Potential underlying condition	Associated signs and symptoms
Relevant recent trauma	Upper cervical ligamentous insufficiency, fracture, cervical myelopathy	Occipital headache and numbness, severe limitation during active ROM in all directions, tenderness over vertebral structures, signs of cervical myelopathy
Age <20 years	Congenital anomalies (e.g. cervical spina bifida)	Weakness of the limbs, orthopedic abnormalities (i.e. club foot, hip dislocation, scoliosis), bowel and bladder dysfunction, abnormal eye movement, pressure sores, skin irritations
Age >50 years	Fracture, neoplastic conditions, carotid or vertebral artery insufficiency	See 'relevant recent trauma', 'cancer in medical history', and 'cerebrovascular symptoms'
Systemic disease: Rheumatoid arthritis, Inflammatory arthritis, Ankylosing spondylitis, Down syndrome, TB, Herpes zoster, Osteoporosis	Carotid or vertebral artery insufficiency, upper cervical ligamentous insufficiency, fracture, infection, inflammatory or systemic disease	Headache, fever, raised blood pressure, resting pulse >100 bpm, burning pain, itching, increased resting respiration, unilateral skin rash, fatigue
Cancer in medical history	Neoplastic conditions	Previous history of cancer, constant pain showing no relief with bed rest or no improvement in symptoms after 4 weeks of treatment, night pain, unexplained weight loss, age >50 years, trouble swallowing, headaches, vomiting
Cerebrovascular symptoms	Carotid or vertebral artery insufficiency	Dizziness or lightheadedness related to neck movement, double vision, nausea, vomiting, weakness of the limbs, drop attacks, dysarthria, dysphasia, positive cranial nerve signs
Infectious symptoms	Osteomyelitis, retropharyngeal or epidural abscess, epiglottitis, meningitis, spondylo-discitis, skin infection	Symptoms and signs of infection (e.g. fever, chills, night sweats), risk factors for infection (e.g. underlying pathological process, in case of immunosuppression, an open wound, intravenous drug use, exposure to infectious disease)
(Widespread) neurological signs and symptoms	Cervical myelopathy	Widespread (i.e. in both arms and/or legs) neurological signs and symptoms, including multisegmental weakness and/or sensory disturbances, bowel and bladder dysfunction, unsteady gait, Hoffman's reflex, Babinski sign, hyperreflexia, spasticity
Thoracic pain	Cardiac involvement, neoplastic conditions	Concurrent chest pain, diaphoresis, shortness of breath
Use of corticosteroids	Fracture	See 'relevant recent trauma'

Abbreviations: ROM, range of motion; TB, tuberculosis; bpm, beats per minute.

neck pain, the therapist should respond appropriately, most likely redirecting the patient's care to another specialist.[27]

Once serious pathology or disease underlying the patient's neck pain has been ruled out, it is important to discern neuropathic conditions from NSNP.[28, 32] Possible causes of neuropathic pain in the cervical spine are disc herniation with radiculopathy (lower motor neuron syndrome) and cervical myelopathy (upper motor neuron syndrome).[26, 29] A grading system of possible, probable or definite neuropathic pain can guide the healthcare practitioner in this diagnostic process.[26, 33, 34] The findings from the subjective and physical examination, and the results of auxiliary testing will determine whether the diagnosis of definite neuropathic pain is retained.[26, 33, 34] Only in case of definite neuropathic pain, the neck pain is labeled as specific neck pain.[33, 34]

Because neck pain is a prevalent and often disabling problem, it is not surprising that numerous methods are routinely used to mitigate symptoms.[28, 29] The treatment for patients with serious underlying diseases is often more aggressive, with strong support in the literature.[29] Conflicting evidence regarding conservative and invasive treatments for patients with neuropathic pain makes targeted interventions more challenging.[28, 29] In line with the overall objective of this thesis, the diagnostic reasoning process and management of specific neck pain will not be discussed in further detail.

Nonspecific neck pain – assessment

When there is no apparent cause of concern for pain caused by malignant, metabolic or infectious disorders,[35] most clinicians will usually be able to diagnose NSNP from the description of the pain, and by examining the patient.[36] Consequently, the additional costs originating from auxiliary testing, such as blood tests or medical imaging, can hardly be justified.[7, 36, 37] Indeed, there is no test that can prove or confirm NSNP. In fact, some argue that tests can actually do more harm than good in case of NSNP. This is referred to as a nocebo response.[25] For example, the technical jargon used to report on plain radiographs or scans can sometimes sound alarming, when in fact the test is just displaying what would be normal for a given age. Auxiliary tests may only be advised in certain situations in which symptoms or signs suggest there may be a more serious underlying cause for the neck pain.[28, 29, 36]

The inability to pinpoint the source of the pain makes NSNP especially challenging to diagnose. Moreover, medical diagnoses usually do not guide physiotherapy interventions very well.[38] The generic terminology used to describe this condition (e.g. Trapezius myalgia, cervicalgia) leaves the therapist with few clues to start an accurate treatment. Historically, this challenge was undertaken starting from a 'biomedical model of pain', where an often dogmatic approach led musculoskeletal physiotherapists to excessively focus on specific 'causal' structures.[25, 39] This has undeniably generated meaningful analyses, aimed at validating the tissues as sources of the pain,[39] and expanded the development of specific hands-on techniques (e.g. manipulation techniques,[40, 41] postero-anterior mobilizations,[41-45] myofascial trigger point treatments,[46-49] etc.), all of which are still being used. Unfortunately, this structural emphasis of physiotherapy does not yield fruitful results for a great deal of patients with NSNP.[25, 50] An increasing body of opinion urged to put an end to the exaggerated focus on structure-related diagnostics, and symptomatic treatment methods.[25, 50-52] Particularly, as this way of working distracts from an early activation and restoration of function, activity and participation,[50] which are presumed to be the higher purposes of physiotherapy.[53]

To fully apprehend the complex matter of NSNP, the clinician could only benefit from a **well-structured and complete reference frame**. To assist healthcare professionals, the International Classification of Functioning, Disability and Health (ICF) provided a unified and integrated framework to link the onset, course and prognosis of the patient's neck pain with its management (i.e. assessment, diagnosis, treatment, and self-management).[22, 54, 55] Where the ICF has moved away from being a 'consequences of disease' classification (version of 1980) to become a 'components of health' classification,[54] the 'biomedical model of pain' was replaced by the 'bio-psychosocial model of pain'.[52, 56] This paradigm shift served as a prelude that offered different reasoning strategies (see below) in which the multifactorial and multidimensional character of health disorders was embodied,[25, 56-63] and led to breakthrough clinical approaches with significantly better outcomes.[52]

A contemporary understanding of the **biopsychosocial model** involves consideration of the complex and dynamic influences that physiological, psychosocial, and environmental factors may have on patients' perceptions and health behaviors.[52, 56] Attention to environmental factors (e.g. unfavorable ergonomics producing excessive load and irritation of injured or sensitized tissues) and psychosocial factors (e.g. emotions and cognitions related to the patient's notion of the problem) are not new. Typically, these factors have been addressed from the perspective of how they may be hampering the normal recovery process, and how they contribute to the patient's pain state.[56]

These aspects can obviously not purely be derived from a superficial patient assessment. On the contrary, evidence on the relative contribution of the subjective exam, physical, and additional investigations in making **medical** diagnoses, highlights the importance of **detailed history-taking**.[64-67] In more than 75% of the samples studied, the history led to the final diagnosis.[64-66, 68] However, these findings may vary depending on the disorder being considered.[65] Although data on the relative contribution of the subjective exam in physiotherapists' diagnostic decision-making is lacking, similar results could be expected.

Based on good clinical practice, a comprehensive history classically assembles information on the location, radiation, severity, and quality of the symptoms, aggravating and alleviating factors, circadian rhythm, associated symptoms (e.g. movement restrictions, headache, dizziness, nausea), onset, evolution, past medical history, psychosocial influences, and results from previous testing and treatments.[8, 26, 28, 37, 67, 69, 70] It can screen for red flags, provide important clues regarding etiology, help differentiate neck pain from other possible sources of somatic referral into the neck region, reveal restrictions in activities and participation, clarify the expectations of the patient regarding the treatment, assist in identifying physical or psychosocial restrictions to recovery, and provide information relevant to the decision to pursue further diagnostic work-up.[8, 22, 26-28, 30, 37, 67, 69, 70]

Following the patient's history, the **physical examination** is often used to confirm or reject the former formulated hypotheses,[28, 64-66] but is rarely pathognomonic.[28] The basic elements of the physical examination of the neck comprises inspection, palpation, postural and movement assessment, and can be complemented with additional tests, including articular, myofascial, and neurological function and provocation tests, and/or a sensorimotor control assessment.[8, 26, 28, 37, 69-71] When deemed appropriate, complementary testing of adjacent areas, such as the shoulder girdle, thoracic and lumbar spine, and/or temporomandibular joints, can be performed.[8, 26, 69]

From an analysis of the patient's history and relevant physical examination outcomes, the therapeutic goals and tools can be determined.[57] To provide patients with NSNP the best possible care, it has become clear that clinicians should be able to address the various and diverse issues that inevitably arise from their comprehensive patient evaluations.[22, 56] How patient classification strategies and clinical reasoning models can assist in managing patient problems, whilst taking into account the biopsychosocial dimensions of their pain, is addressed in the succeeding sections.

Nonspecific neck pain - management

As previously described, the course of NSNP is affected by multiple personal and environmental factors.[22] In a modern biopsychosocial approach to neck pain, the clinician is expected to capture and interpret all the issues, that may be important in the establishment and/or maintenance of the condition. Ideally, therapists should use their clinical skills and prior experience and integrate it with the best available evidence, and the patient's values.[72-75] This process is defined as **evidence-based medicine (EBM)** and has a real impact on clinical decision-making.[75, 76] Consequently, this should lead to **evidence-based practice**, i.e. the consistent use of current best evidence from scientific research into the clinical reasoning process of the individual health professional.[75]

However, for the practitioner, it is not always evident to extract the satisfactory information from the abundance of scientific literature, often fragmented and difficult to interpret.[75] To assist clinicians in this noble process, **EBM guidelines** are designed to identify the interventions supported by current best evidence, and to find the suitable outcome measures to assess the changes resulting from these physiotherapy interventions.[73] These EBM guidelines are not to be confused with other, less rigorously developed clinical guidelines.[75] Where the former produce recommendations based on a carefully weighted synthesis of evidence and a grading of the strength of evidence, the latter might include evidence from studies without assessing the study quality or the use of grading systems.[75] Moreover, when the available evidence is limited, some guidelines include the results from consensus or expert opinion studies, which obviously lessens the strength of evidence and therefore, weakens the confidence in the recommendations made.[77] Although it is desirable for clinicians to consider recommendations presented in clinical guidelines, other factors (e.g. patient preferences, comorbidities, affordability, and availability of care) are important for the actual implementation of EBM into physiotherapy practice.[77]

According to the most recent American Physical Therapy Association (APTA) guideline on neck pain (updated in 2017), once an indication for physiotherapy has been established, NSNP is best treated with a wide spectrum of multimodal treatment options.[37] The treatment recommendations are assigned a grade of confidence (ranging from A to F) based on their strength of evidence. Appendix 1 provides a description of the grading system used by the APTA to determine the level of evidence, and Appendix 2 specifies the criteria used to determine the confidence in the evidence and magnitude of effect. All of the treatment recommendations below received a grade B (moderate evidence), except for those indicated with a C, who were assigned a grade C (weak evidence).

Interventions identified to address acute neck pain (i.e. less than 6 weeks) comprise patient education[B] and reassurance[B], exercises for the neck/shoulder girdle/trunk to reduce pain and increase mobility[B], cervical and thoracic manipulation/mobilization plus mixed exercise[B] (e.g. flexibility, stretching, neuromuscular, postural, strengthening, endurance, aerobic conditioning, functional), cervical manipulation/mobilization without exercise[C], transcutaneous electrical nerve stimulation[C], C1-C2 self-sustained natural apophyseal glide[C] (self-SNAG), laser[C] and short-term use of a cervical collar[C] (in case of acute neck pain with radiating pain).[37] Patients with **subacute neck pain** (i.e. 6-12 weeks) may be best treated with neck/shoulder endurance exercises[B], cervical manipulation/mobilization without exercise[B] (in case of neck pain with headache), thoracic/cervical manipulation/mobilization without exercise[C], and C1-C2 self-SNAG[C].[37] When patients suffer from **chronic neck pain** (i.e. more than 12 weeks) a multimodal approach of education and counseling to encourage participation in occupational and exercise activities, cervical/cervicothoracic/thoracic manipulation/mobilization in combination with dry needling, laser or intermittent traction, and mixed exercise[B] are recommended by the APTA.[37]

These recommendations largely converge with the regulations included in less recently updated guidelines of the Belgian Health Care Knowledge Centre (KCE)[31] and other international guidelines on neck pain,[36, 70] even though there can be regional differences. Yet, these well-documented and often extensive practice guidelines are susceptible to several weaknesses. First, healthcare research is not always able to capture the dynamic or individualized nature of less clear diagnoses, as is often the case in patients with NSNP.[37] Research-validated knowledge should inform clinicians but cannot be their only guide for clinical decision-making. Although the results of meta-analyses, randomized controlled trials, and other forms of empirical research will continue to contribute to the body of information that guides clinical practice, clinicians also need skilled reasoning to use that information wisely (see below).[78] The variables of a particular research study frequently do not sufficiently match the unique patient presentation for the findings to be used in a highly prescriptive manner.[78] Individual differences are particularly significant in treatment planning, as are individual beliefs, goals, and contexts.[78] In addition, healthcare science attempts to classify and quantify the scientific aspects of patient care but cannot adequately seize the intuitive and responsive processes commonly associated with the treatment processes. This will obviously limit the application of practice guidelines in certain scenarios.[37] Furthermore, although the APTA-guidelines discuss the major problem of the recurrent nature of neck pain and its conversion into chronicity, treatment recommendations typically merely consider the relief of an episode of pain.[37] Finally, some important areas of neck pain management (e.g. treatment of sensorimotor control impairments) are not covered in the APTA-recommendations because the available evidence did not meet their threshold for inclusion (i.e. there were no available systematic reviews or meta-analyses on the management of sensorimotor control impairments in adult persons with NSNP, published in peer-reviewed journals prior to August 2016).[37] In case these practice guidelines do not provide the guidance needed to approach a specific clinical case, therapists are encouraged to conduct a literature search themselves.[75] After all, evidence-based practice is rapidly growing in the rehabilitation domain.[72]

Despite the efforts made to support practitioners during their patient management, there seems to be plenty of **room for improvement**, since about one third of people who experience a first-time onset of neck pain, continue to report healthcare utilization for their neck pain at a 5-year follow-up.[79] Perhaps classifying patients with NSNP into distinctive categories entails the key to successfully improve diagnostic procedures, assist educational programs, and/or guide clinicians towards more efficient management?

CLASSIFICATION OR CLASSIFICTION?

The sense & nonsense of classifying patients

In the context of rehabilitation sciences, numerous classification strategies have been introduced to distinguish clinically relevant subgroups of patients presenting with otherwise heterogeneous disorders, such as NSNP.[22, 37, 80-92] Sample heterogeneity has been identified as a possible reason for some treatments failing to demonstrate efficacy in randomized controlled trials.[93] Indeed, within group variability can decrease the chance of finding a significant treatment effect due to the reduced proportion of the sample for which the treatment is intended.[93] Various researchers have highlighted the importance of finding homogeneous subgroups in patients with spinal pain as a **research priority**.[37, 72, 81, 93]

The idea of such classification approaches, potentially improving treatment efficiency and effectiveness by matching patients with optimal therapies, is appealing. Usually, a multistep process is obeyed, involving studies of derivation, validation and analysis of impact, to inform classification development.[81] Spinal pain is being categorized based on diverse conceptual constructs: pathoanatomical classification models,[94-99] classifications based on an association with particular events or precipitating factors,[98, 100-112] models founded on the impact of neck pain on patients' personal lives,[22] stratifications related to treatment responsiveness,[23, 82, 86, 113] subgrouping based on location and presumed source of symptoms,[37, 85] and classifications according to the underlying neurophysiological mechanisms responsible for its generation and/or maintenance.[39, 62, 114]

Only few of the existing classification systems have reached the final stage of impact-analysis.[23, 115-117] This preliminary nature suggests that further research in this area is needed and no single optimal system has been established yet.[23] To substantiate the calls for additional insights into this matter, and in addition to some of the limitations of the practice guidelines addressed above, some researchers highlight a number of **shortcomings of the current classifications**: (1) classifications based solely on the duration of pain may be too simplistic and may not recognize the presence of other important clinical features of certain pain presentations,[25] (2) certain pain classifications remain largely grounded in the medical/disease-oriented paradigm, and as such, may not be the most useful methods clinically since such approaches do not account for the variability in clinical presentations of pain nor for the multidimensionality of the pain experience,[115] (3) rigid classification models do not allow for capturing the dynamic and intuitive nature of spinal disorders, leading to cases that remain with an elusive diagnosis,[37] whereas classifications are bound to minimize the number of subgroups because, as the number of subdivisions increases, the interrater reliability decreases,[116, 118] and (4) most subgrouping approaches have been based on unproven theories, are poorly validated, or remain unreplicated in other studies.[119]

In summary of the issues raised, fundamental to interpreting scientific classification studies on spinal pain is agreeing on **a parsimonious, clinically meaningful set of distinct case definitions.**[22, 116, 119] To reach that ultimate goal, classification strategies need to be **reliable** in that a given patient would be classified in the same manner by two or several clinicians, and should proof **valid,** so that the findings match reality and can be replicated in other settings.[93, 119, 120] Despite the plethora of classifications in recent research, little classifications are readily applied in clinical practice and there has not been a tangible reduction in the prevalence of NSNP or its serious long-term consequences.[119] Hence, at the time this work embarked, the literature only started to reveal preliminary classification systems that had the acceptable flexibility corresponding with clinical practice, and included contemporary clinical reasoning used in musculoskeletal physiotherapy.

The publications and reflections of some prominent researchers in the field of pain related to physiotherapy (i.e. Louis Gifford, David Butler, Lorimer Moseley, Mark Jones, and Keith Smart and colleagues, to name a few),[25, 39, 56, 58-62, 114, 115, 121-128] blended with the gathered experience of a group renowned colleagues at Ghent University, provided some persuasive arguments to attempt to approach the diagnostic reasoning process of NSNP from a different perspective. Interestingly, the promising work of Smart et al., analyzing which clusters of clinical criteria can be used as reliable and valid indicators of a predominant pain mechanism in patients with low back pain,[114, 115, 129, 130] suggested that subgrouping patients into categories based on the prevailing pain mechanisms, may have the potential to facilitate clinical decision-making, guide treatment and impact outcomes.[114, 129, 130] Such categorization requires ways of thinking[63] and step-wise decision-making described in classification systems. This mechanistic approach to categorize patients suffering NSNP has caught many researchers' interest,[39, 62, 114] including mine. Therefore, it was considered appropriate to undertake a comparable scientific quest, with the intention to obtain a similar diagnostic reasoning strategy for NSNP.

Before the main objectives of this thesis are reached, these clinical reasoning models will be briefly explained. But first the reader is provided with a short intermezzo on basic pain physiology, to allow full understanding of the subsequent chapters.

ABOUT NOCICEPTION, SENSITIZATION, PLASTICITY OF THE NERVOUS SYSTEM & OTHER (INTERESTING BUT) COMPLICATED STUFF

Short interlude on basic pain physiology

According to the International Association for the Study of Pain (IASP), all types of musculoskeletal pain share similar underlying mechanisms, manifestations, and potential treatments, despite the wide-ranging conditions and symptoms.[131] Accordingly, it seems desirable for the modern musculoskeletal physiotherapist to have a basic comprehension of those fundamental neurophysiological mechanisms.

Nociceptor activation, sensitization & hyperalgesia in acute pain

From a stress biology perspective, the perception of acute pain is a protective and obvious favorable reaction of the human body to a harmful stimulus. With this pain sensation, the body intends to warn its host that something might be wrong, to prevent aggravation of the situation and restore homeostasis.[25, 132] When a noxious stimulus (i.e. a stimulus that is damaging or threatens damage to normal tissues) stimulates a nociceptor located in the skin, muscles, tendons, radices or peripheral nerves, ligaments or capsules surrounding facet joints, intervertebral discs, bones, or visceral organs, this signal is transmitted from the periphery to the central nervous system (CNS) through somatosensory pathways.[133-135] The neural process of encoding these noxious stimuli is called **nociception**. Consequences of encoding (i.e. outputs) may be autonomic (e.g. elevated blood pressure), neuroendocrine (e.g. elevated stress hormone levels), immunologic (e.g. diminished immune responses due to negative emotional states), and/or behavioral (e.g. motor withdrawal reflex or more complex nocifensive behavior).[25, 39, 121, 136] Pain sensation is not necessarily implied, but when it does, this pain is labelled **nociceptive pain**. That is, pain that arises from actual or threatened damage to non-neural tissue, occurring with a normally functioning somatosensory nervous system,[134] unlike peripheral **neuropathic pain**, that is caused by a lesion or disease of the peripheral somatosensory nervous system.[136]

Nociceptors have unique response properties that depend on the tissue that they innervate. These unique properties, in part, provide the basis for differences in clinical acute pain states after different injuries.[133] **Peripheral sensitization** is the neuroplastic adaptation of peripheral nociceptive nerves (C-fibers) in which the response to normal input stimuli is enhanced. Nociceptor sensitization produces **primary hyperalgesia** at the site of injury, which generates ongoing pain at rest, and enhanced pain during and after the acute onset of the injury.[132, 133]

Sensory input during and after the actual or perceived damage can enhance the responses of pain transmitting neurons in the CNS, amplifying the clinical pain experience. This increased responsiveness of nociceptive neurons in the CNS to normal or subthreshold afferent input can lead to **central sensitization**. Central sensitization amplifies transmission of input from peripheral tissues and produces **secondary hyperalgesia**, an increased pain response evoked by stimuli applied to tissue outside the area of injury.[132-134]

Clinically, sensitization may only be inferred indirectly from phenomena such as hyperalgesia or **allodynia**, i.e. an unexpectedly painful response to a stimulus that does not normally provoke pain.[134]

Pain processing & neuroplasticity in chronic pain

Many patients with chronic musculoskeletal pain (e.g. patients with fibromyalgia, whiplash associated disorders, temporomandibular dysfunctions, etc.) are characterized by alterations in CNS processing, resulting in central sensitization, and generalized or widespread hypersensitivity.[132, 137] This unfortunate physiological state stems from the former described peripheral mechanisms amplified with a complex mash-up of **central mechanisms**: (1) impaired functioning of brain-orchestrated descending inhibitory mechanisms,[138] (2) (over)activation of descending and ascending pain enhancing pathways,[139] and (3) altered sensory processing in the brain.[137]

Once central sensitization is established, this process might be difficult to reverse due to structural and functional reorganization of the nervous system, both peripherally and centrally.[140, 141] This ability of the nervous system to rewire its connections is known as **neuroplasticity**.[140] Any new input may now serve as a fresh source of peripheral nociceptive input, which maintains or aggravates the process of central sensitization.[137, 142] In addition, behavior, thoughts, and emotional dispositions may also cause and reinforce neuroplastic changes, amplify the experience of pain, and perpetuate a vicious cycle of nociception, pain, distress, and disability.[52, 143]

Owing to these maladaptive neuroplastic circumstances, the previous term to label this pain state, central pain, was recently replaced by **nociplastic pain**.[144, 145] It is officially adopted as IASP taxonomy and defined as pain that arises from altered nociception despite no clear evidence of actual/threatened tissue damage or evidence for disease/lesion of the somatosensory system causing activation of peripheral nociceptors.[134]

To conclude, the initiation, transmission, modulation, and perception of pain is governed by complex interactions of various simultaneous neurophysiological mechanisms and processes occurring throughout the peripheral and CNS. The activity of these systems can be regulated by parallel processing systems, such as the motor, neuroendocrine and immune systems.[25, 121] The balance and totality of pathophysiological activity within all these systems ultimately determines the patient's pain experience.[62, 115, 121]

The following section presents a clinical reasoning model that encompasses these underlying neurophysiological processes, to provide clinicians with a better explanation for clinical manifestations of pain and movement dysfunction that are not promptly explained by the biomedical model.[115, 121]

CAN WE DO BETTER?

Benefits of pain mechanisms-based reasoning models & classifications

Authors from both the physiotherapy, medical and scientific disciplines have encouraged a pain mechanisms-based classification, in response to the growing advancements in pain science and the apparent boundaries of the biomedical model in explaining many clinical presentations of pain.[57-59, 62, 115, 121, 146-148] This evolution of concepts and thinking towards explanations that acknowledge the neurobiological and psychosocial complexities of pain and disability, has led to more **comprehensive reasoning models**.[115]

Clinical reasoning in physiotherapy

Clinical reasoning in physiotherapy is characterized by a broad and **multidimensional** nature.[149, 150] To reach an informed diagnosis parallel rounds of thought occur interchangeably and simultaneously.[149] During this dynamic reasoning approach information is gathered on precautions and contra-indications to assessment and treatment, impaired structures, tissue mechanisms, (mal)adaptive behavior of signs and symptoms, impact on functioning and participation, and complemented with consideration of the prevailing pain mechanisms underlying the patient's pain presentation.[26, 63] From a biopsychosocial perspective, appraisal of the cognitive, emotional, behavioral, attitudinal, and sociological aspects of the patient's pain experience need further inquiry to identify valuable psychosocial contributions and/or potential barriers to recovery (i.e. yellow flags).[26, 63, 149]

All these different aspects of decision-making do, to varying degrees, provide some descriptive depth to the diagnostic process and help the therapist to collect the info needed to generate a plausible hypothesis concerning the patient's pain. Depending on adequate knowledge of applied pathophysiology and **pattern recognition** of clinical criteria gathered from the subjective examination,[59, 63, 121] physiotherapists can formulate one initial hypothesis or differential hypotheses. These early hypotheses are then tested with the additional information collected from the physical examination.[26, 59, 63] Upon accurate interpretation of the clinical findings, and modification and confirmation of the most plausible hypothesis, the therapist has to decide whether or not certain aspects of the patient's problem are amenable to physiotherapy, and if physiotherapy is indicated.[59] If so, the process of clinical reasoning is continued by determining the optimal treatment decisions, as well as during the course of treatment through **continuous reassessment**.[26, 59, 63, 128]

This clinical reasoning process is not unique to our profession, but it has become an integral part of the identity of contemporary healthcare. As far as physiotherapy is concerned, this professional identity is not always unambiguously defined. It is often characterized or defined by the treatments physiotherapists perform.[38] The problem with this characterization of our profession is that it places us in the role of technicians who are defined by what we do (e.g. masseurs, or bonesetters), rather than by our distinct body of knowledge. Such popular mainstream definitions ignore our assessment and clinical reasoning skills that have been refined in order to accurately diagnose and manage our patients.[38] Therefore, **clinical decision-making is embedded in physiotherapy**, and patients' management can no longer be interpreted as merely hands-on treatment.

Pain mechanisms-based reasoning models

Clinical reasoning and decision-making informed by pain mechanisms-based classifications seem intrinsic to the provision of qualitative physiotherapy care. Thus far, several models have been developed for the clinician to reach a pain mechanism-driven hypothesis.

The 'input/processing/output' model

The 'Mature Organism Model' proposed by Gifford expanded the mechanisms-based approach by integrating the science of pain physiology and stress biology with the biopsychosocial model.[25, 60, 62, 149] This integrated model of pain and disability describes the numerous and interrelated biological processes involved in the initiation, maintenance and perception of pain, together with the physiological and behavioral reactions to it.[149] Figure 2 represents the human organism in which the organism is constantly sampling its environment and its tissue health, and is sending this information to the CNS. The brain then scrutinizes the incoming information and responds as necessary. These responses or 'outputs' can produce a visible effect (i.e. altered behavior) or invisible effect (i.e. altered physiology). The changes brought about are then re-sampled and re-evaluated to see if they were successful, and the sampling-processing-responding loop continues endlessly.[25, 39, 56, 62] Fundamental to this conceptual model is the recognition that **all input, processing, and output mechanisms occur simultaneously in any pain state**.[25, 56, 60, 62] However, not all mechanisms will necessarily be dysfunctional (i.e. contributing to the problem and/or be counterproductive to recovery). There may be a **clinical dominance** of one mechanism over the others.[25, 56, 60, 62] By pattern generation, the clinician can distinguish between adaptive (i.e. helpful) and maladaptive (i.e. unhelpful) responses and consequently, a reasoned decision about the prevailing mechanism can be made.[121]

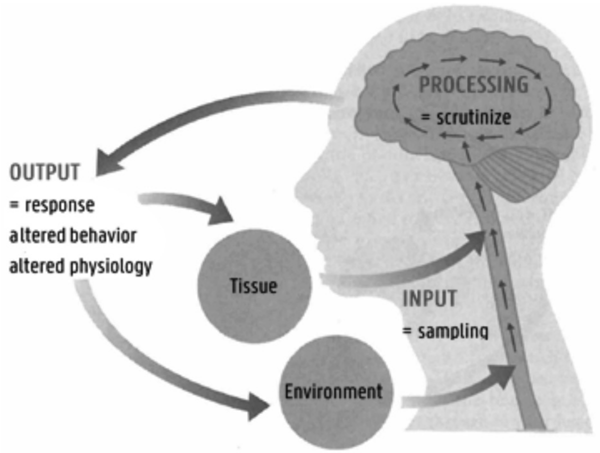

FIGURE 2 The 'Mature Organism Model'. Adapted from Gifford[25]

The 'nociceptive/peripheral neuropathic/central pain mechanisms' model

It is acknowledged that the Mature Organism Model helps to clarify the links between the different pain mechanisms and to consider the multiple factors and levels involved in all pain presentations.[56] The use of such a mechanisms-based classification has been identified as a part of the multidimensional pain-oriented clinical reasoning process in experienced physiotherapists.[63, 115, 128, 149] An early exploratory study of Smart and Doody[128] on how experienced physiotherapists approach these neurophysiological pain mechanisms showed a trend towards integration of basic pain physiology into aspects of clinical decision-making regarding the assessment, treatment, and prognosis of patients presenting with musculoskeletal disorders.[128] Although, there was no direct evidence of reasoning grounded within the input/processing/output or stress biology perspectives as originally conceptualized in the Mature Organism Model by Gifford.[128] This finding raised questions regarding the level of awareness and/or usefulness of reasoning in the original concepts of input/processing/output amongst musculoskeletal physiotherapists. Therefore, the authors decided to redefine the reasoning in relation to pain mechanisms into more apparent **nociceptive, peripheral neuropathic,** and **central (i.e. nociplastic) mechanisms**.[128, 149]

The interpretation and integration of the different models

From the above one could broadly summarize the neurophysiological mechanisms responsible for the generation and/or maintenance of pain into: (1) peripheral **input** pain patterns, including nociceptive pain and peripheral neuropathic pain, (2) central **processing** pain patterns of nociception, comprising ascending pain pathways, nociplastic pain and central sensitization, descending pain control, and the cognitive–affective mechanisms of pain, and (3) the influences of the autonomic, motor, neuroendocrine and immune systems on nociception, originally labelled as the **output** pain patterns.[25, 60, 62, 121, 128] Appendix 3 and 4 list the clustered clinical criteria associated with the input, processing, and output pain patterns and nociceptive, peripheral neuropathic, and central (i.e. nociplastic) pain mechanisms, respectively, as adopted from the available literature.[25, 26, 39, 60, 62, 114, 125-127, 129]

A key reasoning issue is the relevance of an unique finding within the clinical presentation of the individual patient.[62] Excessive emphasis on findings that support a particular hypothesis, might lead to disregarding findings that do not support it, possibly leading to incorrect interpretations.[56, 57, 59] During the clinical reasoning process, the clinician is therefore encouraged to use his/her integrative knowledge and clinical experience to remain open-minded and to see things in perspective.[56, 121] Besides, stand-alone clinical tests provide only marginal value in diagnosis and usually do not reveal excellent results in terms of psychometric properties.[28, 151] That is why **clustering test results** increases the diagnostic value.[67, 151]

It is important for the healthcare professional to understand that patients with NSNP often exhibit signs and symptoms that fit more than one classification, and that the most relevant subjective and physical examination findings frequently change during the episode of care.[37, 85] With recognition that these **categories are not exclusive nor exhaustive**, assigning an individual patient into the category that best fits the patient's current clinical picture relies on clinical reasoning and judgment of the clinician.[37] Thus, continual reflection and re-evaluation of the patient's clinical findings, within a **dynamic** reasoning model, is essential for providing the optimal interventions throughout the management progression.[37]

Benefits of pain mechanisms-based classifications

Emanating from the mounting research on pain mechanisms, the perks of mechanistic reasoning are said (by their proponents) to be vast.[25, 62, 115, 121, 132, 137, 149, 152-155] Apparently conceived as a revulsion towards the former biomedical model, pain mechanisms-based classifications are ought **to assist and contribute to clinicians' understanding** of clinical manifestations of pain and movement dysfunction where the biomedical model fails to deliver.[25, 115, 121] Indeed, this approach accounts for the factors underlying the unpredictability and complexity of clinical presentations of pain, such as the modulation of nociception, and psychological influences.[115] Another proposed advantage is that it addresses the misleading notion of pain being either physical or psychological.[115] This integrated approach recognizes the importance of the cognitive-affective mechanisms of pain and how these influence, and are closely interconnected with, the other pain mechanisms involved in the processing and modulation of pain information.[115] The inseparable connection between the psychological and physiological components of pain is supported by a growing body of evidence which suggests that psychosocial factors are as (or more) important than physical factors in predicting outcome and determining which patients are at risk of developing chronic pain.[115, 132, 156, 157] While early evidence for the face and construct/ clinical validity of several of these assertions has been reported,[114, 128-130, 149] additional evidence underpinning these claims in other patient populations, e.g. patients with NSNP, is still required.

Clinically, this approach has been promoted based on its perceived capability **to facilitate effective decision-making associated with the treatment and follow-up** by directing therapeutic interventions towards the predominant pain mechanisms, and providing a scientific rationale for its management.[57, 62, 114, 121, 149] However, the assumption that pain mechanisms-based classifications can significantly improve clinical outcomes has yet to be substantiated empirically.[114]

Do we need another classification for nonspecific neck pain?

While the case for a mechanisms-based classification for pain has been well made, the burden of proof lies with its promoters to establish its validity for use in clinical practice in defined populations with NSNP.[115] The proposed conceptual model of **dysfunction patterns**, described in the following chapters, is therefore **not** to be contemplated as **an alternative classification** to the existing classifications. Instead, it could serve as a parallel reasoning model, acting as a generator to increase our understanding of mechanisms underlying NSNP.[146]

Given that all mechanisms underlie the patient's pain experience and some dominate the clinical presentation,[121] it is proposed to appoint a **predominant pain mechanism**, rather than labeling the patient's condition as a definite verdict. This subtle, yet critical, nuance reflects the relative contributions of the different mechanisms in action. Whilst Smart et al.[129, 130] have demonstrated diagnostic accuracy of clustered criteria for pain mechanisms discernable in LBP patients, limited evidence is available on which clinical criteria clinicians should rely their diagnostic process on in case of NSNP. To enable physiotherapists and other healthcare practitioners to define the prevailing pain mechanism in patients with NSNP, we need to verify if we can use the same criteria or if we need a different set of **reliable and empirically validated clinical criteria** with which to distinguish one category of pain mechanisms from another.[115]

One could argue that, for some, the biopsychosocial model took the dogma out of musculoskeletal physiotherapy, and paved the path for pain mechanisms-based reasoning models. However, putting things in perspective, a more structure-oriented approach might apply under specific circumstances.[26] As a remainder of the biomedical thinking model, physiotherapists often feel the need and attempt to validate somatic tissues and nerves as definitive sources of patients' pain.[25, 39, 149] Although the tissue-based attitude has been criticized[60, 115] (see above), this reasoning approach can still serve proper diagnostic work-up as one of the parallel rounds of thought.[95, 146] For the practicing physiotherapist it may not always be clear what factors take the upper hand of the patient's pain, as a result of which certain traditionalists refuse to adopt a mechanistic approach, and certain believers might overshoot and dismiss valuable treatment options. A nuance seems in place. It is evident that the practitioner would benefit from an easy to use model that (1) is based on **common procedures** for subjective and physical examination,[26, 69] (2) imposes order on information from scientific origin and organizes it into **clinically relevant patterns** to make it accessible in the clinical setting,[59, 158] (3) **integrates** the different concepts of thought,[56, 58, 63] and (4) provides a reference frame from which the therapist can **adapt and complement** to result in a individually tailored approach.[158]

During the design, development and realization of the proposed reasoning model into dysfunction patterns, all of the above described models and approaches were considered. Starting from the available scientific evidence, recurrently nourished with empirical criticism and support, an overarching conceptual model with meaningful subgroups of people with neck pain was established. Although promising, the proof of concept requires confirmation in proper designed clinical trials, as included in the current thesis.

THESIS AIMS & OUTLINE

The overall objective of this doctoral dissertation is to contribute to a better understanding and recognition of unique characteristics of individual patients with NSNP and to expand the current knowledge on this highly prevalent condition. Furthermore, this thesis aspires to contribute to the development of a sound clinical reasoning underlying the diagnostic process to guide targeted and efficient treatment of patients with NSNP.

The current thesis addresses this subject and consists of three major parts:

PART I CLINICAL CRITERIA FOR NONSPECIFIC NECK PAIN

The available literature indicates that classifications based on identifying the underlying pain mechanisms driving the disorder are clinically useful to improve diagnostic decision-making and enhance treatment efficiency. Consequently, clinicians should be provided with a set of pertinent criteria that helps them to identify the prevailing pain mechanisms. The first aim of the present thesis is to identify these clinical criteria. Chapter 1 introduces the conception of the proposed reasoning model and elaborates on the Delphi-design used to identify the subjective and physical examination criteria. Furthermore, these criteria suggestive for the pain mechanisms-based clinical patterns are discussed against the available literature.

PART II PSYCHOMETRIC PROPERTIES OF THE PROPOSED REASONING MODEL

The second aim is to evaluate the reliability and validity of the suggested reasoning model. In Chapter 2 the interrater reliability of the classification strategy is assessed, as a preliminary step towards classification validation. Subsequently, a complementary analysis of the discriminative validity of the proposed reasoning model is presented in Chapter 3. The sensitivity, specificity, predictive values, likelihood ratios, and overall classification accuracy are evaluated in a consecutive sample of NSNP patients.

PART III EXPLORING THE ARTICULAR DYSFUNCTION PATTERN IN PATIENTS WITH NONSPECIFIC NECK PAIN

The third and final aim of this thesis is to provide the (novice) therapist with a clinical algorithm that steers the assessment and directs towards proper treatment selection in the event of a predominant articular dysfunction pattern. To conclude, Chapter 4 shares an empirical approach, based on years of standardized assessment and management of patients with NSNP who are likely to respond to mobilization and/or manipulation.

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PART I

CLINICAL CRITERIA FOR NONSPECIFIC NECK PAIN
A Delphi-study

CHAPTER 1

Subjective & clinical assessment criteria suggestive for five clinical patterns discernible in nonspecific neck pain patients. A Delphi-survey of clinical experts

Vincent Dewitte, PT [a], Wim Peersman, PhD [b], Lieven Danneels, PT, PhD [a], Katie Bouche, MD, PhD [c], Arne Roets, MSP, PhD [d], Barbara Cagnie, PT, PhD [a]

[a] Department of Rehabilitation Sciences, Ghent University, Corneel Heymanslaan 10, 3B3, 9000 Ghent, Belgium
[b] Department of Family Medicine and Primary Health Care, Ghent University, Corneel Heymanslaan 10, 6K3, 9000 Ghent, Belgium
[c] Centre for Musculoskeletal and Neurological Rehabilitation, Ghent University Hospital, Corneel Heymanslaan 10, K7, 9000 Ghent, Belgium
[d] Department of Developmental, Personality and Social Psychology, Ghent University, Henri Dunantlaan 2, 9000 Ghent, Belgium

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Abstract

Background: Nonspecific neck pain (NSNP) patients form a heterogeneous group with different musculoskeletal impairments. Classifying NSNP patients into subgroups based on clinical characteristics might lead to more comprehensive diagnoses and can guide effective management.
Objective: To establish consensus among a group of experts regarding the clinical criteria suggestive of a clinical dominance of ‘articular’, ‘myofascial’, ‘neural’, ‘central’ and ‘sensorimotor control’ dysfunction patterns (DPs) distinguishable in patients with NSNP.
Study Design: Delphi-study.
Methods: A focus group with ten academic experts was organized to elaborate on the different DPs discernible in neck pain patients. Consecutively, a 3-round online Delphi-survey was designed to obtain consensual symptoms and physical examination findings for the five distinct DPs resulting from the focus group.
Results: A total of 21 musculoskeletal physical therapists from Belgium and The Netherlands experienced in assessing and treating neck pain patients completed the 3-round Delphi-survey. Respectively, 33 (response rate, 100.0%), 27 (81.8%) and 21 (63.6%) respondents replied to Rounds 1, 2 and 3. Eighteen ‘articular’, 16 ‘myofascial’, 20 ‘neural’, 18 ‘central’ and 10 ‘sensorimotor control’ clinical indicators reached a predefined ≥80% consensus level.
Conclusion: These indicators suggestive of a clinical dominance of ‘articular’, ‘myofascial’, ‘neural’, ‘central’, and ‘sensorimotor control’ DPs may help clinicians to assess and diagnose patients with NSNP. Future validity testing is needed to determine how these criteria may help to improve the outcome of physical therapy interventions in NSNP patients.

Key words: Consensus, cervical spine, clinical reasoning, clinical patterns.

Introduction

Neck pain is experienced by people of all ages.[1-3] In most cases it is, however, not due to a serious disease or neck problem, and often the exact cause for the pain remains unclear. This is frequently referred to as 'nonspecific neck pain' (NSNP). In the absence of a precise pathological etiology[4, 5] different alternative methods have been developed to classify patients into subgroups.[6, 7]

It has been demonstrated that classifying patients into subgroups and providing them with matched management strategies may improve the outcome of physical therapy interventions.[8, 9] Several authors have proposed classification strategies for neck pain patients mainly based on specific clinical features.[7-11] Werneke and colleagues ground their categorization on changes in pain location (centralization, noncentralization, partial reduction) in response to a McKenzie-based assessment.[10] Wang et al. categorize patients into one of four main categories (i.e., radicular arm or neck pain, referred arm or neck pain, cervicogenic headaches, or neck pain only) with numerous subcategories depending on the results of several key tests.[11] The authors call attention to the coexistence of patterns and mention that during the course of treatment other patterns may emerge as the initial symptomatology resolves. Childs et al. propose a treatment-based classification that places patients into one of five subgroups (i.e., mobility, centralization, exercise and conditioning, pain control, or headache).[8] This subgrouping is based on the anticipation of an initial treatment approach. In 2008, the Orthopaedic Section of the American Physical Therapy Association (APTA) published its clinical guidelines on neck pain, starting from the classification of Childs et al.[8, 9] Only slight adjustments were made in the pain control category, dividing it into neck pain with movement coordination impairments and neck pain with mobility deficits.[9]

In addition to the abovementioned classification patterns based on clinical features, attempts have also been made to classify patients based on the dominant pain mechanism. It should be noted that a mechanism-based classification is not to be considered an alternative to the existing classifications. Instead, it could serve as a parallel reasoning model, acting as a generator to increase our understanding of mechanisms underlying neck pain.[12]

Pain mechanisms are broadly categorized into input mechanisms, including nociceptive pain and peripheral neurogenic pain; processing or central mechanisms, comprising central pain, central sensitization and cognitive-affective mechanisms of pain; and output mechanisms, including autonomic, motor, neuroendocrine, and immune systems.[13] All these mechanisms occur at the same time, however there may be a clinical dominance of one mechanism over the others. By pattern generation, a reasoned decision about the dominant mechanism(s) in operation can be made.[14]

With the biopsychosocial model as a starting point, it is clear from the scientific literature and clinical practice that a multi-dimensional approach is required to deal with the diversity of factors present in musculoskeletal disorders.[15-17] The relative contribution of the different dimensions and their dominance associated with the disorder will differ for each patient.[17] An estimation of the prevailing pain mechanism is therefore relevant and allows for a diagnosis and mechanism based classification guiding appropriate management of the disorder.[16, 18]

Despite the growing body of studies on pain mechanisms, evidence on clinical criteria associated with pain mechanisms in NSNP patients is noticeably absent in the current literature. Smart and colleagues recently published several papers on clinical judgments and criteria associated with nociceptive, neuropathic and central pain in patients with low back pain.[19-22] They did, however, not include the output mechanism. The output mechanism is typically interpreted as a response to the input and processing mechanisms. In some patients, output pain mechanisms can be considered as pain evoking mechanisms, and might become the clinical dominant mechanism in operation.[14]

In what follows, a more detailed and dynamic classification system is proposed based on the three pain mechanisms in relation to neuromusculoskeletal dysfunctions, as these are the key features within musculoskeletal physical therapy. "More detailed" refers to a refinement of the input pain mechanism into dysfunctions of the articular, myofascial, and nervous system. In addition, an output dysfunction pattern (DP) related to impaired sensorimotor control is included. A "dynamic classification" points towards the fact that patterns coexist and may shift throughout the course of the treatment.

In order to delineate what empirical criteria are associated with each DP a Delphi-survey was conducted. The goal was to generate a set of pertinent clinical criteria, derived from subjective and physical examination, upon which clinicians decide to assume a dominant DP underlying the clinical presentations of neck pain. By identifying accurate and useful diagnostic criteria for neck pain, more informed decisions regarding the management of these conditions can be made.[23]

Methods

Ethics approval

Ethical approval to conduct this study was granted by the Ethics Committee of the Ghent University Hospital. Experts' consent to participate was inferred from their voluntary participation.[19]

Study design

A 3-round online Delphi-survey was designed to obtain a consensus on indicators for five distinct clinical patterns in neck pain patients. The Delphi-technique is a structured process that uses a series of questionnaires or 'rounds' to gather information which are reiterated until 'group' consensus is reached.[24-27] The Delphi-approach provides a suitable methodology from which to commence the process of classification system development and validation by providing clinically meaningful classification criteria with a high degree of face and content validity.[28] Prior to the Delphi-study a focus group was organized and charged with the assignment to elaborate on the distinct DPs discernible in neck pain patients, with the mechanisms-based classification of pain as a starting point.

Participants

The focus group consisted of 10 academic experts within the field of musculoskeletal physical therapy with an average of 18.2 years of clinical experience and an average of 16.2 years of academic teaching experience. These experts were recruited from the teaching board of different postgraduate educational programs in musculoskeletal physical therapy in Belgium, and selected upon their expertise related to the topic. The 10 academic experts all combine clinical work with their teaching assignment and have all updated and integrated knowledge by regular training and attendance at international congresses within the field of the different aspects in musculoskeletal physical therapy. Focus group demographics are presented in Table 1.

TABLE 1 Demographics of participants at the focus group (n =10)

Gender	Male = 7 Female = 3
Mean (SD) age, years	43.7 (8.3)
Mean (SD) years of teaching experience	16.2 (6.9)
Mean (SD) years of clinical experience	18.2 (10.0)

Abbreviations: SD, standard deviation.

Delphi-participants were recruited from both the Belgian (Dutch speaking members) and Dutch association for manual therapy, assuming substantial relevant clinical knowledge and expertise in assessing and treating neck pain patients in this group of professionals.

Prior to the first round, a 4-week period was considered during which the therapists were informed as to the purpose of the study and invited to participate. Additional information on the DPs was provided to assure that the experts were familiar with the concept of pain mechanisms. An invitation to participate was sent to 500 eligible candidates of which 86 therapists expressed interest in participating. From the 86 interested clinicians a heterogeneous sample of therapists was selected based on the following criteria: musculoskeletal physical therapists that assess and treat an average of 15 neck pain patients per week, with a minimum of two years of clinical experience in assessing and treating neck pain patients. Both recently graduated therapists and more experienced therapists (aged between 24 and 63 years old) were included in this study to avoid bias in appraising merely experts graduated with the same educational background. Forty-nine therapists did not meet the inclusion criteria and four opted out. A final survey sample of 33 expert musculoskeletal physical therapists were invited to participate to the online Delphi-survey. Participant demographics are presented in Table 2.

TABLE 2 Demographics of participants (Round 1) at the Delphi-survey (n =33)

Gender	Male = 23 Female = 10
Mean (SD) age, years	39.8 (11.4)
Mean (SD) years of experience	15.6 (11.1)
Mean (SD) number of neck pain patients assessed/treated per week	24.0 (11.0)
Country of residence	Belgium = 12 The Netherlands = 21

Abbreviations: SD, standard deviation.

Procedure

Prior to the focus group the academic experts were provided with the design, and intentions of the gathering, accompanied with some examples of published research with similar study designs. The focus group discussion started from an integrated reasoning model which was primarily based on the concepts of 'input - processing - output' pain mechanisms and 'nociceptive - neuropathic - central' pain mechanisms. By integrating both pain mechanism concepts and implementing the different concepts within the field of musculoskeletal physical therapy, the academic experts came to five clinical patterns in which the expert team found out that most of the patients with NSNP fit in. However, as clinicians, the team was fully aware that these five patterns cannot account for the entire heterogeneity present in patients suffering from NSNP, and therefore preferred to express this in terms of a 'dominance of patterns'.

The qualitative data collected through the focus group was used to inform the first round of the Delphi-survey.[26] The survey consisted of three rounds of questionnaires. All 33 experts were emailed a personal internet link to an online survey (developed in LimeSurvey 2.00+), which enabled them to respond to the questions. Participants had seven weeks to complete each round. Follow-up reminder emails were sent to non-respondents to maximize response rates.[29] At Round 1, the experts were provided with a brief definition of the dominant DPs of interest (Table 3 and Figure 1), in order to assure that all experts interpreted the questions with the same background. Second, they were asked to suggest and list subjective and physical examination criteria that they found to be indicative for a dominance of the particular DP. The retrieved data from Round 1 were qualitatively analyzed (see "Data analysis") with the intention to create a summary of redefined criteria with respect to the diversity of answers provided in Round 1 for inclusion into Round 2.

In Round 2 experts were asked to rate the level to which they considered the suggested subjective and physical examination criteria (in)significant by means of a five-point Likerttype scale (4 =essential, 3 =rather important, 2 =rather unimportant, 1 =not important, 0 =no answer) for each DP. Responses were analyzed with descriptive statistics to determine the level of agreement and consensus for each criterion. Additionally, participants were asked to rate to what extent the redefined criteria reflected their answers from Round 1.

TABLE 3 Definitions of the dysfunction patterns

Dysfunction pattern	Definition
Articular DP	Neck disorders in which you presume the dominant cause of nociception/pain refers to an articular structure dysfunction (facet joint, capsuloligamentous structure, disc, etc.)
Myofascial DP	Neck disorders in which you presume the dominant cause of nociception/pain refers to a myofascial structure dysfunction (muscle, fascia, tendon, etc.)
Neural DP	Neck disorders in which you presume the dominant cause of nociception/pain refers to a neural structure dysfunction (nerve root, peripheral nerve, etc.)/ neuropathic pain
Central DP	Neck disorders in which you presume the dominant underlying cause is not related to a structural cause, but refers to a pain processing dysfunction (e.g. hyperalgesia due to central sensitization)
Sensorimotor control DP	Neck disorders in which you presume the dominant underlying cause refers to a sensorimotor control dysfunction, whereby a continuous source of nociceptive or neuropathic input remains

Abbreviations: DP, dysfunction pattern.

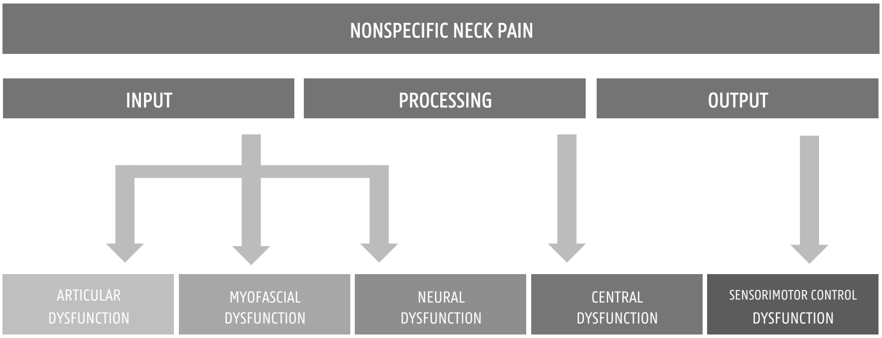

FIGURE 1 Pain mechanisms and dysfunction patterns

A predefined consensus level of ≥80% agreement was set as a cut-off point to determine and establish consensus for a particular criterion, which means that 80% or more of the experts had to rate the criterion as either essential (4) or rather important (3) as a clinical indicator of its respective DP. Indicators that reached a consensus level of 80% or more after Round 2 were considered consensual and omitted from the list for further evaluation, to decrease the work load for the experts in Round 3.

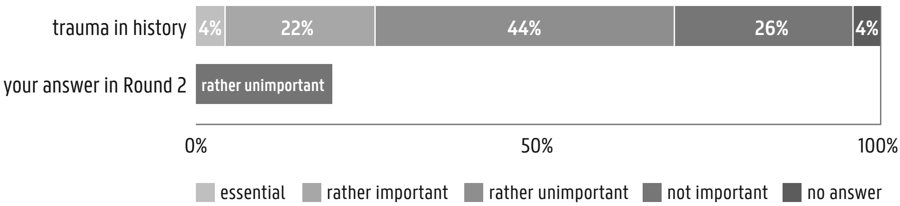

FIGURE 2 Graphical illustration of Round 2 respondent data for a subjective examination criterion for a 'central dysfunction pattern'

In the final round, participants were given the opportunity to re-rate their judgment of (in) significance for the remaining criteria from Round 2 after viewing their own responses from Round 2 and graphical illustrations showing the distribution of the group response per criterion. Figure 2 illustrates a graphic for a single criterion (trauma in history). Response data were then re-analyzed for levels of agreement and consensus. All experts remained anonymous towards each other. The researchers however could link the data to the respective experts, in order to feed back the personal results of the experts in Round 3 to enable them to reconsider their answers in view of the group responses. The questionnaire ran from May 2014 to January 2015.

Data analysis

The retrieved data from Round 1 were qualitatively analyzed via content analysis[30] by two researchers (first and last author): both investigators independently identified and grouped related topics with variable wording in order to reduce the amount of criteria. In selecting appropriate wording, whenever possible, replication of the exact phrases used by the majority of the experts was aspired. The results of the two researchers were compared and differences were analyzed. In case of disagreement the points of difference were discussed in order to reach consensus. Upon mutual agreement a final list of specific clinical indicators was generated and was included into Round 2.

The response data from the experts' significance ratings from Round 2 and 3 were analyzed with descriptive statistics.

Results

Respectively, 33 (response rate, 100.0%), 27 (81.8%) and 21 (63.6%) respondents replied to Rounds 1, 2 and 3. Six experts dropped out between the first and second round and 6 more after completing the second round, resulting in an attrition rate of 36.4%. Tables 4a and 4b summarize the obtained 'subjective' and 'clinical examination' criteria. To enhance comprehensibility the criteria are displayed according to a modified assessment form presented by Petty.[31] Consensus levels of agreement (percentage) for Round 2 and 3 are listed per DP.

Round 1

The qualitative content analysis of Round 1 respondent data generated a total of 37 'articular' (23 'subjective' and 14 'clinical examination'), 46 'myofascial' (26 'subjective' and 20 'clinical examination'), 47 'neural' (28 'subjective' and 19 'clinical examination'), 37 'central' (19 'subjective' and 18 'clinical examination'), and 39 'sensorimotor control' (23 'subjective' and 16 'clinical examination') different clinical criteria, which were presented to the Delphi-experts in Round 2.

Rounds 2 and 3

At Round 2, participants were asked to rate to what extent the redefined criteria reflected their answers from Round 1. Respectively, 48.2% and 44.4% of the experts reported 'almost full' and 'full' recognition of their former formulated criteria. Only 7.4% of the experts mentioned that their answers were 'merely partially' represented in the redefined criteria.

After Round 2, 13 'articular' (4 'subjective' and 9 'clinical examination'), 10 'myofascial' (4 'subjective' and 6 'clinical examination'), 16 'neural' (10 'subjective' and 6 'clinical examination'), 15 'central' (11 'subjective' and 4 'clinical examination'), and 8 'sensorimotor control' (3 'subjective' and 5 'clinical examination') clinical criteria reached the preset ≥80% agreement consensus level (indicated with (R2) in Tables 4a and 4b).

After Round 3, 7 additional subjective and 13 additional clinical examination criteria reached consensus, resulting in a total of 18 'articular', 16 'myofascial', 20 'neural', 18 'central' and 10 'sensorimotor control' clinical indicators (indicated with (R3) in Tables 4a and 4b).

Of the 74 clinical criteria only 3 subjective examination criteria and 5 physical examination criteria show overlap in DPs. Overlap could only be found between input and output pain mechanisms and between the three input DPs.

TABLE 4a Subjective examination criteria that reached consensus

	Subjective examination criteria
Body chart/ symptom distribution/ area of symptoms	**Clear pain distribution, localized to the neck region** Predominant unilateral pain* **Pain referred in a distribution pattern familiar to the target muscle** **Pain and/or stiffness localized to the area of the muscle (insertion)** **Pain referred in a clear distribution pattern familiar to a peripheral nerve or cervical nerve root (dermatome or myotome pattern of distribution)** **Peripheral symptoms (arm pain/symptoms) exceed neck pain** **Referred pain below the elbow** **Widespread, non-anatomical/nonspecific distribution of pain**
Aggravating/easing factors	**Predominant movement restriction towards extension and/or rotation** **Mechanical pattern to aggravating and easing factors, with pain provocation in response to stretch and/ or compression** Careful movements/activities reduce pain* **Pain/symptoms caused by overuse and/or long lasting loading** **Pain provocation in response to stretch** **Pain provocation in response to static postures** **Pain/symptom provocation on specific activities/postures that load the impaired side** **Pain/symptom provocation in response to coughing, sneezing, valsalva maneuvers** **Unpredictable, variable, disproportionate non-mechanical nature to aggravating and easing factors** **Spontaneous (i.e. stimulus-independent) pain and/or paroxysmal pain (i.e. sudden recurrences and intensifications of pain)** **Uncontrollable pain/complaints with no or insufficient response to antalgic medication and/or postures** **Pain/symptom provocation on static, one-sided loading and/or more specific activities/postures (e.g. desktop-workers, car driver, ...), whereas dynamic (low load) exercises/activities result in pain reduction and/or functional improvement**
Quality of symptoms	**Absence of neurological symptoms** **Sharp, stabbing, shooting pain** **Pain variously described as pins and needles, ants, electrical, toothache-like pain, altered sensations in arm and/or hand** **Spontaneous (i.e. stimulus-independent) pain/ pain at rest** **Muscle weakness (not caused by pain inhibition), sometimes objectified by EMG results** **Pain of high severity and irritability (high scores on VAS or NRS)**
24-hour behavior	Pain/complaints increase(s) during the day* **Night pain/disturbed sleep** **Pain persisting beyond expected tissue healing/pathology recovery times**
History of condition/ evolution of symptoms	**History of (long) lasting complaints (recurrent, in episodes)**
Special questions (RF, YF,...)	**Positive identification of various maladaptive psychological factors/YF (e.g. major life events in past history, distress, catastrophisation, fear-avoidance behavior, passive coping strategies, irrational thoughts on diagnosis/complaints** **Disproportionate/abnormal, non-mechanical, unpredictable intolerance to visual perception of light, mechanical, thermal triggers and/or sound** **Positive identification of lowered immune responses and/or tolerance to activities** **Medical shopping**
Additional testing	**Medical imagery: findings do not relate to the patient's complaints (i.e. no structural cause)** **Surveys can reveal supporting evidence: high scores on HADS, TSK, CSI, NDI, etc.**

Abbreviations: RF, red flags; YF, yellow flags; EMG, electromyography; VAS, visual analogue scale; NRS, numeric rating scale; HADS, Hospital Anxiety and Depression Scales; TSK, Tampa Scale for Kinesiophobia; CSI, Central Sensitization Inventory; NDI, Neck Disability Index). Clinical criteria highlighted in bold are unique to the dysfunction pattern. Clinical criteria indicated with a * are found in several dysfunction patterns. (R2), criterion that reached consensus after Round 2; (R3), criterion that reached consensus after Round 3.

ARTICULAR DYSFUNCTION Consensus level of agreement (%)	MYOFASCIAL DYSFUNCTION Consensus level of agreement (%)	NEURAL DYSFUNCTION Consensus level of agreement (%)	CENTRAL DYSFUNCTION Consensus level of agreement (%)	SENSORIMOTOR CONTROL DYSFUNCTION Consensus level of agreement (%)
88.9 (R2)	-	-	-	-
85.2 (R2)	-	81.5 (R2)	-	-
-	**96.3 (R2)**	-	-	-
-	**92.6 (R2)**	-	-	-
-	-	**100.0 (R2)**	-	-
-	-	**88.9 (R2)**	-	-
-	-	**85.2 (R2)**	-	-
-	-	-	**100.0 (R2)**	-
88.9 (R2)	-	-	-	-
85.7 (R2)	-	-	-	-
85.7 (R3)	81.0 (R3)	-	-	-
-	**88.9 (R2)**	-	-	-
-	**92.6 (R2)**	-	-	-
-	**85.7 (R3)**	-	-	-
-	-	**88.9 (R2)**	-	-
-	-	**85.2 (R2)**	-	-
-	-	-	**85.2 (R2)**	-
-	-	-	**81.0 (R3)**	-
-	-	-	**92.6 (R2)**	-
-	-	-	-	**85.7 (R2)**
95.2 (R3)	-	-	-	-
-	-	**92.6 (R2)**	-	-
-	-	**96.3 (R2)**	-	-
-	-	**81.5 (R2)**	-	-
-	-	**81.5 (R2)**	-	-
-	-	-	**88.9 (R2)**	-
-	81.0 (R3)	-	-	88.9 (R2)
-	-	-	**85.2 (R2)**	-
-	-	-	**96.3 (R2)**	-
-	-	-	-	**88.9 (R2)**
-	-	-	**96.3 (R2)**	-
-	-	-	**96.3 (R2)**	-
-	-	-	**88.9 (R2)**	-
-	-	-	**85.7 (R3)**	-
-	-	-	**81.5 (R2)**	-
-	-	-	**81.5 (R2)**	-

TABLE 4b Physical examination criteria that reached consensus

	Physical examination criteria
Observation	Antalgic posture* Insufficient posture, unable to maintain a corrected posture* **Placing the painful arm on top of the head results in pain relief (Bakody's sign)**
Palpation	**Increased muscle tension** **Presence of (active) myofascial trigger points/taught bands** **Hyperalgesia** **Allodynia (painful response to non-painful stimuli)**
Active/passive movement testing	**Associated with unilateral compression and/or stretch pain** **Provocation in response to combined movement testing (3D-extension/3D-flexion)** **Predominant movement restriction towards extension and/or rotation** **Restricted ROM on passive and active movement testing** **Relaxation of relevant myofascial structures does not result in an increased passive ROM** **Traction reduces pain/symptoms** Active movement testing provokes symptoms and reveals ROM restrictions* Impaired quality of movement* **Relaxation of relevant myofascial structures does result in an increased passive ROM** **Mechanical pattern to aggravating and easing factors, with pain provocation in response to stretch and/or compression** **Provocation of peripheral pain/symptoms in response to ipsilateral rotation, ipsilateral side bending and extension of the neck (positive Spurling's test)** **Variable findings in active movement assessment** **Muscular imbalance with increased activity of superficial/global neck muscles** **Pain/symptom provocation with repeated movement testing**
Myofascial assessment	**Localized, unilateral increased muscle tension** **Pain/symptom provocation/local twitch response on palpation of relevant myofascial structures (trigger point(s))** **Pain/symptom provocation in response to stretch of relevant myofascial structures (positive muscle length tests)** **Reduced muscle power and/or endurance of impaired muscles**
Articular assessment	**Intervertebral movement restriction at the impaired segment (aberrant end feel)** **Pain/symptom provocation/muscle tension on palpation of relevant articular structures (positive UPA)** **No clear intervertebral movement restriction(s)**
Neurological assessment	**Negative findings on neurological function and provocation testing** **Positive neurological findings (i.e. altered deep-tendon reflexes, sensation and motor strength)** **Positive neurodynamic tests** **Pain/symptom provocation in response to palpation of the nerve** **Positive cluster of Rubinstein † / Positive cluster of Wainner ‡** **Positive slump test** **Absence of clear neurological findings**
Sensorimotor control assessment	Muscular imbalance with impaired cervical and/or scapulothoracic neuromuscular control and/or proprioception*
Other	**Inconsistent and ambiguous findings/diagnostics that vary over sessions** **Disproportionate/abnormal, reaction during and after the patient's assessment and/or treatment**

Abbreviations: 3D, 3-dimensional; ROM, range of motion; UPA, unilateral posteroanterior provocation test.
Clinical criteria highlighted in bold are unique to the dysfunction pattern. Clinical criteria indicated with a * are found in several dysfunction patterns. (R2), criterion that reached consensus after Round 2; (R3), criterion that reached consensus after Round 3.

† Positive cluster of Rubinstein:[53] positive Spurling's test, traction/neck distraction, and Valsalva maneuver are indicative of a cervical radiculopathy, while a negative upper-limb tension test is used to rule it out.

‡ Positive cluster of Wainner:[48] positive Spurling's test, traction reduces irradiating symptoms, rotation ROM towards the painful side is restricted (less than 60° ROM), positive upper limb tension test.

ARTICULAR DYSFUNCTION Consensus level of agreement (%)	MYOFASCIAL DYSFUNCTION Consensus level of agreement (%)	NEURAL DYSFUNCTION Consensus level of agreement (%)	CENTRAL DYSFUNCTION Consensus level of agreement (%)	SENSORIMOTOR CONTROL DYSFUNCTION Consensus level of agreement (%)
81.0 (R3)	-	100.0 (R2)	-	-
-	85.2 (R2)	-	-	88.9 (R2)
-	-	**81.0 (R3)**	-	-
-	**96.3 (R2)**	-	-	-
-	**92.6 (R2)**	-	-	-
-	-	-	**88.9 (R2)**	-
-	-	-	**96.3 (R2)**	-
88.8 (R2)	-	-	-	-
92.6 (R2)	-	-	-	-
92.6 (R2)	-	-	-	-
95.2 (R2)	-	-	-	-
96.3 (R2)	-	-	-	-
81.0 (R3)	-	-	-	-
96.3 (R2)	-	88.9 (R2)	-	-
81.0 (R3)	-	-	-	92.6 (R2)
-	**81.0 (R3)**	-	-	-
-	-	**92.6 (R2)**	-	-
-	-	**96.3 (R2)**	-	-
-	-	-	-	**81.0 (R3)**
-	-	-	-	**85.2 (R2)**
-	-	-	-	**85.7 (R3)**
85.2 (R3)	-	-	-	-
-	**100.0 (R2)**	-	-	-
-	**88.9 (R2)**	-	-	-
-	-	-	-	**85.2 (R2)**
92.6 (R2)	-	-	-	-
92.6 (R2)	-	-	-	-
-	81.0 (R3)	-	-	-
-	**90.5 (R3)**	-	-	-
-	-	**85.2 (R2)**	-	-
-	-	**96.3 (R2)**	-	-
-	-	**81.0 (R3)**	-	-
-	-	**85.7 (R3)**	-	-
-	-	**81.0 (R3)**	-	-
-	-	-	**85.7 (R3)**	-
-	85.2 (R2)	-	-	96.3 (R2)
-	-	-	**100.0 (R2)**	-
-	-	-	**92.6 (R2)**	-

Discussion

This study reveals an expert consensus-derived list of clinical indicators associated with a dominance of 'articular', 'myofascial', 'neural', 'central', and 'sensorimotor control' DPs in patients with NSNP.

These five patterns were carefully selected based on clinical relevance considerations during a focus group with academic experts. An advantage of this approach is that the five clinical patterns were clearly defined before the Delphi-survey started. This straightforward approach entitled participants to propose unambiguous criteria, but on the other hand limited their freedom of choice to edit the patterns.

A much debated topic is the ability of a 'simple' classification construct to capture the heterogeneity of neck pain.[32, 33] Perhaps the shortcomings of a lot of classifications of neck pain patients do not lie in the construct of the distinct categories, but in the strict manner these categories are approached. Therefore, the expected merit of classifying neck pain patients relies highly on the clinical reasoning process. Based on a thorough subjective and physical examination, a cluster of indicators might raise suspicion of a particular clinical pattern or may prelude a shift towards another DP. Mutually Wang et al., Childs et al., and Fritz and Brennan have insisted on the importance of continuous reassessment as an essential part of this reasoning process in order to obtain successful outcome.[7, 8, 11]

Sterling and Woolf et al. previously called to differentiate mechanisms underlying the patient's pain condition and to then direct treatment toward these mechanisms.[12, 32] The proposed classification system is a response to their call by distinguishing five clinical DPs based on the three pain mechanisms in relation to neuromusculoskeletal dysfunctions. The results of this study do not empower us to make treatment recommendations, but are to be considered a preliminary step towards classification validation by providing clinically meaningful criteria with a high degree of face and content validity.[28] Similar to previous Delphi-studies, the results suggest that clinicians may be able to distinguish between the proposed DPs based on a cluster of criteria that reveal the predominant underlying mechanism of the patient's neck pain.[20-22]

Regarding the 'input'-related dysfunctions, the authors are aware that an anatomical-based classification of symptoms seems undesirable. Nevertheless, despite the assumption that pathoanatomical factors are of low importance in clinical decision making,[34] their relevance cannot be erroneously disregarded.[35] It is clinically important to distinguish between different tissues.[12] Therefore the experts from the focus group found it interesting to subdivide the 'input' pain mechanism into 'articular', 'myofascial' and 'neural' as there are characteristic clinical features related to each of these structures. The 'input'-related criteria seem to largely correspond with the available literature on dysfunctions of the articular,[36-41] myofascial,[19, 42-44] and neural[7, 19, 41, 45-55] system. Although some 'input'-criteria overlap, most criteria that reached consensus were unique to the respective DPs.

All Delphi-experts agreed upon the importance of 'pain/symptom provocation/local twitch response on palpation of trigger point(s)' as an indicator for a dominant myofascial DP. The importance of myofascial trigger points has been extensively debated over the last few years. While some investigators question the existence of a 'myofascial pain syndrome' and myofascial trigger points,[56] others recognize the central role of trigger points to the diagnostic process.[44]

Differentiating neuropathic from nociceptive pain is probably the most important clinical distinction to make, as stated by Cohen.[41] The International Association for the Study of Pain (IASP) definition of neuropathic pain – "pain initiated or caused by a primary lesion or dysfunction in the nervous system"[57] is questioned in the literature,[58, 59] and Treede et al. therefore proposed a grading system that considers the wide range of clinical representations within neural pain conditions.[58] Given the scope of this study, we asked the Delphi-experts what clinical criteria they associated with a dominant neural underlying problem. Apart from the literature, 'predominant unilateral pain', 'peripheral symptoms (arm pain/symptoms) exceed neck pain', and 'active movement testing provokes symptoms and reveals ROM restrictions' were additional criteria suggested by the Delphi-experts in this study. Furthermore, a positive slump test was rated as an important criterion. Albeit the clear relationship between this test and neuropathic pain in the lower limb,[60] no evidence was found in the literature concerning neck pain.

With regard to the central DP, the literature is less extensive compared to the literature on low back pain, even though psychosocial and psychological factors also play an important part in neck pain.[32, 61, 62] A comparable study on clinical criteria associated with 'nociceptive', 'peripheral neuropathic' and 'central' mechanisms of musculoskeletal pain was conducted by Smart et al.[19] The 'central' features most commonly agreed upon in their survey were similar to those identified by our expert panel. Recently, Nijs and colleagues published an algorithm for the classification of central sensitization in pain patients.[55] They proposed guidelines for the differential classification between neuropathic, nociceptive, and central sensitization pain. Together with this algorithm our findings might increase diagnostic distinction between dominant central and dominant input and/or output mechanisms, as these may require different management strategies.[55]

Sensorimotor control impairment is considered as a condition in which faulty movement can induce pathology (e.g. neck complaints).[63-66] Alternatively, predominant mechanical pain may lead to mal-adaptive physical compensations which may become a mechanisms for ongoing pain.[17] This interrelationship between 'input' and 'output' mechanisms may render it difficult to clearly distinguish between a dominant 'input' dysfunction or a dominant 'sensorimotor control' dysfunction. The identification of criteria related to a predominant 'sensorimotor control' dysfunction is, however, of great importance as persistence of motor deficits may render the patient at risk of developing recurrent complaints.[2, 32, 67] This cohesion is also reflected in our criteria list, where four items were present in both the 'input'-related dysfunctions and the 'sensorimotor control' dysfunction: 'pain/complaints increase(s) during the day', 'insufficient posture, unable to maintain a corrected posture', 'impaired quality of movement', and 'muscular imbalance with impaired cervical and/or scapulothoracic neuromuscular control and/or proprioception'. Based on clinical reasoning, their relevance and/or dominance to either category is to be determined.

Limitations and future research

The preliminary findings from this study should be interpreted in light of a number of limitations. Even though the Delphi-method can be particularly useful for informing clinical decision making in situations of clinical uncertainty[19, 27, 68, 69], as in the debate on diagnostic procedures for the neck, several limitations are associated to its use. First, no standardized guidelines are available for defining and selecting experts. Consequently, the credibility and expertise of participants must be inferred and assumed from their professional properties.[19] Different expert-panels may generate alternative clinical indicators. Second, to reduce the workload of the participants no additional criteria could be included after Round 1 and criteria that reached consensus level after Round 2 were omitted from the survey in Round 3. This may have influenced the content validity of findings. Cook et al. also mentioned the 'stand-alone principle' as a weakness inherent to the Delphi-technique.[70] As the experts were asked to rate their level of agreement variable-by-variable, it is possible that some clinical diagnoses may only be made based on combinations of specific indicators. Subsequently, using a cluster of criteria is likely a better application of our findings for clinical practice.

None of the proposed DPs are believed to be distinct clinical entities. Inherent to the clinical reasoning process underlying pain mechanisms, several of these clinical patterns can coexist.[14] Therefore, further reliability and validity testing is needed to ascertain the diagnostic value of the proposed criteria and to provide insights on which criteria are essential or introduce a shift towards another DP. Additional studies are required to find out whether or not this pain mechanism-based approach results in a better management of NSNP patients.

Conclusion

This Delphi-study of 21 experts in musculoskeletal physical therapy identified several clinical criteria indicative for five distinct DPs. The results of this study are in line with a number of other studies and might be a preliminary step towards a more pertinent definition of clinical patterns in patients with NSNP. However, further research on validity testing is needed before these indicators and DPs can be recommended for clinical use.

Conflict of interest

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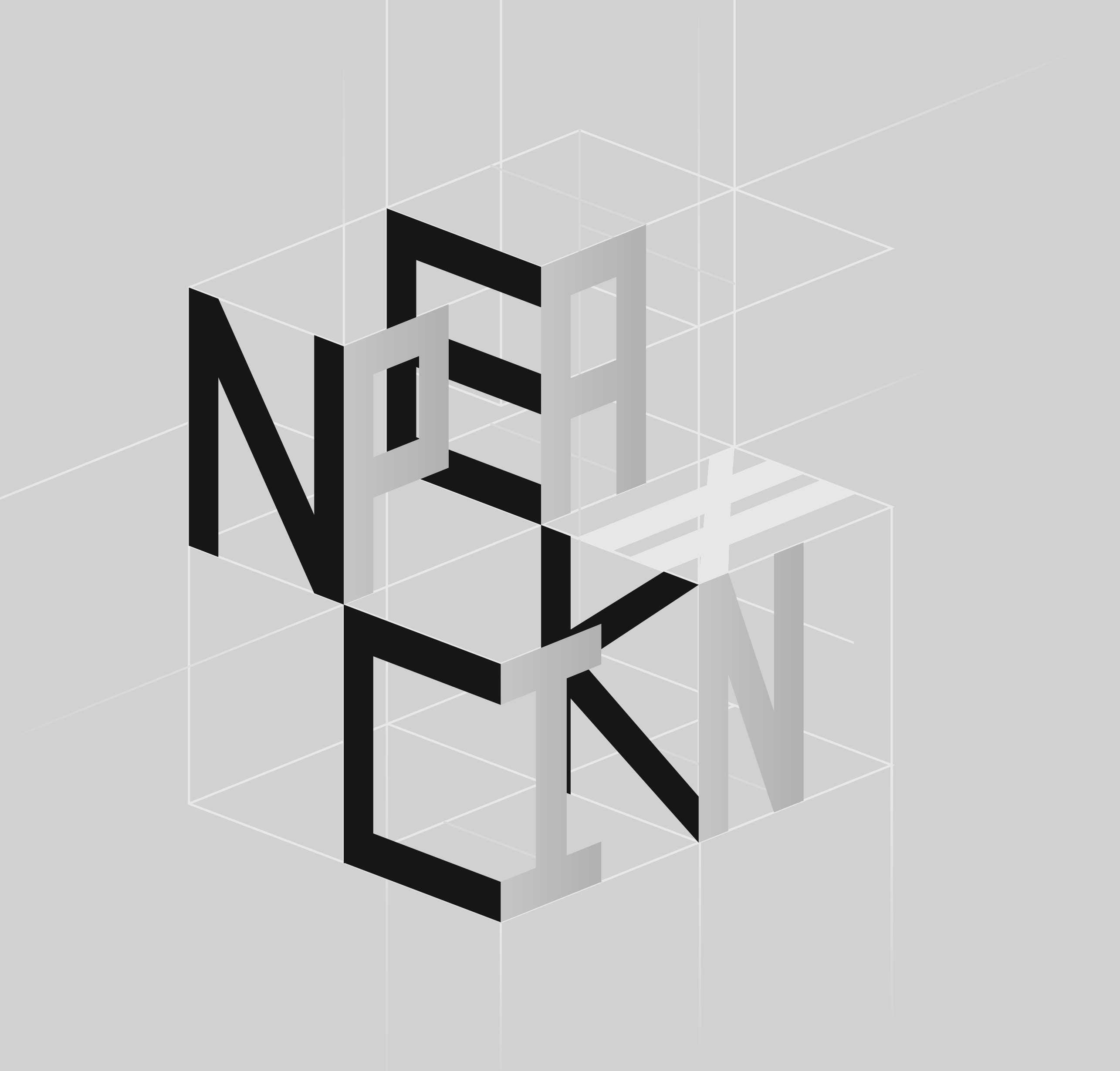

PART II

PSYCHOMETRIC PROPERTIES OF THE PROPOSED REASONING MODEL

CHAPTER 2

The interrater reliability of a pain mechanisms-based classification for patients with nonspecific neck pain

Vincent Dewitte, PT [a,*], Robby De Pauw, PT [a,*], Lieven Danneels, PT, PhD [a], Katie Bouche, MD, PhD [b], Arne Roets, MSP, PhD [c], Barbara Cagnie, PT, PhD [a]

[a] Department of Rehabilitation Sciences, Ghent University, Corneel Heymanslaan 10, 3B3, 9000 Ghent, Belgium
[b] Centre for Musculoskeletal and Neurological Rehabilitation, Ghent University Hospital, Corneel Heymanslaan 10, K7, 9000 Ghent, Belgium
[c] Department of Developmental, Personality and Social Psychology, Ghent University, Henri Dunantlaan 2, 9000 Ghent, Belgium
* equally contributed first authors

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Abstract

Objective: To examine the interrater reliability and agreement of a pain mechanisms-based classification for patients with nonspecific neck pain (NSNP).

Design: Observational, cross-sectional reliability study with a simultaneous examiner design.

Setting: University hospital-based outpatient physical therapy clinic.

Participants: A random sample of 48 patients, aged between 18 and 75 years old, with a primary complaint of neck pain was included.

Interventions: Subjects underwent a standardized subjective and clinical examination, performed by one experienced physical therapist. Two assessors independently classified the participants' NSNP on 3 main outcome measures.

Main Outcome Measures: The Cohen's kappa, percent agreement, and 95% confidence intervals (CIs) were calculated to determine the interrater reliability for (1) the predominant pain mechanism; (2) the predominant pain pattern; and (3) the predominant dysfunction pattern (DP).

Results: There was almost perfect agreement between the two physical therapists' judgements on the predominant pain mechanism, kappa =.84 (95% CI, .65-1.00), p< .001. There was substantial agreement between the raters' judgements on the predominant pain pattern and predominant DP with respectively kappa =.61 (95% CI, .42-.80); and kappa =.62 (95% CI, .44-.79), p< .001.

Conclusion(s): The proposed classification exhibits substantial to almost perfect interrater reliability. Further validity testing in larger neck pain populations is required before the information is used in clinical settings.

Key words: Neck pain, physical therapy, classification, reproducibility of results.

Introduction

Neck pain is a common problem and often becomes chronic.[1, 2] In the Global Burden of Disease 2010 study measured by years lived with disability, neck pain ranked fourth out of all 291 conditions studied.[3-5] Among subjects with neck pain, 37% report persistent problems and 23% report a recurrent episode.[6] Patients with neck pain account for up to 20% of all patients seen in outpatient physical therapy, which leaves physical therapists with the challenging task to make a reasoned diagnosis and to identify the important issues to be addressed during treatment.[7]

Neck complaints are usually not due to a serious disease or pathology, and often the exact cause for the pain remains unclear, a condition frequently referred to as 'nonspecific neck pain' (NSNP).[8, 9] In the absence of a precise pathological etiology,[10, 11] classifications based on pathoanatomy may not be the most effective method to guide treatment. Similar to low back pain (LBP), a classification based on information collected from the subjective and clinical examination may be useful in identifying subgroups and guiding treatment choices in NSNP patients.[8, 12]

Defining the prevailing underlying neurophysiological mechanisms can help physical therapists in diagnosing and directing management goals.[13-16] Dewitte et al. recently published classification criteria for NSNP,[8] based on underlying pain patterns described by Gifford (i.e. the 'Mature Organism Model' including input, processing and output).[15] In the approach of Dewitte et al., clinicians classify the patients' NSNP based on subjective and physical examination criteria into one of five dysfunction patterns (DPs) (i.e. articular DP, myofascial DP, neural DP, central/ nociplastic DP, and sensorimotor control DP). The definitions and criteria on which clinicians decide to classify the patients' NSNP are presented in detail elsewhere.[8] These criteria show substantial overlap with the criteria of Smart et al., by which clinicians determine pain mechanisms-based classifications of pain (i.e. nociceptive pain, neuropathic pain, and central pain).[17] Both classification strategies can inform us about the neurophysiological mechanisms and are part of the parallel rounds of thought that characterize the essential reasoning process for a sound diagnosis.[18] The DPbased classification holds the potential to guide treatment towards distinct clinical DPs with a high degree of face and content validity.[19]

To date, this classification has not yet been tested on psychometric properties. Accepting reliability as a prerequisite for validity,[20] the aim of this study was to investigate the interrater reliability and agreement of the clinical judgements associated with: (1) the pain mechanisms; (2) the pain patterns; and (3) the DPs driving the patients' NSNP. The authors hypothesized that the proposed classification would show acceptable interrater reliability, as a preliminary step towards classification validation.

Methods

Participants and setting

This cross-sectional reliability study was carried out at an outpatient physical therapy clinic of the Ghent University Hospital, between September 2017 and February 2018. Ethical approval to conduct this study was granted by the Ethics Committee of the Ghent University Hospital in accordance with the guidelines of the Declaration of Helsinki.

Subjects were referred by general practitioners and physical therapists from local hospitals, general practitioners' clinics, and outpatient physical therapists' clinics. The referring practitioners were informed on the inclusion and exclusion criteria, prior to the start of the study. All volunteers of any race or sex, aged between 18 and 75 years old, who experienced acute, subacute or chronic neck pain (± arm pain) were considered eligible for inclusion. Subjects were excluded if they were diagnosed with any serious pathology (i.e. cancer, metastasis, untreated fractures, history of diabetes or pathology of the central nervous system, non-musculoskeletal neck pain) that could compromise proper assessment or affect clinical reasoning. After the first screening for eligibility by the referring practitioners, subjects who expressed interest in participating were double-checked for eligibility by the researchers before enrolment in the study.

All participants were informed about the aims and procedure of the study and gave signed informed consent before testing. Forty-eight patients were recruited based on sample size calculations for detecting a kappa coefficient of .5 with a two-tailed test at an alpha level of .05 with 80% power.[21] Based on the sample of 48 participants, a lower limit of .351 can be expected for the 95% CI of the .5 kappa coefficient.

The raters were two experienced physical therapists (first two authors), with both a postgraduate degree in Manual Therapy and respectively 13 and 6 years of clinical experience.

Procedure

A simultaneous examiner design was used to collect the data. Each patient was interviewed and examined by examiner 1, while examiner 2 observed the assessment to assure that both examiners had the same information. Several other reliability studies have used this approach to avoid variable responses or results due to repeated testing.[20, 22, 23] The assessment was performed based on accepted clinical practice.[24] The subjective examination consisted of questions related to demographic data; localization, intensity, quality, onset and evolution, circadian rhythm, provocation, and reduction of the pain; associated complaints (movement restrictions, headache, dizziness, nausea, other); medical diagnosis and history; results of technical examinations (medical imagery, blood tests, etc.), and questionnaires (Neck Disability Index and Central Sensitization Inventory); general health; red and yellow flags; restrictions in activities and participation; and medication and/or previous therapy. The physical examination included a postural and movement assessment, and was complemented with additional articular, myofascial, neurological, and/or sensorimotor control assessments. Following the assessment, both raters classified the patient's NSNP description on three outcome measures: (1) predominant pain mechanism (i.e. nociceptive, peripheral neuropathic or central/nociplastic pain);[14, 16, 17, 25] (2) predominant pain pattern (i.e. input, processing or output);[15] and (3) predominant DP (i.e. articular DP, myofascial DP, neural DP, central/nociplastic DP, and sensorimotor control DP).[8]

Both researchers had six years of previous experience with the proposed clinical reasoning model. Before participation, however, the raters studied an assessment manual with definitions and guidelines for the standardized assessment and thoroughly discussed the interpretation of all subjective and physical examination criteria. The assessment protocol was piloted in two 'dummy trials' to ascertain equal understanding of the diagnostic procedure. To ensure that the raters were blind to each other's judgements, both researchers independently registered the participants' classification in separate databases, without knowing each other's decision.

Data analysis

The data analysis was performed using RStudio for Windows version R 3_4_1 (RStudio, Boston, MA, USA). To assess interrater reliability of the classification, Cohen's kappa and percentage of overall agreement with 95% confidence intervals (CIs) were calculated. Percentage of overall agreement was defined as the percentage of cases in which both raters agreed on the condition being present in the total study population (n =48). To explore the nature of agreements in the physical therapists' judgements, identification agreement and exclusion agreement were examined. Identification agreement was defined as the percentage of cases in which both raters agreed on the condition being present, in the subset of cases that were labelled by at least one rater as being present. Finally, exclusion agreement was defined as the percentage of cases in which both raters agreed on the condition being absent, in the subset of cases that were labelled by at least one rater as being absent.

Interpretations of kappa values were based on categories outlined by Landis and Koch[26] (Supplementary Table 1). For the purpose of this study 'clinically acceptable' reliability was defined as kappa >.60 or in the absence of kappa, a percentage agreement of ≥80%.[20, 27, 28]

Results

Forty-eight patients with NSNP participated in this study. Patient characteristics are detailed in Table 1. There was almost perfect agreement between the two physical therapists' judgements on the predominant pain mechanisms, kappa =.84 (95% CI, .65-1.00), p< .001. There was substantial agreement between the raters' judgements on the predominant pain patterns and predominant DPs with respectively kappa =.61 (95% CI, .42.80); and kappa =.62 (95% CI, .44-.79), p< .001. The percentages, proportions, and 95% CIs of the percentage of overall agreement, identification agreement, and exclusion agreement are displayed in Table 2. For example, in 92.11% (35 out of 38)

TABLE 1 Characteristics of the included subjects (n =48)

	Sample size (n)	Proportion (%)		
Gender				
Male	13	27.08		
Female	35	72.92		
Predominant pain location				
Neck without upper limb	16	33.33		
Neck and unilateral proximal arm	6	12.50		
Neck and unilateral distal arm (below elbow)	9	18.75		
Neck and bilateral proximal arm	5	10.42		
Neck and bilateral arm, below elbow	4	8.33		
Neck pain and headache	38	79.17		
Widespread pain sample	8	16.67		
Neck and other (TMJ, Tx, abdominal)	26	54.17		
Work status				
Full-time	40	83.33		
Part-time	2	4.17		
Unemployed	3	6.25		
Retired	3	6.25		
	Mean	**Median**	**Range**	**IQR**
Age (years)	36.52	30.50	(19.00 - 65.00)	(24.00 - 49.00)
Height (centimeters)	171.27	172.00	(154.00 - 191.00)	(164.00 - 178.00)
Weight (kilograms)	69.71	69.00	(48.00 - 110.00)	(60.25 - 77.75)
BMI (kg/m²)	23.74	22.49	(18.75 - 35.38)	(20.40 - 26.52)
Average symptom intensity (NRS) over previous 7 days	3.92	4.00	(1.00 - 8.00)	(2.00 - 5.00)
Worst symptom intensity (NRS) over previous 7 days	6.13	7.00	(1.00 - 10.00)	(5.00 - 8.00)
NDI score	10.89	9.50	(2.00 - 31.00)	(7.00 - 13.00)
CSI score	34.57	34.00	(8.00 - 68.00)	(26.00 - 41.00)
Duration of current episode (weeks)	155.69	3.00	(0.00 - 1404.00)	(0.29 - 260.00)

Abbreviations: TMJ, temporomandibular joint complaints; Tx, musculoskeletal thoracic complaints; IQR, interquartile range; BMI, body mass index; NRS, numeric pain rating scale; NDI, Neck Disability Index; CSI, Central Sensitization Inventory.

TABLE 2 Interrater reliability of the 3 main outcome measures in patients with nonspecific neck pain (n =48)

Classification	Kappa (95% CI)	Percentage of overall agreement†, % (proportion) (95% CI)	Identification agreement‡, % (proportion) (95% CI)	Exclusion agreement§, % (proportion) (95% CI)
Predominant pain mechanism	.84 (.65 - 1.00)*	93.75 (45/48) (.87 - 1.00)		
Nociceptive pain			92.11 (35/38) (.84 - 1.00)	76.92 (10/13) (.54 - .99)
Peripheral neuropathic pain			100.00 (2/2) (NA)	100.00 (46/46) (NA)
Central pain			72.73 (8/11) (.46-.99)	92.50 (37/40) (.84 - 1.00)
Predominant pain pattern	.61 (.42 - .80)*	75.00 (36/48) (.63 - .87)		
Input			60.00 (15/25) (.41 - .79)	69.70 (23/33) (.54 - .85)
Processing			72.73 (8/11) (.46 - .99)	92.50 (37/40) (.84 - 1.00)
Output			54.17 (13/24) (.34 - .74)	68.57 (24/35) (.53 - .84)
Predominant dysfunction pattern	.62 (.44 - .79)*	70.83 (34/48) (.58 - .84)		
Articular DP			55.56 (5/9) (.23 - .88)	90.70 (39/43) (.82 - .99)
Myofascial DP			41.18 (7/17) (.18 - .65)	75.61 (31/41) (.62 - .89)
Neural DP			100.00 (2/2) (NA)	100.00 (46/46) (NA)
Central DP			72.73 (8/11) (.46 - .99)	92.50 (37/40) (.84 - 1.00)
Sensorimotor control DP			52.17 (12/23) (.32 - .73)	69.44 (25/36) (.54 - .84)

Abbreviations: DP, dysfunction pattern; 95% CI, 95% confidence interval; NA, not applicable.

* $p < .001$.

† Percentage of overall agreement, percentage of cases in which both raters agreed on the condition being present in the total study population (n=48).

‡ Identification agreement, percentage of cases in which both raters agreed on the condition being present in the subset of cases that were labelled by at least one rater as being present.

§ Exclusion agreement, percentage of cases in which both raters agreed on the condition being absent in the subset of cases that were labelled by at least one rater as being absent.

of the cases both raters agreed on the predominant pain mechanism being nociceptive pain, in the subset of cases that were labelled by at least one rater as being nociceptive pain. Accordingly, in 76.92% (10 out of 13) of the cases both raters agreed on the predominant pain mechanism not being nociceptive pain, in the subset of cases that were labelled by at least one rater as not nociceptive pain.

Discussion

This is the first study to examine the interrater reliability and agreement of the clinical judgements associated with predominant pain mechanisms, pain patterns, and DPs in patients with NSNP. The interrater reliability of the prevailing pain pattern and DP was substantial. The classification into predominant pain mechanism showed almost perfect reliability. These findings provide preliminary evidence that the proposed classification has acceptable clinical reliability, as a step towards classification validation. The standardized assessment protocol, the fixed examiner, and the previous experience with the proposed classification all presumably contributed to the interrater reliability observed in this study.

To our knowledge, there are no previous studies available on interrater reliability of clinical judgements associated with predominant pain patterns, and DPs in patients with NSNP. Therefore, it is difficult to compare our findings to the existing literature. A number of articles have reported the reliability of various components of the subjective or physical examination for patients with neck pain.[29-38] Surprisingly, only few studies have reported reliability of components of both the subjective and physical examination.[29, 33] Yet, obtaining a history can influence reliability of the physical examination.[32]

Predominant pain mechanism

Consistent with a previous study investigating the reliability of clinical judgements associated with the predominant pain mechanisms in LBP patients,[20] the current study found clinically acceptable reliability for this outcome measure.

Studying the sub-categories, judgments related to the peripheral neuropathic pain (PNP) category seemed to have perfect agreement. As Cohen stated, differentiating PNP from nociceptive pain is probably the most important clinical distinction to make.[39] Yet, this must be interpreted with caution, as there were only 2 out of 48 subjects identified with a dominance of PNP (as mentioned in Table 2). This high degree of clustering patients in nonPNP categories has most likely inflated the kappa value for the PNP category. Other reliability studies exploring the identification of clinical indicators for PNP (in LBP patients) found only fair to moderate levels of interrater reliability.[20, 40]

The examiners in this study seemed to identify patients' pain states more reliable as predominant nociceptive as compared to the exclusion of predominant nociceptive pain. The opposite was found for the central/nociplastic pain state. This could be supported by the fact that a dominance of nociceptive pain typically has clear criteria on which physical therapists base their judgements (e.g. 'pain localized to the area of injury/dysfunction', 'clear, proportionate mechanical/anatomical nature to aggravating and easing factors', 'pain is usually intermittent and sharp with movement/mechanical provocation', etc.).[41] On the other hand, a predominant central/nociplastic pain mechanism is usually characterized by the lack of a consistent clinical pattern (e.g. 'disproportionate, non-mechanical, unpredictable pattern of pain provocation in response to multiple/nonspecific aggravating/easing factors').[42] Caution is warranted when interpreting these assumptions, since the indicators for pain mechanisms in LBP patients may not generally apply to patients with neck pain. Nevertheless, the 'central/nociplastic' features discernible in NSNP patients most commonly agreed upon in the Delphi-survey by Dewitte et al.[8] were similar to those identified in LBP patients by Smart et al.[42]

Predominant pain pattern and dysfunction pattern

The pain pattern classification and DP classification show comparable, clinically acceptable kappa values. The agreement levels seem to reveal a trend in that exclusion agreements are higher than identification agreements. From a probability point of view, it seems evident that the exclusion of a condition by two raters yields better conformity, compared to the identification of a condition. For the identification of the predominant pain pattern, both raters had to agree on one out of three categories (i.e. input, processing or output), resulting in a 3/9 chance to agree. On the other hand, for the exclusion agreement they had 4/9 chances to agree on the absence of the prevailing pain pattern. Analogue reflections apply to the predominant DP classification. The two physical therapists had only 5/25 chances to agree on the identified DP, in contrast to the 16/25 chances to agree on the absence of the remaining DPs.

It is important that a dominance of central/nociplastic DP/processing mechanism, underlying a patient's NSNP, can be ruled out, since these patients require a different approach.[43] Because the processing pain pattern and central/nociplastic DP are defined in a similar way, they both attained identical, clinically acceptable agreement levels.

The input and output pain patterns did not reach the percentage agreement level of ≥80% for clinical acceptance, neither did the myofascial and sensorimotor control DPs. Possibly this could be explained by the interrelationship between input and output patterns, and the considerable overlap in clinical indicators that define the myofascial and sensorimotor control DPs.[8] Prolonged sensorimotor control dysfunctions may induce myofascial dysfunctions,[44-46] but changes in myofascial structure and function may generate sensorimotor control problems.[47] This may render it difficult to clearly distinguish between a dominant myofascial DP or sensorimotor control DP, as both 'dysfunctions' appear to merge.

Study Limitations

This study has several limitations. Firstly, the simultaneous examiner design may have caused bias towards overestimated interrater agreement values. Indeed, this design excludes the possible variability in assessments and patient–therapist interactions, that could occur in an independent-examiner design, which might result in lower levels of agreement.[20]

Secondly, the raters in this study had six years of experience with the classification under study. As such, the study results may not generalize to novice therapists or clinicians less familiar with mechanisms-based approaches.

Thirdly, the sample studied in the current study showed a preponderance of female patients (72.92%), and patients with headache (79.17%). A purposive, intentionally diverse sample might have been better to support the robustness of the reliability estimates. However, these patient characteristics appear to be typical for patients presenting with NSNP and correspond with the prevalence reported in the available literature.[1, 2, 39, 48-51]

Finally, we did not test reliability of unique criteria. Consequently, we cannot comment on the capacity of a stand-alone criterion for a definitive decision regarding the classification. This is, however, beyond the scope of this study. In practice, most clinicians do not make clinical decisions based on a single test finding. Using clusters provide more promising findings and are more closely associated to clinical decision making.[52]

Conclusions

The current study investigated the interrater reliability and agreement of a pain mechanism-based classification for patients with NSNP. Present findings suggest that physical therapists, acquainted with the classification strategy, are able to provide reliable ratings of individuals' predominant pain mechanisms, pain patterns, and DPs underlying their NSNP. These results require careful interpretation. They are to be seen as clinically-oriented indirect classifications, based on a cluster of signs and symptoms, that presumably reflect the underlying pain generating mechanism, rather than a direct classification based on neurophysiology.[20] The extent to which physical therapists can validly associate clinical patterns with the underlying pathophysiological mechanisms is still unclear.[53] Future studies examining the clinical utility of mechanisms-based classifications of NSNP, by means of clinical trials with larger patient samples and various independent examiners, are the necessary next step to justify this approach for clinical use.

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Supplementary Tables

SUPPLEMENTARY TABLE 1 Interpretation of kappa values suggested by Landis & Koch[26]

Kappa	Interpretation
<.00	Poor
.00 – .20	Slight
.21 - .40	Fair
.41 - .60	Moderate
.61 - .80	Substantial
.81 – 1.00	Almost perfect

CHAPTER 3

Diagnostic accuracy of a pain mechanisms-based reasoning model for nonspecific neck pain

Vincent Dewitte, PT [a,*], Robby De Pauw, PT [a,*], Kayleigh De Meulemeester, PT [a],
Lieven Danneels, PT, PhD [a], Katie Bouche, MD, PhD [b], Arne Roets, MSP, PhD [c], Barbara Cagnie, PT, PhD [a]

[a] Department of Rehabilitation Sciences, Ghent University, Corneel Heymanslaan 10, 3B3, 9000 Ghent, Belgium
[b] Centre for Musculoskeletal and Neurological Rehabilitation, Ghent University Hospital, Corneel Heymanslaan 10, K7, 9000 Ghent, Belgium
[c] Department of Developmental, Personality and Social Psychology, Ghent University, Henri Dunantlaan 2, 9000 Ghent, Belgium
* equally contributed first authors

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Abstract

Objectives: The aim of this study was to evaluate the diagnostic value of a pain mechanisms-based reasoning model for patients with nonspecific neck pain (NSNP).

Methods: In a cross-sectional, diagnostic accuracy study a random sample of 191 consecutive patients, aged between 18 and 75 years old, with a primary complaint of neck pain was assessed using a standardized assessment protocol. After the assessment, the subjects' NSNP was classified on two levels: (1) predominant pain pattern (input, processing, output) and (2) predominant dysfunction pattern (DP).

Results: Binomial logistic regression analyses with Lasso penalty identified distinct clusters of 22, 5, and 20 clinical criteria predictive of a predominant input, processing, and output pain pattern, respectively. Additional clusters of 10, 6, 5, and 20 clinical criteria were found to be predictive of a predominant articular DP, neural DP, central DP, and sensorimotor control DP, respectively. No cluster of clinical criteria could be identified for the myofascial DP. The obtained clusters showed overall high levels of diagnostic accuracy (sensitivity, specificity, positive/negative predictive values, positive/negative likelihood ratios, overall diagnostic accuracy).

Discussion: This study offers preliminary evidence for the diagnostic accuracy of a pain mechanisms-based reasoning model for NSNP. Several discriminatory clusters of subjective and physical examination criteria were identified as predictive of the proposed classification categories. Further evaluation of construct and criterion validity in larger neck pain populations is required before the information is used in clinical settings. The study protocol was registered at http://clinicaltrials.gov (NCT03147508).

Key words: Neck pain, reasoning model, pain mechanisms, validity

Introduction

Neck pain is a common condition that causes substantial disability and is associated with high costs.[1] Regardless the increased expenditure on the treatment of spinal pain, the results are not favorable.[2, 3] Evidence shows that no proportionate improvements in health outcomes can be observed, despite the growing costs over time.[3] For the majority of patients, a specific diagnosis cannot be made due to the multifactorial etiology, whereby neck pain is labelled as nonspecific (NSNP).[2, 4-7] To encounter the heterogeneity that characterizes NSNP patients, several classifications have been proposed in the literature.[8-12]

In the absence of a clear pathological etiology,[7, 13] classifications based on pathoanatomy are largely ineffective to guide treatment. Therefore, efforts have been made to classify patients' pain based on the prevailing pain mechanisms.[4, 14-16] Such a mechanistic approach has been actively encouraged in an attempt to exploit the growing understanding of the underlying neuro-physiological processes responsible for pain generation and/or maintenance.[16-23] It holds the potential to explain the variability of clinical manifestations of pain, and can facilitate targeted treatment selection associated with the predominant pain mechanism.[17, 23-25] However, most of the available diagnostic tools generally lack specificity for identifying the pain driver defined in terms of pain mechanisms, and treatment rarely targets such drivers.[16] These complex and often abstract concepts do not easily translate into clinical practice. Herein, the work of Smart and colleagues is to be acknowledged.[15, 20] Their pragmatic view on this area of research enabled them to provide the clinician with a set of subjective and physical examination criteria related to a dominance of pain mechanisms in patients with low back pain.[15, 20]

Recently, a new reasoning model was proposed by Dewitte et al. where patients with NSNP are classified on two levels: (1) the predominant pain pattern (including input, processing and output);[25] and (2) the predominant dysfunction pattern (DP) (i.e. articular DP, myofascial DP, neural DP, central DP, and sensorimotor control DP).[4] When the classification in DPs was established, the classification into input, processing, and output served as the foundation.[4] It was deemed appropriate to refine the input pain pattern into distinct categories (i.e. articular, myofascial, and neural DP). The researchers anticipated on the identification of unique criteria that could link the patients' NSNP to potentially relevant symptomatic structures, in case of a predominant input pattern. Each category refers to a clinical representation of the patient's NSNP that is assumed to reflect a dominance of the underlying pain mechanisms. Preferably one should look for a dominance of one of these mechanisms, because they all occur simultaneously. Yet, one mechanism might be clinically dominant over the others.[17] The information collected from both subjective and physical examination, could inform clinicians to identify these subgroups in NSNP patients.[7, 11] By pattern generation, a reasoned decision about the dominant mechanisms in operation can be made, since these mechanisms are typically defined by clusters of findings.[14, 17]

Preceding interrater reliability testing revealed acceptable clinical reliability, with substantial agreement between physiotherapists' judgements on the predominant pain pattern with kappa =.61 (95% CI, .42-.80), p <.001; and substantial agreement between the raters' judgements on the predominant DP with kappa =.62 (95% CI, .44-.79), p <.001.[26] However, further measurement properties are to be determined before the proposed reasoning model can be recommended for clinical use.[20, 27] Consequently, diagnostic accuracy in terms of sensitivity, specificity, overall diagnostic accuracy, predictive values, and likelihood ratios are required.[28, 29]

In the ongoing process of reasoning model development, the objective of this study was to evaluate the diagnostic accuracy of a pain mechanisms-based reasoning model for patients with NSNP, aspiring the identification of discriminative clusters of clinical criteria associated with the proposed categories. The authors hypothesized that the proposed reasoning model would demonstrate acceptable validity, and yield clusters of clinical criteria, to improve clinicians' understanding of the patients' NSNP and assist substantiated assessment and clinical reasoning.

Materials and methods

Study design

This cross-sectional, diagnostic accuracy study was conducted in accordance with the STARD 2015 guidelines for reporting diagnostic accuracy.[30]

Setting and participants

This study was carried out in an outpatient physiotherapy clinic of the Ghent University Hospital, between September 2017 and February 2018. The study was approved by the Ethics Committee of the Ghent University Hospital in accordance with the guidelines of the Declaration of Helsinki.

Twelve experienced physiotherapists with a postgraduate degree in Manual Therapy, including the first three authors and the last author, were responsible for the data collection. The mean number of years of clinical experience was 9.0 (SD 5.31, range 4-20). All investigators had a minimum of three years of previous experience with the proposed clinical reasoning model.

Subjects were referred by general practitioners and physiotherapists from local hospitals, general practitioners' clinics, and outpatient physiotherapists' clinics. All volunteers of any race or sex, aged between 18 and 75 years old, who experienced acute, subacute or chronic neck pain (± arm pain) were considered eligible for inclusion. Subjects were excluded if they were diagnosed with any serious pathology (i.e. cancer, metastasis, untreated fractures, history of diabetes or pathology of the central nervous system, non-musculoskeletal neck pain) that could compromise proper assessment or affect clinical reasoning. Before joining the study, all participants were informed about the aims and procedure of the study and gave signed informed consent. Figure 1 presents a flowchart of the patient recruitment.

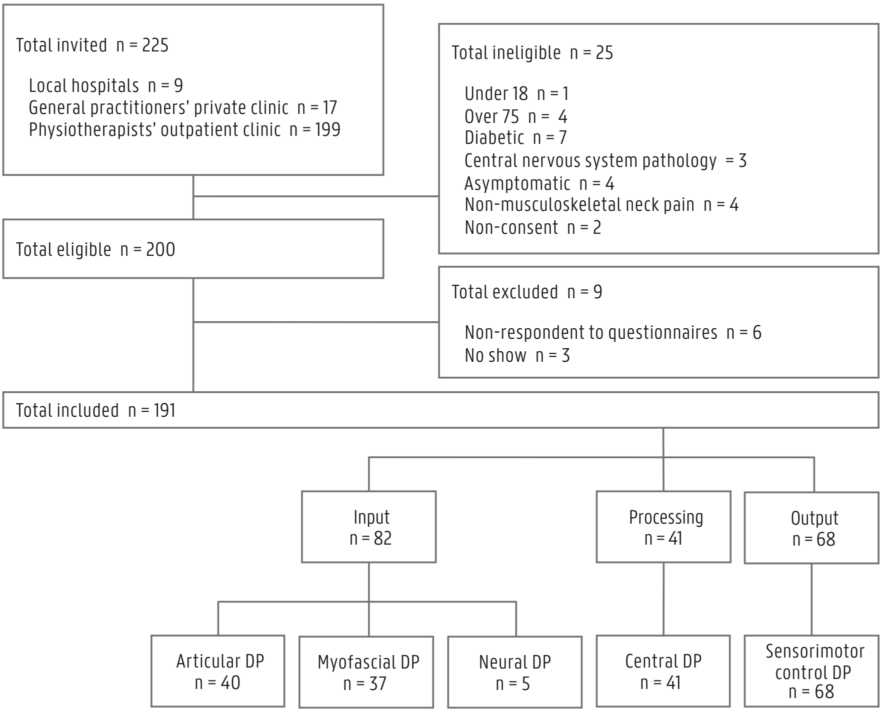

FIGURE 1 Flowchart of patient recruitment

Instrumentation and procedures

Patient data was collected via a standardized assessment form. The assessment was performed based on general clinical practice guidelines.[31] The subjective examination consisted of questions related to demographic data; localization, intensity, quality, onset and evolution, circadian rhythm, provocation, and reduction of the pain; associated complaints (movement restrictions, headache, dizziness, nausea, other); medical diagnosis and history; results of technical examinations (medical imagery, blood tests, etc.), and questionnaires (Neck Disability Index and Central Sensitization Inventory); general health; red and yellow flags; restrictions in activities and participation; and medication and/or previous therapy. The physical examination included a postural and movement assessment, and was complemented with additional tests, including articular, myofascial, and neurological function and provocation tests, and/or a sensorimotor control assessment.

Following the assessment, the physiotherapists classified the patient's NSNP description on two outcome measures: (1) predominant pain pattern (i.e. input, processing or output);[25] and (2) predominant DP (i.e. articular DP, myofascial DP, neural DP, central DP, and sensorimotor control DP).[4] The physiotherapists formulated their decisions based on experienced clinical judgement regarding the expected predominant mechanisms underlying the patient's NSNP. The discriminative validity of a classification is traditionally measured by comparing the results of the index test (i.e. new classification) with a gold standard (i.e. reference test).[29, 32] Unfortunately, there is no diagnostic gold standard available. In the absence of such a gold standard, the best proxy reference standard (i.e. the best available method to establish the presence or absence of a condition of interest[33] may be expert clinical judgement.[20, 34] Before participation, all therapists consulted an assessment manual with definitions and guidelines for the standardized assessment, to ensure that everyone interpreted the subjective and physical examination findings in a similar way.

Statistical data analysis

The high number of clinical criteria identified in a previously published study by Dewitte et al.[4] hinders the application of classical logistic regression models. Therefore, binomial logistic regression analysis with Lasso penalty was undertaken to identify meaningful criteria associated with the included groups of pain patterns and DPs. This approach is widely used in domains with high dimensional datasets, however, it is not robust to highly correlated predictors.[35] To tackle multi-collinearity among predictor variables, the two-by-two association was assessed and tested at a 5% significance level.[36] Significant correlations with a Cramer's V ≥.80 were clustered and merged into new uncorrelated variables. The data-analysis consisted of a three-staged approach. Firstly, eight high dimensional models were estimated to identify clinical predictors for each clinical outcome (pain patterns: input, processing, and output; dysfunction patterns: articular DP, myofascial DP, neural DP, central DP, and sensorimotor control DP) and to determine the most predictive criteria. Secondly, these binomial models were evaluated for their predictive capacity. Lastly, descriptive measures for proportions were given for each of the identified clinical criteria. All data-analyses were performed using RStudio for Windows version R 3.4.1 (RStudio, Boston, MA, USA).

Identification of clinical predictors

First, the dataset was randomly split into two components, a training dataset and a test dataset containing respectively 80% and 20% of all observations. A binomial logistic regression model including a lasso estimator,[35] which uses the l1 penalized least squares criterion to obtain a sparse solution of only a subset of all included predictors, was estimated using the training dataset. The l1 penalty was selected to minimize the amount of deviance based on a 10-fold cross validation algorithm.[37] The final selected l1 equals the largest value of l1 such that error was within 1 standard error of the minimum. By introducing a l1 penalty into the model, some predictors shrank towards zero, and the remaining non-zero predictors were thus evaluated by the model as the most important clinical identifiers with high discriminative capacity.

Predictive characteristics of the model

After the model estimation, its accuracy and predictive features were evaluated based on the test-dataset, which contained 20% of all observations. Subsequently, a prediction in terms of probability was established based on the selected clinical criteria.[38] These probabilities were then labeled (e.g. articular DP versus non-articular DP) based on an optimal cut-off point between sensitivity and specificity. Measures for diagnostic accuracy were calculated based on the training dataset unless the labeled predictions resulted in the same label for each observation (i.e. neural DP). In that instance, the measures of diagnostic accuracy were calculated on the full dataset which contained both the training- and test-datasets. Measurements for diagnostic accuracy included sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (LR+), negative likelihood ratio (LR-), and overall diagnostic accuracy.[29] Exact twosided 95% confidence intervals (CI) using the Pearson-Klopper method were additionally supplemented[39], except for the LR+ and LR-, where 95% CI were provided based on their asymptotic normality properties. In case of zero cell counts, an adjustment by adding .5 to each of the cells (known as Haldane-Anscombe correction) was performed.[40]

Descriptive measures for proportions

Odds ratios (ORs) were calculated for each of the identified clinical criteria in the lasso binomial regression model. Two-sided 95% CI were additionally supplemented along the ORs (with Haldane-Anscombe correction in case of zero cell counts), and a Fisher's exact test at a significance level of .05 ($\alpha < .05$) was performed to test the null hypothesis of independence.

Results

Of the 225 consecutive patients invited to participate, 191 entered the study. Their results were included for final analysis. Based on the exclusion criteria, 34 patients were ineligible (Figure 1). Table 1 presents the characteristics of the included subjects. The predictive characteristics of the model were assessed, based on the criteria obtained from a previous Delphi-study. The criteria included for further analysis are depicted in Table 2. Since criterion 35 ('Bakody's sign') and criterion 44 ('Traction reduces pain/symptoms') were absent in all subjects, and criterion 45 ('Active movement testing provokes symptoms and reveals ROM restrictions') was present in all subjects, these criteria were omitted from the list for further analysis.

The ORs of the clinical criteria identified by the logistic regression model are presented in Table 3. Only for the myofascial DP no clinical criteria were identified. Based on the univariate analysis of independence, not all criteria were found to be significant (Table 3), although these criteria were present in the cluster identified for a dominance of its respective pain pattern or DP. This indicates that these clinical criteria should be incorporated when making decisions on the dominance of the particular pain patterns or DPs. Details on diagnostic accuracy measures are presented in Table 4. Diagnostic accuracy measures were calculated based on the two-by-two contingency tables found in Supplementary Tables 1-7.

TABLE 1 Characteristics of the included subjects by pain classification (n =191)

Variable	Input pain pattern n =82 (42.9%)	Processing pain pattern n =41 (21.5%)	Output pain pattern n =68 (35.6%)
Sex (Female)	54 (65.9%)	36 (87.8%)	47 (69.1%)
Age (y), Mean (SD, Range)	45.0 (15.1, 21-75)	41.3 (13.5, 20-67)	33.1 (10.9, 20-70)
Predominant pain location			
Neck	9 (11.0%)	0 (0.0%)	10 (14.7%)
Neck/Uni Prox Arm (AE)	19 (23.2%)	6 (14.6%)	5 (7.4%)
Neck/Uni Dist Arm (BE)	12 (14.6%)	8 (19.5%)	4 (5.9%)
Neck/Bi Prox Arm (AE)	4 (4.9%)	10 (24.4%)	5 (7.4%)
Neck/Bi Dist Arm (BE)	3 (3.7%)	5 (12.2%)	1 (1.5%)
Neck/Other (TMJ, Tx, abdom)	35 (42.7%)	32 (78.0%)	27 (39.8%)
Head	50 (61.0%)	39 (95.1%)	52 (75.0%)
Wide spread	4 (4.9%)	23 (56.1%)	0 (0.0%)
Work status			
Full-time	64 (78.0%)	28 (68.3%)	65 (95.6%)
Part-time	3 (3.7%)	5 (12.2%)	2 (3.0%)
Unemployed	1 (1.2%)	6 (14.6%)	0 (0.0%)
Retired	14 (17.1%)	2 (4.9%)	1 (1.5%)
Average Sx intensity (NRS) over previous 7d, Mean (SD, Range)	4.1 (1.9, 0-8)	4.9 (1.8, 1-8)	3.7 (1.7, 1-8)
Worst Sx intensity (NRS) over previous 7d, Mean (SD, Range)	6.0 (2.1, 0-10)	6.9 (1.9, 1-10)	5.7 (2.0, 1-10)
NDI score, Mean (SD, Range)	10.9 (5.4, 0-24)	16.9 (7.2, 2-33)	9.2 (3.7, 2-18)
CSI score, Mean (SD, Range)	33.0 (11.4, 8-66)	45.0 (11.5, 12-68)	32.0 (9.9, 11-57)
Duration of current episode (weeks), Mean (SD, Range)	243.0 (389.0, 0.14-2080)	513.0 (526.0, 0.14-2080)	255.0 (434.0, 0.14-1820)
<4 weeks	21 (25.6%)	3 (7.3%)	25 (36.8%)
4-12 weeks	4 (4.9%)	1 (2.4%)	1 (1.5%)
>12 weeks	57 (69.5%)	37 (90.2%)	42 (61.8%)

continued

TABLE 1 Continued

Variable	Articular DP n =40 (20.9%)	Myofascial DP n =37 (19.4%)	Neural DP n =5 (2.6%)	Central DP n =41 (21.5%)	Sensorimotor control DP n =68 (35.6%)
Sex (Female)	23.0 (57.5%)	30.0 (81.1%)	1.0 (20.0%)	36.0 (87.8%)	47.0 (69.1%)
Age (y), Mean (SD, Range)					
Predominant pain location	46.7 (16.6, 22-75)	43.9 (13.6, 21-72)	40.0 (14.3, 25-63)	41.3 (13.5, 20-67)	33.1 (10.9, 20-70)
Neck	6.0 (15.0%)	3.0 (8.1%)	0.0 (0.0%)	0.0 (0.0%)	10.0 (14.7%)
Neck/Uni Prox Arm (AE)	5.0 (12.5%)	9.0 (24.3%)	5.0 (100.0%)	6.0 (14.6%)	5.0 (7.4%)
Neck/Uni Dist Arm (BE)	3.0 (7.5%)	4.0 (10.8%)	5.0 (100.0%)	8.0 (19.5%)	4.0 (5.9%)
Neck/Bi Prox Arm (AE)	1.0 (2.5%)	3.0 (8.1%)	0.0 (0.0%)	10.0 (24.4%)	5.0 (7.4%)
Neck/Bi Dist Arm (BE)	1.0 (2.5%)	2.0 (5.4%)	0.0 (0.0%)	5.0 (12.2%)	1.0 (1.5%)
Neck/Other (TMJ, Tx, abdom)	19.0 (47.5%)	16.0 (43.2%)	0.0 (0.0%)	32.0 (78.0%)	27.0 (39.8%)
Head	21.0 (52.2%)	28.0 (75.7%)	1.0 (20.0%)	39.0 (95.1%)	51.0 (75.0%)
Wide spread	2.0 (5.0%)	2.0 (5.4%)	0.0 (0.0%)	23.0 (56.1%)	0.0 (0.0%)
Work status					
Full-time	29.0 (72.5%)	31.0 (83.8%)	4.0 (80.0%)	28.0 (68.3%)	65.0 (95.6%)
Part-time	2.0 (5.0%)	1.0 (2.7%)	0.0 (0.0%)	5.0 (12.2%)	2.0 (2.9%)
Unemployed	0.0 (0.0%)	0.0 (0.0%)	1.0 (20.0%)	6.0 (14.6%)	0.0 (0.0%)
Retired	9.0 (22.5%)	5.0 (13.5%)	0.0 (0.0%)	2.0 (4.9%)	1.0 (1.5%)
Average Sx intensity (NRS) over previous 7d, Mean (SD, Range)	3.8 (1.81, 1-7)	4.4 (2.1, 1-8)	3.2 (1.8, 0-4)	4.9 (1.8, 1-8)	3.7 (1.7, 1-8)

continued

TABLE 1 Continued

Variable	Articular DP n =40 (20.9%)	Myofascial DP n =37 (19.4%)	Neural DP n =5 (2.6%)	Central DP n =41 (21.5%)	Sensorimotor control DP n =68 (35.6%)
Worst Sx intensity (NRS) over previous 7d, Mean (SD, Range)	5.9 (1.97, 1-9)	6.2 (2.2, 1-10)	5.2 (3.0, 0-7)	6.9 (1.9, 1-10)	5.7 (2.0, 1-10)
NDI score, Mean (SD, Range)	10.3 (5.42,0-22)	11.3 (5.1, 3-24)	12.6 (6.9, 7-24)	16.9 (7.2, 2-33)	9.2 (3.7, 2-18)
CSI score, Mean (SD, Range)	31.5 (10.6, 8-47)	35.4 (11.8, 18-66)	29.8 (14.2, 15-52)	45.0 (11.5, 12-68)	32.0 (9.9, 11-57)
Duration of current episode (weeks), Mean (SD, Range)	261.0 (435.0, 0.14-2080)	230.0 (356.0, 0.29-1508)	194.0 (273.0, 3-624)	513.0 (526.0, 0.14 -2080)	255.0 (434.0, 0.14-1820)
<4 weeks	11.0 (27.5%)	9.0 (24.3%)	1.0 (20.0%)	3.0 (7.3%)	25.0 (36.8%)
4-12 weeks	2.0 (5.0%)	2.0 (5.3%)	0.0 (0.0%)	1.0 (2.4%)	1.0 (1.5%)
>12 weeks	27.0 (67.5%)	26.0 (70.4%)	4.0 (80.0%)	37.0 (90.2%)	42.0 (61.8%)

Abbreviations: Neck/Uni Prox Arm (AE), neck pain with unilateral proximal arm pain above elbow; Neck/Uni Dist Arm (BE), neck pain with unilateral distal arm pain below elbow; Neck/Bi Prox Arm (AE), neck pain with bilateral proximal arm pain above elbow; Neck/Bi Dist Arm (BE), neck pain with bilateral distal arm pain below elbow; Neck/Other (TMJ, Tx, abdom), neck pain associated with temporomandibular joint complaints, musculoskeletal thoracic complaints or abdominal complaints; Sx, symptom; NRS, numeric pain rating scale; NDI, Neck Disability Index; CSI, Central Sensitization Inventory.

TABLE 2 Clinical criteria included for analysis

Criterion	Description
1	Clear pain distribution, localized to the neck region
2	Predominant unilateral pain
3	Pain referred in a distribution pattern familiar to the target muscle
4	Pain and/or stiffness localized to the area of the muscle (insertion)
5	Pain referred in a clear distribution pattern familiar to a peripheral nerve or cervical nerve root (dermatome or myotome pattern of distribution)
6	Peripheral symptoms (arm pain/symptoms) exceed neck pain
7	Referred pain below the elbow
8	Widespread, non-anatomical/nonspecific distribution of pain
9	Predominant movement restriction towards extension and/or rotation
10	Mechanical pattern to aggravating and easing factors, with pain provocation in response to stretch and/or compression (subjective examination)
11	Pain/symptoms caused by overuse and/or long-lasting loading (e.g. static postures)
12	Pain/symptom provocation on static, one-sided loading and/or more specific activities/postures (e.g. desktop-workers, car driver, ...), whereas careful movements/activities (low load) exercises/ activities result in pain reduction and/or functional improvement
13	Pain provocation in response to stretch
14	Pain/symptom provocation on specific activities/postures that load the impaired side
15	Pain/symptom provocation in response to coughing, sneezing, valsalva maneuvers
16	Unpredictable, variable, disproportionate non-mechanical nature to aggravating and easing factors and/or disproportionate/abnormal, non-mechanical, unpredictable intolerance to visual perception of light, mechanical, thermal triggers and/or sound
17	Spontaneous (i.e. stimulus-independent) pain/ pain at rest
18	Uncontrollable pain/complaints with no or insufficient response to antalgic medication and/or postures
19	Absence of neurological symptoms
20	Sharp, stabbing, shooting pain
21	Pain variously described as pins and needles, ants, electrical, toothache-like pain, altered sensations in arm and/or hand
22	Muscle weakness (not caused by pain inhibition), sometimes objectified by EMG results
23	Pain of high severity and irritability with high scores on VAS or NRS (i.e. worst NRS>7)
24	Pain/complaints increase(s) during the day
25	Night pain/disturbed sleep
26	Pain persisting beyond expected tissue healing/pathology recovery times
27	History of (long) lasting complaints (recurrent, in episodes)
28	Positive identification of various maladaptive psychological factors/YF (e.g. major life events in past history, distress, catastrophizing, fear-avoidance behavior, passive coping strategies, irrational thoughts on diagnosis/complaints)
29	Positive identification of lowered immune responses and/or tolerance to activities
30	Medical shopping
31	Medical imagery: findings do not relate to the patient's complaints (i.e. no structural cause)

continued

TABLE 2 Continued

Criterion	Description
32	Surveys can reveal supporting evidence: high scores on HADS, TSK, CSI, NDI, etc.
33	Antalgic posture
34	Insufficient posture, unable to maintain a corrected posture
35	Placing the painful arm on top of the head results in pain relief (Bakody's sign)
36	Increased muscle tension
37	Presence of (active) myofascial trigger points/taught bands
38	Hyperalgesia and/or allodynia (painful response to non-painful stimuli)
39	Associated with unilateral compression and/or stretch pain
40	Provocation in response to combined movement testing (3D-extension/3D-flexion)
41	Predominant movement restriction towards extension and/or rotation
42	Restricted ROM on passive and active movement testing
43	Relaxation of relevant myofascial structures does result in an increased passive ROM and/or pain/symptom provocation in response to stretch of relevant myofascial structures (positive muscle length tests)
44	Traction reduces pain/symptoms
45	Active movement testing provokes symptoms and reveals ROM restrictions
46	Impaired quality of movement
47	Mechanical pattern to aggravating and easing factors, with pain provocation in response to stretch and/or compression (physical examination)
48	Provocation of peripheral pain/symptoms in response to ipsilateral rotation, ipsilateral side bending and extension of the neck (positive Spurling's test)
49	Variable findings in active movement assessment
50	Muscular imbalance with increased activity of superficial/global neck muscles
51	Pain/symptom provocation with repeated movement testing
52	Localized, unilateral increased muscle tension
53	Pain/symptom provocation/local twitch response on palpation of relevant myofascial structures (trigger point(s))
54	Reduced muscle power and/or endurance of impaired muscles and/or muscular imbalance with impaired cervical and/or scapulothoracic neuromuscular control and/or proprioception
55	Intervertebral movement restriction at the impaired segment (aberrant end feel)
56	Pain/symptom provocation/muscle tension on palpation of relevant articular structures (positive UPA)
57	No clear intervertebral movement restriction(s)
58	Absence of clear neurological findings on neurological function and provocation testing
59	Clear neurological findings (i.e. altered deep-tendon reflexes, sensation and motor strength)
60	Pain/symptom provocation in response to palpation of the nerve
61	Positive slump test
62	Inconsistent and ambiguous findings/diagnostics that vary over sessions
63	Disproportionate/abnormal reaction during and after the patient's assessment

Abbreviations: YF, yellow flags; EMG, electromyography; VAS, visual analogue scale; NRS, numeric rating scale; HADS, Hospital Anxiety and Depression Scales; TSK, Tampa Scale for Kinesiophobia; CSI, Central Sensitization Inventory; NDI, Neck Disability Index; 3D, 3-dimensional; ROM, range of motion; UPA, unilateral posteroanterior provocation test.

Input pain pattern

Twenty-two criteria were identified as predictive for the dominance of the input pain pattern. The most predictive criterion was 'Muscle weakness (not caused by pain inhibition)' with an OR of 26.8, which implies that the odds for the presence of muscle weakness were 26.8 times higher compared to the odds for the absence of muscle weakness in patients whose NSNP was labeled with a dominance of an input pain pattern. The achieved sensitivity of 92% in this cluster indicates that 92% of the patients whose NSNP was classified as predominant input, based on the reference standard of clinical judgement, were classified correctly by the model, while 8% of patients' NSNP classified as predominant input were falsely classified.

Processing pain pattern and central dysfunction pattern

A cluster of five criteria was identified as predictive for the dominance of a processing pain pattern. These clinical criteria were, as expected, identical to those identified for the dominance of a central DP. According to the processing pain pattern model, the strongest predictor was the presence of 'Inconsistent and ambiguous findings' with an OR of over 80, suggesting the odds for the presence of this criterion was more than 80 times higher than the odds for the absence of this criterion. This was followed by the presence of 'Hyperalgesia and/or allodynia' with an OR of approximately 60. The achieved specificity of 98% in this cluster implies that 98% of the patients whose NSNP was classified, based on the reference standard of clinical judgement, as a predominant non-processing pain pattern were classified correctly by the model. The LR+ of over 34 suggests that the processing cluster is over 34 times more likely to be found in a patient whose NSNP predominantly reflects a processing pain pattern compared to a non-processing pain pattern.

Output pain pattern and sensorimotor dysfunction pattern

A cluster of 20 clinical criteria was identified to be predictive for a dominant output pain pattern. Due to the definitions used, the criteria of the output pain pattern were identical to those related to a dominance of a sensorimotor control DP. The most important clinical criterion was the presence of 'Reduced muscle power/endurance/impaired neuromuscular control' with an OR of over 129. Another important clinical predictor was the presence of 'Widespread pain' with an OR of .026, which suggest that the odds for absence of widespread pain is over 38 times higher compared the odds for the presence of widespread pain in patients whose NSNP was labeled as a predominant output pain pattern. The overall accuracy of 84% suggests that 84% of all cases were classified correctly by the cluster of clinical criteria in this model, while only in 16% patients were classified incorrectly. The LR- of .11 indicates that the likelihood of the cluster being absent in patients identified with a predominant output pain pattern compared to a non-output pain pattern, is .11. The NPV of 94% indicates that the probability for a patient without this particular cluster not to have a prevailing output pain pattern, is 94%.

TABLE 3 Descriptive odds ratios for the criteria in the classification models

Criteria	OR	95% CI Lower	95% CI Upper	p-value
Input pain pattern				
5 Pain referred in peripheral nerve/Cx nerve root distribution pattern	2.106	.881	5.183	.070
8 Widespread pain	.193	.047	.600	.001
10 Mechanical pattern to aggravating and easing factors (subj. exam)	1.730	.827	3.647	.119
13 Pain provocation in response to stretch	2.277	.862	6.329	.075
14 Sx provocation on specific activities/postures that load impaired side	.353	.182	.670	<.001
22 Muscle weakness (not caused by pain inhibition)	26.877	1.534	470.788	<.001
23 High scores on VAS or NRS (i.e. worst NRS>7)	.697	.374	1.289	.243
32 Surveys can reveal supporting evidence (high scores on CSI, NDI, etc.)	.438	.204	.904	.021
34 Insufficient posture, unable to maintain a corrected posture	.349	.168	.711	.003
38 Hyperalgesia and/or allodynia	.045	.003	.771	.002
39 Associated with unilateral compression and/or stretch pain	4.293	2.072	9.219	<.001
41 Predominant movement restriction towards extension/ rotation	2.496	1.274	4.961	.004
42 Restricted ROM on passive and active movement testing	5.176	1.666	21.504	.001
43 Relaxation of relevant muscles results in increased ROM	.223	.114	.429	<.001
47 Mechanical pattern to aggravating and easing factors (phys. exam)	.228	.097	.505	<.001
49 Variable findings in active movement assessment	9.074	1.933	86.072	.001
50 Muscular imbalance with increased activity of global neck muscles	.094	.010	.402	<.001
52 Localized, unilateral increased muscle tension	1.774	.950	3.331	.055
54 Reduced muscle power/endurance/impaired neuromuscular control	.238	.116	.474	<.001
55 Intervertebral movement restriction at the impaired segment	2.836	1.493	5.498	<.001
62 Inconsistent and ambiguous findings	.122	.023	.423	<.001
63 Disproportionate/abnormal reaction	.186	.020	.858	.016
Processing pain pattern				
8 Widespread pain	44.932	13.387	199.483	<.001
28 Positive identification of various YFs	14.526	6.124	36.646	<.001
38 Hyperalgesia and/or allodynia	59.855	8.289	2611.318	<.001

continued

TABLE 3 Continued

Criteria	OR	95% CI Lower	95% CI Upper	p-value
Processing pain pattern				
62 Inconsistent and ambiguous findings	80.821	21.361	464.438	<.001
63 Disproportionate/abnormal reaction	33.414	7.006	320.430	<.001
Output pain pattern				
8 Widespread pain	.026	.002	.436	<.001
14 Sx provocation on specific activities/postures that load impaired side	1.507	.795	2.863	.223
15 Sx provocation in response to coughing/sneezing/valsalva maneuvers	.122	.007	2.181	.098
16 Unpredictable/disproportionate aggravating and easing factors	.047	.001	.296	<.001
21 Pain variously described as pins and needles	.173	.032	.601	.001
24 Pain/complaints increase(s) during the day	3.081	1.474	6.808	.001
28 Positive identification of various YFs	.175	.057	.449	<.001
29 Lowered immune responses and/or tolerance to activities	.104	.012	.435	<.001
34 Insufficient posture, unable to maintain a corrected posture	2.781	1.242	6.753	.009
39 Associated with unilateral compression and/or stretch pain	.402	.171	.882	.017
41 Predominant movement restriction towards extension/ rotation	.232	.092	.527	<.001
42 Restricted ROM on passive and active movement testing	.321	.125	.796	.009
43 Relaxation of relevant muscles results in increased ROM	4.152	2.022	8.976	< .001
47 Mechanical pattern to aggravating and easing factors (phys. exam)	4.084	1.571	12.609	.002
49 Variable findings in active movement assessment	.127	.003	.883	.020
50 Muscular imbalance with increased activity of global neck muscles	7.471	2.668	24.287	<.001
54 Reduced muscle power/endurance/impaired neuromuscular control	129.524	7.842	2139.271	<.001
55 Intervertebral movement restriction at the impaired segment	.551	.289	1.046	.067
58 Absence of clear neurological findings (function/ provocation tests)	18.889	1.110	321.337	.003
62 Inconsistent and ambiguous findings	.024	.001	.397	<.001
Articular dysfunction pattern				
17 Spontaneous (i.e. stimulus-independent) pain/ pain at rest	.043	.003	.718	.003
28 Positive identification of various YFs	.255	.062	.773	.008

continued

TABLE 3 Continued

Criteria	OR	95% CI Lower	95% CI Upper	p-value
Articular dysfunction pattern				
34 Insufficient posture, unable to maintain a corrected posture	.288	.129	.641	.001
39 Associated with unilateral compression and/or stretch pain	3.340	1.504	7.436	.002
41 Predominant movement restriction towards extension/rotation	2.260	1.028	4.940	.033
49 Variable findings in active movement assessment	5.963	1.684	22.423	.002
51 Pain/symptom provocation with repeated movement testing	4.422	1.338	14.670	.007
54 Reduced muscle power/endurance/impaired neuromuscular control	.277	.125	.605	<.001
55 Intervertebral movement restriction at the impaired segment	5.847	2.251	18.048	<.001
57 No clear intervertebral movement restriction(s)	.117	.013	.487	<.001
Myofascial dysfunction pattern				
There were no criteria associated with a myofascial dysfunction pattern				
Neural dysfunction pattern				
6 Arm symptoms exceed neck pain	92.568	7.955	4857.556	<.001
22 Muscle weakness (not caused by pain inhibition)	126.459	10.421	6732.219	<.001
48 Positive Spurling's test	81.478	7.103	4253.610	<.001
58 Absence of clear neurological findings (function/ provocation tests)	.017	.001	.187	<.001
59 Clear neurological findings	106.977	9.029	5649.428	<.001
60 Pain/symptom provocation in response to palpation of the nerve	37.043	2.330	490.327	.005
Central dysfunction pattern				
8 Widespread pain	44.932	13.387	199.483	<.001
28 Positive identification of various YFs	14.526	6.124	36.646	<.001
38 Hyperalgesia and/or allodynia	59.855	8.289	2611.318	<.001
62 Inconsistent and ambiguous findings	80.821	21.361	464.438	<.001
63 Disproportionate/abnormal reaction	33.414	7.006	320.430	<.001
Sensorimotor control dysfunction pattern				
8 Widespread pain	.026	.002	.436	<.001
14 Sx provocation on specific activities/postures that load impaired side	1.507	.795	2.863	.223
15 Sx provocation in response to coughing/sneezing/valsalva maneuvers	.122	.007	2.181	.098
16 Unpredictable/disproportionate aggravating and easing factors	.047	.001	.296	<.001
21 Pain variously described as pins and needles	.173	.032	.601	.001

continued

TABLE 3 Continued

Criteria	OR	95% CI Lower	95% CI Upper	p-value
Sensorimotor control dysfunction pattern				
24 Pain/complaints increase(s) during the day	3.081	1.474	6.808	.001
28 Positive identification of various YFs	.175	.057	.449	<.001
29 Lowered immune responses and/or tolerance to activities	.104	.012	.435	<.001
34 Insufficient posture, unable to maintain a corrected posture	2.781	1.242	6.753	.009
39 Associated with unilateral compression and/or stretch pain	.402	.171	.882	.017
41 Predominant movement restriction towards extension/rotation	.232	.092	.527	<.001
42 Restricted ROM on passive and active movement testing	.321	.125	.796	.009
43 Relaxation of relevant muscles results in increased ROM	4.152	2.022	8.976	<.001
47 Mechanical pattern to aggravating and easing factors (phys. exam)	4.084	1.571	12.609	.002
49 Variable findings in active movement assessment	.127	.003	.883	.020
50 Muscular imbalance with increased activity of global neck muscles	7.471	2.668	24.287	<.001
54 Reduced muscle power/endurance/impaired neuromuscular control	129.524	7.842	2139.271	<.001
55 Intervertebral movement restriction at the impaired segment	.551	.289	1.046	.067
58 Absence of clear neurological findings (function/provocation tests)	18.889	1.110	321.337	.003
62 Inconsistent and ambiguous findings	.024	.001	.397	<.001

Abbreviations: OR, odds ratio; CI, confidence interval; YFs, Yellow Flags; Cx, cervical; subj. exam, subjective examination; Sx, symptom; VAS, Visual Analogue Scale; NRS, Numeric Rating Scale; CSI, Central Sensitization Inventory; NDI, Neck Disability Index; ROM, range of motion; phys. exam, physical examination.
The criterion descriptions were shortened. Full descriptions are listed in Table 2.
In case of zero cell counts, an adjustment by adding 0.5 to each of the cells (known as Haldane-Anscombe correction) was performed.[39]

Articular dysfunction pattern

Ten criteria were identified as predictive for a dominance of an articular DP. The odds for the presence of '**Intervertebral movement restriction at the impaired segment**' in patients whose NSNP was judged as a predominant articular DP was almost six times higher than the odds for the absence of that criterion. The achieved overall diagnostic accuracy of 58% indicates that only in 58% of all cases patients' NSNP was labeled correctly as a predominant articular DP or non-articular DP. The PPV of 29% indicates that the probability of a patient with this particular cluster of criteria having a dominance of an articular DP, is 29%.

Neural dysfunction pattern

A total of six criteria was identified as predictive for the dominance of a neural DP. '**Muscle weakness (not caused by pain inhibition)**' and '**Clear neurological findings**' were identified as the most important clinical predictors with an OR of respectively 126 and 107. The NPV of 100% indicates that the probability of a patient without this particular cluster of criteria having a dominance of a non-neurological DP, is 100%.

Discussion

To our knowledge this is the first study to investigate the diagnostic value of a pain mechanisms-based reasoning model for patients with NSNP. A preceding Delphi-study resulted in an expert consensus-derived list of clinical criteria associated with a dominance of the proposed classification categories. From this list, several discriminatory clusters of subjective and physical examination criteria were identified as predictive of the predominant pain pattern and DP.

When the input pattern dominates the pain presentation, the complaint is typically driven by de peripheral somatosensory dimension of the pain. Hence, the patient's complaints are largely explained by dysfunctional tissues, and the clinical representation corresponds to a nociceptive or neuropathic pain mechanism.[41] This is reflected in our findings, in which some input criteria overlap with the criteria linked to a predominant articular or neural DP. The clustered input predictors comprise criteria that lower the plausibility for a central or output pain pattern, along with criteria that predict higher odds to be classified into the input pattern. The latter seem to reflect a rather incoherent compilation of various clinical representations of NSNP. This appears logical because the input pattern encompasses the articular, myofascial, and neural DPs. In contrast, the clusters related to the articular and neural DPs reveal a more comprehensive entity of criteria that relate to the additional articular and/or neurological assessment.

Despite the fact that the refinement of the input pattern into the articular DP resulted in criteria that are assumed to be related to articular structures, this articular DP model lost diagnostic accuracy compared to the input model. The lowered absolute values of the PPV may be partially explained by a low disease prevalence in the test population (Supplementary Table 4, 6 subjects on a total of 31).[42] However, an additional explanation appears in order, since the other diagnostic accuracy measures are not affected by disease prevalence. From a probabilistic point of view, it seems logical that introducing 3 options (i.e. articular, myofascial and neural) instead of 1 option (i.e. input) affected the accuracy measures of the articular DP model. Then again, perhaps the ramification of the input pain pattern into distinct DPs that refer to apparent anatomical structures may clinically be less favorable than initially anticipated.

Although evidence supports the identification of myofascial structures as possible sources of NSNP,[43, 44] confusion remains on the diagnostic criteria on which physiotherapists have to base their decision regarding a myofascial pain syndrome.[44, 45] Regrettably, the results of this cross-sectional study bring little clarification on this matter. The subjects whose NSNP was judged to be predominant myofascial, displayed considerable variability in clinical features. Consequently, it was impossible to withhold a clear cluster of criteria related to a dominant myofascial DP. Myofascial pain syndrome is frequently associated with anxiety-depressive disorders found in patients with cervical pain.[46, 47] Furthermore, patients with Trapezius myalgia can also lead to disturbed muscle activation patterns.[48] This could possibly explain, why some of the clinicians were in doubt to make clear distinction between a predominant myofascial DP and a central or sensorimotor control DP, respectively.

The cluster of criteria identified for the neural DP is consistent with the results reported in the literature.[49-54] These findings should be interpreted cautiously, since the prevalence of this subgroup in the studied sample was only 2.6% (Table 1). This might have inflated the ORs and accuracy measures for the neural DP classification model and is reflected in the low PPV.

The results of the processing pain pattern and central DP are identical, since both categories were defined in a similar way.[4] The criteria related to a predominance of central pain processes underlying the patients' NSNP in the present study converge with the results of Smart et al. in patients with low back pain.[20] The comparison of different patient samples with complaints in different symptomatic areas warrants caution. Yet, the central mechanisms are not assumed to depend on symptomatic regional differences.[41]

The output pattern, as originally described by Gifford, comprises autonomic, motor, neuroendocrine, and immune systems to promote survival to any threats (e.g. NSNP) to the organism.[18, 21, 25] At the conception of the DP classification, the output pattern was reduced to the motor system (i.e. sensorimotor DP), since physiotherapy traditionally focusses on impairments of the locomotor system.[4] This does not downgrade the importance of the other output-related mechanisms, but helps to elucidate why the output pain pattern criteria coincide with the sensorimotor control DP criteria. A subjective or physical examination procedure may not allow for the detection of clinical criteria related to the other, 'background' output systems.[17]

There are a number of methodological areas requiring consideration. Firstly, patients were only examined by physiotherapists. It might have been valuable to include a range of clinicians from different disciplines.[34] Yet, physiotherapists are thoroughly trained and well placed to diagnose and manage patients with NSNP.[55]

Secondly, this study included considerably less patients with a recent onset of complaints compared to the sample studied in the study of Smart et al.[20] Obviously, the call for participation in the current study attracted more patients with ongoing NSNP (i.e. recurrent or chronic) (Table 1). Because persevering complaints are typically associated with a predominant central and/or output pain mechanism,[56-58] this non-response bias limited us to make clear statements on the predominant input mechanism and the articular, myofascial, and neural DPs. A purposive, intentionally diverse sample may have been better to support the robustness of the accuracy estimates for these categories.

Thirdly, each clinician collected information on the clinical criteria and then classified the patients' NSNP based on those criteria. It is accepted that this procedure could have introduced clinical review or expectation bias. To prevent such bias, test and reference standard results should have been read successively in a blinded fashion.[42] Unfortunately, the financial resources for this study did not allow us to assess each patient by 2 separate physiotherapists. Besides, the approach used in this study is compatible with the daily routine of current clinical practice.

Finally, this process of reasoning model development started from a Delphi-approach, resulting in a set of clinical criteria which are assumed to have a high degree of face and content validity.[59] Applying lasso regression enabled us to include all criteria into a single model, taking into account the relatively small sample size compared to the numerous clinical criteria. Still, inherent to the low number of included subjects, it is possible that the univariate ORs are inflated.

In summary, this study offers preliminary evidence for the diagnostic accuracy of a pain mechanisms-based reasoning model for NSNP. Several discriminatory clusters of subjective and physical examination criteria were identified as predictive of the proposed classification categories. Yet, these sets of criteria should be evaluated in larger samples of patients with NSNP, by clinicians from different disciplines in which the criteria will be ultimately used. The performance of these criteria is to be compared prospectively with other sets of criteria to attain more accurate estimates of the "true" criteria.[20, 60] Non-specific neck pain remains a difficult area to diagnose, as the signs and symptoms relate to more than one subcategory and vary over time. As often observed in clinical practice, the coincidence of clinical criteria and altered patterns of associations between them, suggest that longitudinal study designs are needed to investigate this further.

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Supplementary Tables

SUPPLEMENTARY TABLE 1 Classification accuracy of the input pain pattern model

	Reference standard positive	Reference standard negative	Total
Cluster positive	12 patients	3	15
Cluster negative	1	15	16
Total	13	18	31

SUPPLEMENTARY TABLE 2 Classification accuracy of the processing pain pattern model

	Reference standard positive	Reference standard negative	Total
Cluster positive	5 patients	0	5
Cluster negative	2	24	26
Total	7	24	31

SUPPLEMENTARY TABLE 3 Classification accuracy of the output pain pattern model

	Reference standard positive	Reference standard negative	Total
Cluster positive	10 patients	4	14
Cluster negative	1	16	17
Total	11	20	31

SUPPLEMENTARY TABLE 4 Classification accuracy of the articular dysfunction pattern model

	Reference standard positive	Reference standard negative	Total
Cluster positive	5 patients	12	17
Cluster negative	1	13	14
Total	6	25	31

SUPPLEMENTARY TABLE 5 Classification accuracy of the neural dysfunction pattern model

	Reference standard positive	Reference standard negative	Total
Cluster positive	5 patients	6	11
Cluster negative	0	180	180
Total	5	186	191

SUPPLEMENTARY TABLE 6 Classification accuracy of the central dysfunction pattern model

	Reference standard positive	Reference standard negative	Total
Cluster positive	5 patients	0	5
Cluster negative	2	24	26
Total	7	24	31

SUPPLEMENTARY TABLE 7 Classification accuracy of the sensorimotor control dysfunction pattern model

	Reference standard positive	Reference standard negative	Total
Cluster positive	10 patients	4	14
Cluster negative	1	16	17
Total	11	20	31

PART III

EXPLORING THE ARTICULAR DYSFUNCTION PATTERN IN PATIENTS WITH NONSPECIFIC NECK PAIN

CHAPTER 4

Articular dysfunction patterns in patients with mechanical neck pain: a clinical algorithm to guide specific mobilization & manipulation techniques

Vincent Dewitte, PT [a], Axel Beernaert, PT [a], Bart Vanthillo, PT [a], Tom Barbe, PT [a],
Lieven Danneels, PT, PhD [a], Barbara Cagnie, PT, PhD [a]

[a] Department of Rehabilitation Sciences, Ghent University, Corneel Heymanslaan 10, 3B3, 9000 Ghent, Belgium

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Abstract

In view of a didactical approach for teaching cervical mobilization and manipulation techniques to students as well as their use in daily practice, it is mandatory to acquire sound clinical reasoning to optimally apply advanced technical skills. The aim of this Masterclass is to present a clinical algorithm to guide (novice) therapists in their clinical reasoning to identify patients who are likely to respond to mobilization and/or manipulation. The presented clinical reasoning process is situated within the context of pain mechanisms and is narrowed to and applicable in patients with a dominant input pain mechanism. Based on key features in subjective and clinical examination, patients with mechanical nociceptive pain probably arising from articular structures can be categorized into specific articular dysfunction patterns. Pending on these patterns, specific mobilization and manipulation techniques are warranted. The proposed patterns are illustrated in three case studies. This clinical algorithm is the corollary of empirical expertise and is complemented by in-depth discussions and knowledge exchange with international colleagues. Consequently, it is intended that a carefully targeted approach contributes to an increase in specificity and safety in the use of cervical mobilizations and manipulation techniques as valuable adjuncts to other manual therapy modalities.

Keywords: Articular dysfunction patterns, clinical reasoning, cervical spine, spinal manipulation

Introduction

For centuries, spinal mobilization and manipulation techniques have been passed down from one generation of manipulators to the next. Although these techniques have undoubtedly evolved over time, their progression has largely been a culmination of imitation and iterative adaptation, leading to a great variety of spinal manipulation techniques.[1] Nowadays, an eclectic approach is used in most of the manual therapy courses, including aspects of Maitland, Kaltenborn-Evjenth, Hartman and other philosophies and principles.

Although recent systematic reviews[2-4] have demonstrated evidence (low to moderate quality) that cervical manipulation and mobilization are beneficial, these reviews highlight the lack of knowledge on optimal techniques and doses.

In view of a didactical approach for teaching students as well as for daily practice, it is mandatory not only to learn advanced technical skills, but also to acquire sound clinical reasoning skills.[5-7] Only if both aspects are integrated, spinal manipulation and mobilization may be considered proficient. In 2003, Hing et al.[8] published a comprehensive paper in Manual Therapy to discuss manipulation of the cervical spine, detailing the teaching strategies developed for cervical spine manipulation in New Zealand, outlining the clinical assessment and providing examples of the procedures in practice. What is missing in this article, and in a lot of handbooks on manual therapy, is the sound clinical reasoning behind manipulation. It is mandatory to (1) recognize key features in subjective examination and clinical examination to identify patients likely to benefit from cervical mobilization and manipulation, and (2) to define optimal techniques pending on the individual presentation of the patient.

Therefore, the aim of this Masterclass is to present a clinical algorithm for guiding therapists in their clinical reasoning to identify patients with predominantly mechanical nociceptive pain arising from the articular structures, who are likely to respond to mobilization and/or manipulation. This clinical algorithm is mainly based on many years of clinical experience using a standardized way in assessing and treating neck pain patients. According to Jones, a form of pattern recognition sprouts, when a well-structured approach is obeyed, and this for many years of clinical practice.[9-11] Considering the empirical foundation of this process, the desire to communicate these prototypes to (international) colleagues arose so that definition and interpretation of similar patterns could be modeled into a more comprehensive and refined form. To our knowledge these symptoms have not been clustered before in distinct dysfunction patterns (DPs) along with specific treatment recommendations. Therefore the authors tried to describe specific findings per DP and, where possible, complemented them with the limited evidence available.

First the reasoning framework of interest to (articular) mechanical neck pain is outlined. In light of this reasoning process, an attempt is made to categorize subjects into a specific articular DP based on the characteristics identified during subjective examination and clinical examination.

This is then linked to specific mobilization and manipulation techniques, which are summarized in a clinical algorithm to guide specific treatment. In the last part of this Masterclass, this clinical algorithm is illustrated by different case studies.

Articular dysfunctions in a broader perspective

Figure 1 represents a model, that enables the therapist to systematically analyze and appraise the impact of the different components as a basis for clinical decisions and aims to contribute to a more efficient way of managing patients.[12] This planetary model is not a new model, but is a didactical representation mainly inspired by an adapted model of the International Classification of Functioning, Disability and Health (ICF). The structure of the ICF is reflected in a vertical plan, whereas the pain mechanisms and psychosocial factors surround this vertical structure reflecting their continuous interaction with the different components of the vertical axis. As musculoskeletal pain is multidimensional in nature[13, 14] this planetary representation endeavors to capture the dynamic character of the reasoning process.

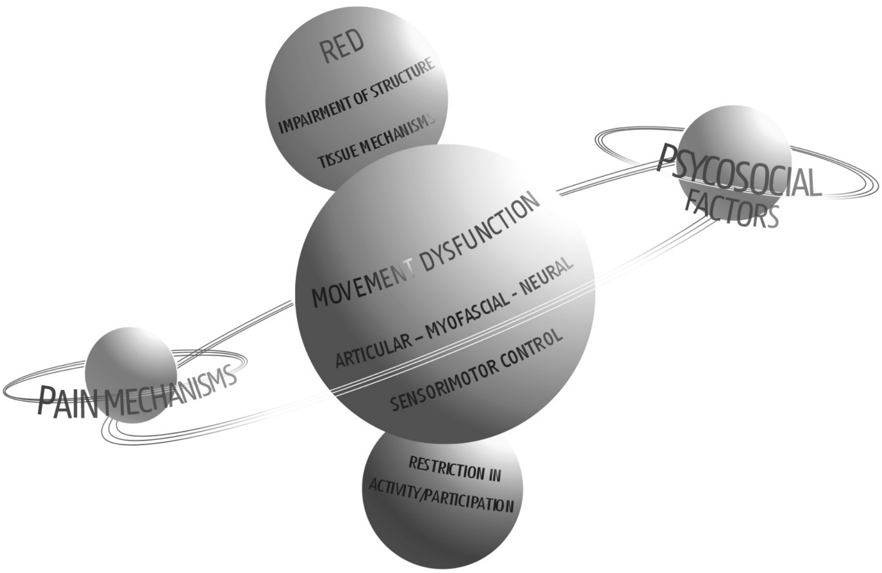

FIGURE 1 Planetary model

The process of clinical decision-making is preferably well structured and stepwise instead of vague and global. If a structured path is followed you can avoid gaps and enhance efficiency in the patient approach.[15] After subjective examination different features should be interpreted. First of all, the importance of excluding red flags prior to further investigation to prevent misdirection and enhance safety is warranted.[5, 16-18] Subsequently, the dominant pain mechanism should be defined.[7, 19, 20] Pain mechanisms have been broadly categorized into: (1) input mechanisms, including nociceptive pain and peripheral neurogenic pain; (2) processing mechanisms, including central pain and central sensitization, and the cognitive–affective mechanisms of pain; and (3) output mechanisms, including autonomic, motor, neuroendocrine and immune system.[7, 19] In case of a dominant input component, hypotheses about the possible nociceptive sources of symptoms can be formulated.[16, 21] Identifying impairments in activity and participation as well as contributing psychosocial factors are also an essential part to give the clinician a fairly comprehensive understanding of the patient's signs and symptoms. Clinical examination is mainly important to further confirm or reject the former formulated hypotheses regarding impairment in structure and function. From a compilation of the subjective examination analysis and the relevant clinical findings emerging from the physical examination, therapeutic goals and tools can be determined.[9] Reassessment at subsequent treatment sessions is necessary to evaluate treatment progression and to readjust the treatment plan if needed. Moreover, the evaluation of perceived treatment effects is an integral part of the reflective reasoning process.[10, 11, 14]

Care is needed to avoid a preoccupation with one structure or diagnosis at the expense of others, as this will be reflected in the management.[9] Nonetheless, given the context of this paper the presented clinical reasoning process is narrowed to and applicable in patients with a dominant input pain mechanism with mechanical nociceptive pain probably arising from articular structures. Even though minor symptoms coming from muscular or neurological structures might be present in patients suffering from mechanical neck pain, the dominant pain source should be articular to justify the use of specific mobilizations and/or manipulations. It is essential to rule out dominant processing mechanisms since manipulative therapy would not be the first choice of treatment in these patients. Furthermore, when there seems to be a dominant output component with maladaptive movement patterns as a generator of the patient's condition, manipulative therapy can be used only secondary to relief patients nociceptive symptoms. In the latter case, the focus should be on the motor control aspect since this might be the source of the vicious circle that could lead to a more chronic condition.

Based on clinical experience and available evidence in the literature,[5, 8, 22-25] the type of clinical presentation that would suggest an amenity to manipulative therapy may include:

- primary complaint of neck pain (defined as pain in the region between the superior nuchal line and first thoracic spinous process);
- a problem that is mechanical in nature and fits with a biomechanical pattern that is regular and recognizable;
- a non-traumatic history of onset suggestive of mechanical dysfunction;
- a limited symptom duration (according to Puentedura et al.[5] less than 38 days);
- limited range of motion (ROM) (direction specific), with a side-to-side difference in cervical rotation ROM of at least 10°;
- pain that has clear mechanical aggravating and easing positions or movements;
- local provocation tests produce recognizable symptoms;

- spinal movement patterns that, when examined actively and passively, suggest a movement restriction that is local to one or two functional spinal units;
- no neurological findings in clinical history or manual assessment;
- no signs of central hyperexcitability;
- no indication that referral to other health care providers is necessary (to exclude red flags);
- a positive expectation that manipulation will help.

The presumption of a predominant articular dysfunction as inherent cause of neck complaints is supported by the prevalence of several of the above listed findings. As there is no particular recipe or protocol for the 'articular patient', the key part in the clinical reasoning process is to make decisions based on information collected in both subjective and clinical examination. The hypothesis of an articular dysfunction is only valid if a cluster of articular symptoms is endorsed. A key reasoning issue is the relevance of an unique finding within the individual presentation of the patient.[7] For example, a stiff neck may be of little relevance in a patient with dominant processing mechanisms, since any attempt to "loosen the joints up" may simply be an additional input to the system that the body is unable to handle.[7] An overemphasis on findings which support the articular hypothesis, might lead to ignoring findings which do not support it, possibly leading to incorrect interpretations.[9, 10, 20]

Given the amount of articular techniques available,[1, 8, 26-29] it is crucial, to define optimal techniques pending on the individual presentation of the patient. In the next chapter we will propose a model of articular DPs mainly based on years of clinical experience in treating neck pain patients. These patterns will guide the manual therapist to choose the appropriate mobilizations and manipulative techniques for the individual patient. This section specifically outlines the mid and lower cervical spine. As the anatomy and clinical biomechanics of the upper cervical spine is far more complex[30] and requires a different approach, this will not be discussed.

Clinical subgroups

Articular DPs are clinically divided into two main categories: a 'convergence' pattern and a 'divergence' pattern. Table 1 gives an overview of the key clinical findings during the subjective and physical examination.

Convergence pattern

A monosegmental convergence pattern is characterized by pain provocation and motion restriction mainly during extension and ipsilateral side bending and rotation. This pattern is associated with unilateral compression pain that can appear at the start, mid- or end range of motion. This clinical pattern is further clarified by combined passive movement testing, which reproduces the patient's symptoms. This will generally be a combination of extension, ipsilateral side bending and rotation. The intervertebral movement tests may give additional information about the quality and quantity of the segmental joint play. Dorsocaudal (downslope) gliding is usually restricted at the same side of the compression pain.

TABLE 1 Features of mono-segmental cervical spine convergence and divergence patterns

	Cervical spine convergence pattern	Cervical spine divergence pattern
Subjective examination	Feeling of locking Movement restriction Unilateral compression pain Often in acute cases Antalgic posture	Feeling of painful strain at end ROM Movement restriction at end ROM Unilateral stretch pain High intensity or severity of symptoms is rare Antalgic posture is uncommon
Physical examination	Active and passive combined extension, ipsilateral side bending, and rotation is limited and evokes comparable signs	Active and passive combined flexion, contralateral side bending, and rotation is limited and evokes comparable signs Passive shoulder elevation in this position does not result in increased ROM/decreased pain
Articular examination	Provocation tests (spring testing) are positive at the impaired segment(s) Intervertebral Movement Tests: ipsilateral downslope restriction Segmental distraction alleviates the pain	Provocation tests are positive at the impaired segment(s) Intervertebral Movement Tests: ipsilateral upslope restriction

A convergence pattern is often found in acute cases and is frequently characterized by a pronounced movement restriction and associated antalgic posture. The head is deviated in flexion and rotation away from the painful side to avoid closing of the zygapophysial (facet) joint. Extension and rotation are highly restricted and painful, associated with hypertonic muscles.

Divergence pattern

A monosegmental divergence pattern is rarely associated with an antalgic posture and high intensity or severity of symptoms is uncommon. This pattern is considered when pain is provoked and movement is restricted during flexion and contralateral side bending and rotation. The divergence pattern is associated with unilateral stretch pain originating from capsuloligamentous structures, usually appearing at the end range of motion. A passive combined movement, including flexion, (contralateral) side bending and rotation will increase the stretch on the capsuloligamentous structures and may produce pain or comparable symptoms. The intervertebral movement test, performing ventrocranial (upslope) gliding is usually restricted at the same side of the stretch pain. In case of a divergence pattern special note is made to differentiate the stretch symptoms between articular and muscular/neural tissue.

Mixed pattern

Clinically a third pattern in the cervical spine can be described and added to the two regular patterns, which is called a 'mixed pattern'. This pattern is characterized by multisegmental and multidirectional dysfunctions that can be diagnosed in a degenerative cervical spine. A degenerative cervical spine is characterized by general stiffness, multisegmental movement restrictions, a mixed pattern of compression/stretch pain and a combination of convergence/divergence patterns.

Mobilization and manipulative techniques

Various segmental mobilizations and manipulative techniques co-exist and have been described in different ways regarding aim, nature and execution.[26, 28, 31] Most manual therapists use the manipulative approach as a progression of localized mobilization techniques. This enables the therapist to work towards an articular barrier adding different components to the mobilization while sensing the tissue responses and the nature of the barrier. This will also enhance safety due to the careful interpretation of pre-manipulative local and general symptoms. In addition, it allows the patient to agree or disagree with the performed procedure through body symptoms (embodied consent), sending signals (implied consent) or verbally (express consent).[32]

Different manipulative approaches can be distinguished, ranging from translatoric and distraction to gapping techniques. It is essential to use techniques that both limit ROM and the applied force in order to enhance safety. Roughly, two fundamentally different approaches can be distinguished: focus and locking approach.

In the focus approach the applied force and amplitude will be limited by adding concomitant components at the involved segment. The different components may consist of flexion or extension, contralateral rotation, ipsilateral side bending, with additional non-voluntary movements such as traction, side glide and compression. The affected segment is placed in a non-physiological position (side bending coupled with rotation to the opposite side) to more easily obtain the articular barrier.[26]

In the locking techniques the adjacent spinal segments caudal or cranial to the affected segment should be placed in a non-physiological position to constrain their movement, whereas the affected segment is placed in a physiological position (side bending coupled with rotation to the same side) so it is more effectively targeted.[31]

The most frequently used manipulative procedures in the mid and lower cervical spine will be described briefly.

Translatoric techniques

Translatoric techniques are defined as an applied glide or thrust parallel to the zygapophysial joint plane and are referred to as 'upslope' or 'downslope' techniques depending on the direction of the thrust. These techniques are termed as such, since the aim is to move the zygapophysial joint either up its slope, simulating "opening" of the joint as would occur during flexion, and contralateral rotation or down the slope, simulating "closing" of the joint as would occur during extension and ipsilateral side bending.[8, 28]

The upslope focus technique (Figure 2) comprises of a cradle or chin hold to the head with the ipsilateral hand contacting the articular pillar of the superior segment. The head is positioned in contralateral rotation and ipsilateral side bending. Slight flexion can be added as a third component. The thrust is directed to the opposite eye (ventrocranial). While performing a manipulation in upslope direction, an indirect downslope movement occurs on the opposite side of the same segmental level (= indirect downslope technique).

The therapist positions the head and cervical spine (cradle hold) with the right hand contacting the articular pillar of the superior segment (C3). The head is positioned in left rotation and right side bending. Slight flexion can be added as a third component. The thrust is directed to the left eye (ventrocranial – white arrow).

FIGURE 2 Upslope focus technique for the right C3/4 segment

This upslope technique can also be performed while using a locking approach. An often-used upslope technique with caudal locking (Figure 3) consists of stabilizing the caudal segments by placing them in a non-physiological position (rotation and contralateral side bending). The affected segment is placed in a physiological position and a translation is given in an upslope direction.

The therapist stabilizes the caudal segments by placing them in a non-physiological position (slight extension, left rotation and right side bending). The affected C3/4 segment is placed in a physiological position (slight extension, left rotation and left side bending) and a translation is given in an upslope direction (white arrow).

FIGURE 3 Upslope technique with caudal locking for the right C3/4 segment

The downslope focus technique (Figure 4) comprises of the therapist adopting a cradle or chin hold of the head with the ipsilateral hand contacting the articular pillar at the superior segment. The head is positioned in contralateral rotation and ipsilateral side bending. Slight extension can be added as a third component. A translatoric thrust is given in the direction of the opposite inferior scapular angle (dorsocaudal).

The therapist positions the head and cervical spine (cradle hold) with the right hand contacting the articular pillar of the superior segment (C3). The head is positioned in left rotation and right side bending. Slight extension can be added as a third component. A translatoric thrust is given in the direction of the opposite inferior scapular angle (dorsocaudal– white arrow).

FIGURE 4 Downslope technique for the right C3/4 segment

Distraction techniques

For the distraction techniques (Figure 5) the premanipulative positioning is similar to the upslope technique, but the applied thrust direction is perpendicular to the joint plane, with the contact hand placed onto the articular pillar of the superior segment.

The therapist positions the head and cervical spine (chin hold) with the right hand contacting the articular pillar of the superior segment (C3). The head is positioned in left rotation and right side bending. Slight flexion or extension can be added as a third component. The thrust direction is perpendicular to the joint plane with the right hand placed onto the articular pillar of the C3 segment (white arrow).

FIGURE 5 Distraction technique for the right C3/4 segment

Gapping technique

Gapping techniques (Figure 6) are indirect techniques, as the aim is to create a separation of the affected zygapophysial joint at the opposite side. The applied force is directed perpendicular to the contact point.

The therapist positions the head and cervical spine (cradle hold) with the left hand contacting the articular pillar of the superior segment (C3). The head is positioned in right rotation and left side bending. Slight extension can be added as a third component. The thrust direction is perpendicular to the contact point with the left hand placed onto the articular pillar of the C3 segment (white arrow).

FIGURE 6 Gapping technique for the right C3/4 segment

Therapeutic guidelines for mobilization and manipulative techniques

In the succeeding paragraph this selection of mobilizations and manipulative techniques will be linked to the aforementioned articular DPs. This is summarized in a clinical algorithm that is presented in Figure 7.

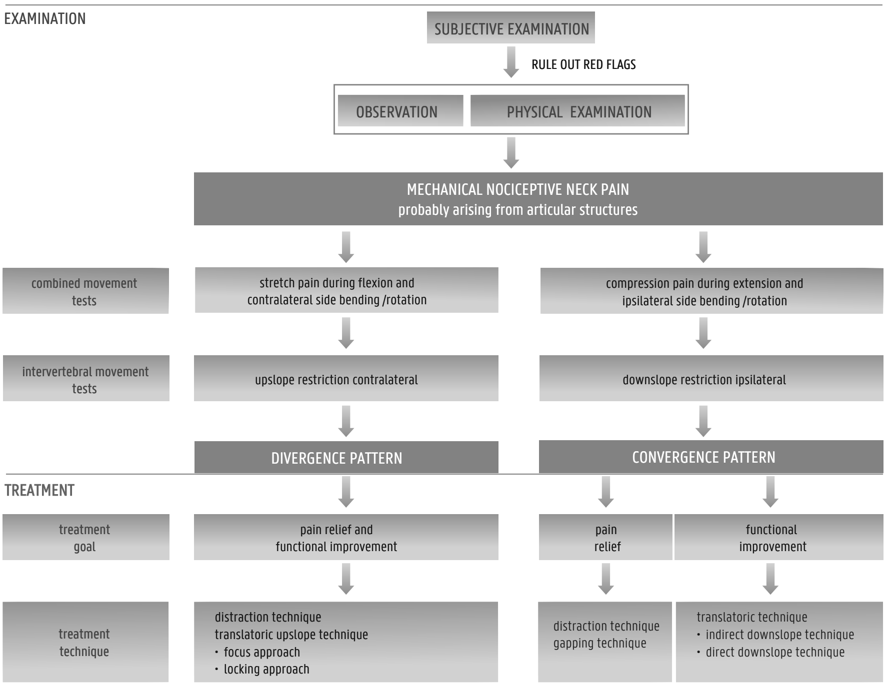

FIGURE 7 Clinical algorithm

Convergence pattern

In a first phase of treating a convergence pattern any compression at the affected side should be avoided since this would aggravate the condition. Therefore, a direct distraction technique and an indirect gapping approach are both indicated. The primary goal in gapping techniques is to obtain pain relief (neurophysiological effect) as the effect on mobility is nonspecific.[1, 33, 34]

In the second stage the remaining function deficits should be addressed. First of all, the use of an indirect downslope technique to restore downslope mobility at the affected side is appropriate. An added benefit in this approach is restoring mobility without creating excessive compressional force on the affected zygapophysial joint. Both the locking and focus upslope technique are applicable but the latter creates more cavitation at the opposite side.

In the final phase, when a painless end range downslope restriction is still present, a direct downslope technique might be warranted. The use of segmental traction as an additional component is often needed to cope with the compressional forces related to this technique.

Divergence pattern

In case of a cervical divergence pattern, the main goal is to restore the upslope translation. Creating a separation by an indirect gapping technique is contraindicated in this case, since this would create unnecessary tension onto the capsuloligamentous structures. Translatoric techniques in the upslope direction are the first choice of treatment in order to restore upslope translation. Both focus and locking techniques can be carried out.

If necessary, one could start off with a distraction manipulation since this does not create an end range distension of the zygapophysial capsula due to the positioning in ipsilateral side bending and contralateral rotation.

Case studies

Supplementary Tables 1, 2 and 3 represent three case studies of individuals with mechanical nociceptive neck pain, each illustrating the importance of subjective examination and clinical examination to guide treatment.

Within the scope of this Masterclass, the analysis of examination findings and therapeutic interventions is limited to those of interest to the discussed pattern. The reader is referred to several more thorough and technical accounts for additional information.[5, 12, 16, 24, 35] The management plan is also directed to the scope of this article, so other interventions will not be discussed.

Conclusion

The intention of this Masterclass was to propose a clinical algorithm to guide (novice) therapists in their clinical reasoning to identify patients with predominantly mechanical nociceptive pain arising from the articular structures, who are likely to respond to mobilization and/or manipulation. This clinical algorithm is the corollary of empirical expertise (collected during years of clinical fieldwork) and complemented by gathered wisdom ranging from in-depth discussions and knowledge exchange with international colleagues.

One could argue that the established framework is a simplified and therefore incorrect image of reality. However, the authors do emphasize that the added value of the proposed articular DPs can only be fully appreciated when this is considered within a broader perspective. Nevertheless, treating patients requires a sense of awareness for subtle distinctions, where adaptation entails the key to success.

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Supplementary Tables

SUPPLEMENTARY TABLE 1 Case study 1 – Convergence pattern

Subjective examination

A 37-year-old female office worker presented with a 2-week history of neck pain and movement restriction, upon referral of a GP. The pain developed gradually over time without a traumatic antecedent. There was no history of similar complaints.
Her chief complaint was neck pain, localized at the right neck-shoulder border, mainly when performing specific neck movements to the right. The patient experienced a feeling of locking while looking over her right shoulder and moving her head towards extension and right rotation.
There was no referred pain to the upper limbs.
The pain at rest was scored 5/10 (VAS), rising to 7-8/10 during certain neck movements such as tilting the head backwards and rotation towards the right. Complaints were localized at the lower third of the Cx spine.
There was no pain at night while sleeping. No technical investigations were performed and medication was not recommended.
None of the reported symptoms were considered to be of significant importance regarding YF or RF detection.

Physical examination

Observation
Subtle antalgic posture: the head slightly bended forward, rotated and side bended to the left. The patient is not aware of this position, and is not able to actively correct her posture when instructed, because of the pain. Neck-shoulder muscles are hypertonic on both sides, although right more than left.
Active and passive movement examination
Extension, right side bending and right rotation are limited and provocative.
End range side bending to the left feels restricted and causes muscle tension.
Passive elevation of the right shoulder improves ROM during left side bending.
Combined passive movement examination
The combination of extension, right side bending and right rotation is limited and painful (comparable sign).
Provocation tests
Central PA on the spinous process at C5/6 segment and the UPA at C5/6 reproduce the symptoms on the right side with localized hyperalgesia only.
Passive physiological intervertebral joint tests
Restricted downslope gliding at the right C5/6 zygapophysial joint.
Neurological examination
Negative.

Hypothesis

The key findings resulting from the subjective and clinical examination endorse the hypothesis for a dominant mechanical nociceptive cause assuming an articular convergence condition of the right zygapophysial joint.

Management plan

The nature of the patient's articular dysfunction indicates that a passive approach, using localized segmental mobilizations and manipulations, is appropriate to reduce symptoms and to increase mobility. Given the severity and intensity of the symptoms, our first technique of choice would be a gapping technique creating a cavity at the right C5/6 zygapophysial joint. This is to avoid compression in the affected zygapophysial joint and to alleviate the pain. In a second phase a translatoric (downslope) technique would be warranted to optimally normalize the downslope gliding.

Abbreviations: GP, general practitioner; VAS, visual analogue scale (0-10; 0 = no pain, 10 = worst pain ever); Cx, cervical; YF, yellow flag; RF, red flag; PA, posterior-anterior provocation; UPA, unilateral posterior-anterior provocation.

SUPPLEMENTARY TABLE 2 Case study 2 – Divergence pattern

Subjective examination

A 45-year-old male plumber, presented upon doctor referral with an inconvenience at the Cx spine, which was present for about 2 months. This burden was localized at the left side of his neck and became painful when performing specific neck movements. The pain developed gradually, without trauma in history.
There was no history of similar complaints.
The patient described his complaint as a bothersome sensation of strain and movement restriction at end range Cx flexion and while bending the head to the right side.
The last 3 days preceding the consultation, the complaint emerged on the left side during functional activities.
The pain at rest was scored 4/10 (VAS), rising to 6/10 during neck flexion and right side bending. The symptoms were localized at the upper third of the neck on the left side.
No other complaints such as headache, temporo-orofacial pain, dizziness, or symptoms in the upper limbs were present.
There was no pain at night while sleeping. No technical investigations were performed and medication was not recommended.
None of the reported symptoms were considered to be of significant importance regarding YF or RF detection.

Physical examination

Observation
Forward head posture when seated. The patient can actively correct posture to good position when facilitated.
Active and passive movement examination
Flexion, right side bending and right rotation are limited at end range of movement and provocative. Passive left shoulder elevation does not alter the restriction nor the symptoms.
Combined passive movement examination
The combination of flexion, right side bending and right rotation is limited at end range of motion and painful (comparable sign).
Provocation tests
The central PA on the spinous process of C2 and the left UPA at C2/3 reproduce the symptoms on the left side.
Passive physiological intervertebral joint tests
Restricted upslope gliding at the left C2/3 zygapophysial joint.
Neurological examination
Negative.

Hypothesis

The key findings resulting from the subjective and clinical examination suggest a dominant mechanical nociceptive cause assuming an articular divergence condition of the left zygapophysial joint.

Management plan

The nature of this articular dysfunction allows us to choose a passive approach, using localized specific mobilizations and manipulations to reduce the patient's symptoms and increase segmental mobility. In this case a translatoric technique (upslope) is preferred to avoid excessive stretch on the capsuloligamentous structures of the left zygapophysial joint capsula and to normalize the upslope gliding.

Abbreviations: GP, general practitioner; VAS, visual analogue scale (0-10; 0 = no pain, 10 = worst pain ever); Cx, cervical; YF, yellow flag; RF, red flag; PA, posterior-anterior provocation; UPA, unilateral posterior-anterior provocation.

SUPPLEMENTARY TABLE 3 Case study 3 – Mixed pattern

Subjective examination

A 62-year-old male engineer presented with a 5-month history of neck pain. He mainly complained of rigidity associated with bilateral neck-shoulder pain, which was more pronounced on the right side compared to the left. The pain was predominantly located at the lower Cx spine without irradiating symptoms to the upper limbs. Two years before the current consultation he received PT intervention for similar complaints with beneficial results on symptom reduction.
There were no traumas in the past.
All end range movements were limited and provocative, scored 4/10 (VAS). The most limited movement was neck extension followed by flexion and rotation without differences between sides. The patient did report having trouble finding a good night's rest, albeit related to frequent urge to urinate (established prostate problem).
Plain radiographs revealed degenerative changes at the lower Cx spine, mainly present at the C5/6/7 level.
Apart from the known prostate problem, the patient reported good physical health. No systemic diseases were documented and based on the patient's subjective examination no other signs of specific pathology could be detected. No pain medication was taken.
None of the reported symptoms were considered to be of significant importance regarding YF detection.

Physical examination

Observation
Forward head posture and protracted shoulders when seated. The patient has difficulties actively correcting his posture, even when facilitated.
Active and passive movement examination
All neck movements elicit pain and are restricted.
Combined passive movement examination
No clear pattern of restriction and/or pain.
Provocation tests
The central PA on the spinous process of C5 and C6 and both left and right UPA's at C5 and C6 reproduce the symptoms. Segmental traction on C5/6 and C6/7 along the longitudinal axis alleviates the symptoms.
Passive physiological intervertebral joint tests
Up and downslope gliding are restricted at the hypomobile C5/6 and C6/7 segments.
Neurological examination
Negative.

Hypothesis

The key findings resulting from the subjective and clinical examination put up evidence for a dominant mechanical nociceptive cause, assuming a mixed pattern of articular convergence and divergence conditions of the zygapophysial joints.

Management plan

The nature of the articular dysfunction demands a more gentle approach and indicates the use of (segmental) traction and/or (midrange) translatoric mobilizations. Given the degenerative condition of the spine, even though medical imagery is present, this does not preclude the possibility of side effects or adverse responses to spinal manipulations. Therefore, specific midrange mobilizations should take precedence on more cumbersome end range mobilizations or (in)direct thrust techniques. Distraction manipulations could be indicated if used with caution.

Abbreviations: GP, general practitioner; VAS, visual analogue scale (0-10; 0 = no pain, 10 = worst pain ever); Cx, cervical; YF, yellow flag; RF, red flag; PT, physical therapy; PA, posterior-anterior provocation; UPA, unilateral posterior-anterior provocation.

The aim of an argument or discussion
should not be victory, but progress.

Joseph Joubert

GENERAL DISCUSSION

MAIN FINDINGS & DISCUSSION OF THE RESEARCH QUESTIONS

The aim of the present thesis was to identify characteristic traits that define patients with nonspecific neck pain (NSNP), and to improve our understanding on how these characteristics could direct clinical reasoning during the physiotherapeutic assessment of this prevalent and challenging condition. This dissertation comprised three major parts. In **Part I** a novel reasoning model into clinical dysfunction patterns (DPs) was presented, together with a set of pertinent consensus-derived criteria, to inform healthcare professionals on distinct classes within patients suffering from NSNP (Chapter 1). **Part II** focused on the psychometric properties of the proposed mechanisms-based reasoning model for NSNP. More specific, an evaluation of its interrater reliability (Chapter 2), and discriminative validity (Chapter 3) was carried out and revealed clinically acceptable reliability and overall high levels of diagnostic accuracy of the reasoning model. Additionally, the results of the diagnostic accuracy of the nociceptive, peripheral neuropathic, and nociplastic pain mechanisms-based classification were provided in appendix (Appendices 5-10) to allow comparison with the results from Chapter 3 in the succeeding paragraphs. Finally, **Part III** explored the clinical reasoning underlying the assessment and management in the event of a prevailing articular DP in patients with NSNP (Chapter 4). Henceforward, the results are discussed in detail with respect to the aims mentioned in the general introduction. Afterwards, the methodological considerations, clinical implications, and directions for future research are reviewed. The general discussion will be closed with the main conclusions of the current thesis.

CLINICAL CRITERIA FOR NONSPECIFIC NECK PAIN

Nonspecific neck conditions are common and originate from multiple possible causes.[1-6] In assistance of clinicians' day-to-day confrontations with patients enduring NSNP, several classification strategies have been developed.[7-21] To tackle the heterogeneity of clinical presentations of spinal pain and to bridge the gaps of the alternative stratification methods, pain mechanisms-based reasoning has been promoted by numerous authors.[22-38] As a result, indications of clinical decision-making related to such a mechanistic approach have been identified in experienced physiotherapists during their professional encounters with patients suffering from musculoskeletal disorders.[37, 39] In contrast to the simplistic, and therefore often unsatisfying or erroneous biomedical model of pain,[26, 27, 38, 40, 41] the alternative approach related to the neurophysiological mechanisms of pain is typically perceived as far more complex. Due to its multidimensional and entangled nature, musculoskeletal physiotherapists might question the usefulness of reasoning in the original concepts of the 'Mature Organism Model' (i.e. the input, processing, and output patterns, as described by Gifford[25, 38, 40, 42]).[37, 39] Smart et al.[37, 39] addressed this matter by suggesting a classification into a nociceptive, peripheral neuropathic, and central pain mechanism, but neglected the magnitude of the output dimension. Therefore, the first aim was to refine the existing pain mechanisms-based classification, into a model that translates this mechanistic approach to clinical patterns. Accordingly, care practitioners should be able to relate their subjective and physical examination findings more straightforwardly to the neurobiological and psychosocial complexities of their patients' pain and disability.[26]

A two-phase sequential design of a focus group and Delphi-survey resulted in the proposed reasoning model of five distinct DPs, enclosed in Chapter 1, including specific clinical criteria that refer to the predominant pain mechanisms. The results from **the Delphi-study seemed to largely correspond** with the results of a similar Delphi-study on nonspecific low back pain (NSLBP) [43] with regard to (1) the number of criteria obtained in the consecutive rounds, (2) the extent to which their formulated criteria from the first round were represented in the redefined criteria for the second round, (3) the overlap found between the input and output related criteria and within the input DPs, and (4) their compliance with the clinical criteria described in the accessible literature.[43, 44] In addition, the physical examination criteria gave the impression to pursue confirmation or rejection of the hypotheses raised following the subjective examination. This strategy characterizes the process of clinical reasoning during the assessment.[22, 45-51]

Although the experts included in both studies had similar professional qualifications, there were a few remarkable disparities in the criteria they agreed upon, apart from the evident anatomical regional differences.[43, 44] For example, the clinical criteria indicating intervertebral disc involvement were only suggested by the experts of the Delphi-study on NSLBP,[43] while the disc has been identified as a possible source for both NSLBP and NSNP.[6, 52-55] While large variations have been reported on the prevalence of disc-related spinal disorders, and NSLBP has been studied more extensively than NSNP,[56-59] cervical disc herniations remain a common source of NSNP.[60] However, this absence of clear clinical criteria for cervical disc-related conditions in the Delphi-study corresponds with the results from a recent review article that underlined the absence of significant history items to rule in disc pathology in the cervical spine.[61] Furthermore, only the experts participating in the Delphi-study on NSNP indicated the supporting evidence of questionnaires in detecting a predominant central pain mechanism. Even though several questionnaires are being recommended by physiotherapy practice guidelines,[19, 62] their routine use might not yet be embedded in daily clinical practice. These differences in criteria identified by the different expert panels reflect the dominance of the experts' opinions.[63] Obviously, **different expert-panels can generate alternative clinical criteria**.[63]

One last finding worth mentioning is the reoccurring **interrelation between input and output related criteria**, highlighted in both Delphi-studies.[43, 44] Referring to the original model of Gifford,[38, 40, 42] this consistent overlap should not surprise, though. The output pain pattern is commonly interpreted as the consequence of the sampling systems of our body (i.e. input mechanisms) and processing mechanisms within the central nervous system (CNS).[27, 38, 40, 42] Yet, this stepwise sequence is only observed when there is a well-defined onset or when we artificially break it down into distinct mechanisms.[38] In reality, **all mechanisms occur simultaneously**.[27, 38, 40, 42] So, instead of presenting them as separate categories (Chapter 1, Figure 1), portraying these neurophysiological processes as a loop or continuum probably yields a more realistic impression (Figure 1 and Appendix 11). From a clinical perspective, it can be quite challenging for the physiotherapist to distinguish the prevailing pain mechanism from the input and output DPs when a patient cannot recall a clear onset of its NSNP (e.g. in case of ongoing or recurrent pain states), at least not predicated upon a unique variable from the subjective or physical exam. The relevance of the signs and symptoms and their dominance to either category can only be determined through profound clinical reasoning.

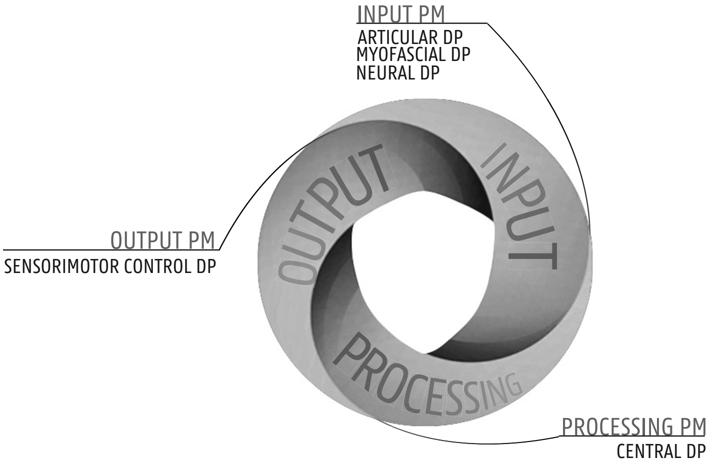

FIGURE 1 The continuum of pain patterns & dysfunction patterns (DP)

To summarize, the general agreement in clinical criteria resulting from the consensus study enclosed in Chapter 1, and those suggested in the literature,[35, 43, 45, 63-65] emphasizes the notion that pain mechanisms are not restricted to anatomical boundaries,[25, 38, 40-42] although regional exceptions might occur.[66] Therefore, caution is warranted when interpreting these clinical criteria, as the clusters identified may not always generalize to musculoskeletal disorders other than NSNP.

PSYCHOMETRIC PROPERTIES OF THE PROPOSED REASONING MODEL

According to Woolf et al.,[28] any classification for pain should be reliable, valid, generalizable and comprehensive, and allow clinicians to identify clinical patterns, aid judgements regarding prognosis, and predict treatment responses. Consequently, the usefulness of any system may be judged against its ability to serve such ends.[26, 28] Accepting reliability as a prerequisite for validity,[67] the aim of Chapter 2 was to assess the interrater reliability and agreement of the clinical judgements associated with the pain mechanisms, pain patterns, and DPs driving the patients' NSNP.

The classification into predominant pain mechanism showed almost perfect reliability (kappa =.84; 95% CI, .65-1.00). There was substantial agreement between the raters' judgements on the predominant pain pattern (kappa =.61; 95% CI, .42-.80), along with substantial agreement regarding the decisions on the predominant DP (kappa =.62; 95% CI, .44.79). The three stratification levels of the proposed reasoning model displayed **acceptable clinical reliability**, with clinically acceptable reliability defined as kappa >.60.[68, 69] Nonetheless, these kappa and agreement values may have been inflated due to a high degree of clustering in the sample. Indeed, only two out of 48 subjects were identified with a prevailing peripheral neuropathic pain mechanism or neural DP.

In line with the aforementioned Delphi-findings, the judgements concerning the input and output pain patterns did not reach the percentage agreement level of ≥80% for clinical acceptance, neither did the myofascial and sensorimotor control DPs (Chapter 2, Table 2). Possibly, this could be explained by the interrelationship between input and output patterns, and the considerable overlap in clinical criteria that define these DPs.[44] Based on additional analyses it was clear that when, for example, the subjects whose NSNP was labeled as a predominant myofascial DP by one of the two raters were omitted from the analysis, the percentage of overall agreement surpassed the 80% threshold for clinical acceptance (87.10%; 95% CI, 75.30-98.90, instead of 70.83%). However, owing to the lack of power, a further widening of CIs could not be prevented. Similar trends were found for the articular DP and sensorimotor control DP (respectively 74.36%; 95% CI, 60.65-88.06 and 88.00%; 95% CI, 75.26-1.00, instead of 70.83%).

The results from the cross-sectional diagnostic accuracy study, detailed in Chapter 3 and Appendices 5-10, provided extra information on the psychometric properties of the suggested reasoning model. Several discriminatory clusters of subjective and physical examination criteria were identified as predictive of the proposed classification categories, to assist substantiated assessment and clinical reasoning in NSNP patients. Tables 1-3 summarize the final clusters of predictive clinical criteria, including their respective accuracy measures. Inherent to the statistical model used, although self-evident, **these clinical criteria should not be used as stand-alone criteria.** Their diagnostic value will only remain standing when a coexistence of as much as possible clustered criteria is identified in the clinical representation of the patients' NSNP.

Some prominent findings emerged when investigating these clusters. The clustered input predictors included criteria that lowered the plausibility for an input pain pattern (indicated with an odds ratio (OR) <1 in Chapter 3, Table 3, and indicated with 'less likely' in Tables 1-3), as well as criteria that predicted higher odds to be classified into the input pattern (OR>1 in Chapter 3, Table 3). As expected, the latter reflected a quite incoherent picture of various clinical representations of NSNP. Therefore, in designing the DP-classification, it was deemed appropriate to arrange the input pattern into the articular, myofascial, and neural subclasses.[44] The articular and neural DP clusters revealed a more comprehensive entity of criteria that generally relate to the additional articular and/or neurological assessment. Unfortunately, no clear myofascial DP cluster could be retained, since the subjects whose NSNP was judged to be predominantly myofascial displayed considerable variability in clinical features. Myofascial impairments are frequently associated with a variety of clinical presentations of NSNP (e.g. patients with disturbed muscle activation patterns, acute neck pain conditions, whiplash associated disorders, etc.)[70-78] This could possibly explain why the clinicians were sometimes in doubt to make clear distinction between a predominant myofascial DP and the other DPs. Although the sub-classification of the input pattern yielded distinct clinical patterns, it did result in a loss of overall diagnostic accuracy of the articular DP compared to the input model. In case of predominant input-related NSNP, it might have been less advantageous than initially anticipated to link the patients' NSNP to distinct articular and/or myofascial structures, compared to the classification into a predominant nociceptive or peripheral neuropathic pain state. The predictive cluster identified for a prevailing nociceptive pain mechanism did show better overall accuracy. Nevertheless, these classifications should not be interpreted as concurrent reasoning models, but could offer additional value during the parallel rounds of thought that enable the therapist to reach an informed diagnosis.[37, 45]

The processing pattern, central DP, and nociplastic pain mechanism were all defined in a very similar way, which explains the identical clusters and psychometric properties obtained. These clusters are in line with the diagnostic criteria stipulated in the body of knowledge on centrally evoked and/or maintained pain conditions.[35, 45, 63-66, 79-81] Likewise, the suggested clusters for a preponderance of a neural DP and peripheral neuropathic pain mechanism disclose identical sets of clinical criteria that overlap with criteria related to neural involvement in NSNP.[45, 82-86] However, they do not match the relevant international consensus documents on the diagnosis of neuropathic pain.[87, 88] This could be explained by the way the neural DP was defined at the start of the research project. The broad definition provided,[43, 44] including both nociceptive and neuropathic pain states, may have distracted the Delphi-experts to suggest specific criteria related to neuropathic pain. Besides, at that moment the leading evidence suggested a rather broad 'diagnostic spectrum' of neuropathic pain,[82, 83] whereas to date these guidelines have been refined[35, 64, 65, 88] and have become part of contemporary clinical reasoning. These considerations do not imply that the neural cluster is insufficient to detect and/or confirm a suspicion of a dominant neural DP in patients with NSNP. It seems more accurate and, hence better clinical practice, to complement the proposed criteria with the aforementioned consensus guidelines to detect neuropathic features in neck pain patients.

These constraints aside, the results of Chapters 2 and 3, and Appendices 510 provide several sets of clinical criteria that appear to have **acceptable reliability and diagnostic accuracy**. Screening for these clusters may help clinicians to identify clinical patterns that hold the possibility to assist judgements regarding prognosis and reasoned management procedures. Further study should elaborate on the present preliminary findings.

TABLE 1 Clinical criteria associated with the input, processing and output pain patterns

Input pattern	Processing pattern
Subjective examination Muscle weakness (not caused by pain inhibition) Less likely if Sx are provoked on specific activities/postures that load impaired side Less likely in case of widespread pain Mechanical pattern to aggravating & easing factors Less likely in case of high scores on VAS or NRS (i.e. worst NRS>7) Less likely when surveys reveal high scores on CSI, NDI, etc. Pain referred in peripheral nerve/Cx nerve root distribution pattern Pain provocation in response to stretch	**Subjective examination** Widespread pain Positive identification of various YFs
Physical examination Less likely in case of hyperalgesia and/or allodynia Less likely when reduced muscle power/endurance/impaired NMC Less likely when muscular imbalance with increased activity of global neck muscles Less likely in case of inconsistent & ambiguous findings Less likely in case of disproportionate/abnormal reaction during/after assessment Variable findings in active movement assessment Less likely if relaxation of relevant muscles results in increased ROM Intervertebral movement restriction at the impaired segment Associated with unilateral compression and/or stretch pain Less likely if insufficient posture, or inability to maintain a corrected posture Restricted ROM on passive & active movement testing Less likely in case of a mechanical pattern to aggravating & easing factors Predominant movement restriction towards extension/rotation Localized, unilateral increased muscle tension	**Physical examination** Hyperalgesia and/or allodynia Inconsistent & ambiguous findings that vary over sessions Disproportionate/abnormal reaction during/after assessment
Diagnostic accuracy Interrater reliability (95% CI): κ =.61 (.42 - .80) Sensitivity (95% CI): .92 (.64 - 1.00) Specificity (95% CI): .83 (.59 - .96) PPV (95% CI): .80 (.52 - .96) NPV (95% CI): .94 (.70 - 1.00) LR+ (95% CI): 5.54 (1.95 - 15.75) LR- (95% CI): .09 (.01 - .61) Overall diagn. accuracy (95% CI): .87 (.70 - .96)	**Diagnostic accuracy** Interrater reliability (95% CI): κ =.61 (.42 - .80) Sensitivity (95% CI): .69 (.29 - .94) Specificity (95% CI): .98 (.83 - 1.00) PPV (95% CI): .92 (.44 - 1.00) NPV (95% CI): .91 (.73 - .98) LR+ (95% CI): 34.37 (2.13 - 556.00) LR- (95% CI): .32 (.11 - .89) Overall diagn. accuracy (95% CI): .91 (.76 - .98)

Abbreviations: Sx, symptoms; CSI, Central Sensitization Inventory; NDI, Neck Disability Index; Cx, cervical; YFs, Yellow Flags; ROM, range of motion; NMC, neuromuscular control; CI, confidence interval; κ, kappa; PPV, positive predictive value; NPV, negative predictive value; LR+, positive likelihood ratio; LR- negative likelihood ratio; Overall diagn. accuracy, overall diagnostic accuracy. The criterion descriptions were shortened. Full descriptions are listed in Chapter 3, Table 2. The criteria are ranked in descending order of importance within their respective category, based on the prediction model.

Output pattern

Subjective examination
Less likely in case of widespread pain
Sx are provoked on specific activities/postures that load impaired side
Less likely if Sx provocation in response to valsalva maneuvers
Less likely in case of unpredictable/disproportionate aggravating & easing factors
Less likely if pain is variously described as pins & needles
Pain/complaints increase(s) during the day
Less likely in case of positive identification of various YFs
Less likely in case of lowered immune responses and/or tolerance to activities

Physical examination
Insufficient posture, unable to maintain a corrected posture
Less likely if associated with unilateral compression and/or stretch pain
Less likely if predominant movement restriction towards extension/rotation
Less likely in case of restricted ROM on passive & active movement testing
Relaxation of relevant muscles results in increased ROM
Mechanical pattern to aggravating & easing factors
Less likely in case of variable findings in active movement assessment
Muscular imbalance with increased activity of global neck muscles
Reduced muscle power/endurance/impaired NMC
Less likely in case of intervertebral movement restriction at the impaired segment
Absence of clear neurological findings (function/provocation tests)
Less likely in case of inconsistent & ambiguous findings

Diagnostic accuracy
Interrater reliability (95% CI): κ =.61 (.42 - .80)
Sensitivity (95% CI): .91 (.59 - 1.00)
Specificity (95% CI): .80 (.56 - .94)
PPV (95% CI): .71 (.42 - .92)
NPV (95% CI): .94 (.71 - 1.00)
LR+ (95% CI): 4.55 (1.86 - 11.14)
LR- (95% CI): .11 (.02 - .75)
Overall diagn. accuracy (95% CI): .84 (.66 - .95)

TABLE 2 Clinical criteria associated with the dysfunction patterns

Articular dysfunction pattern	Neural dysfunction pattern
Subjective examination	**Subjective examination**
Less likely in case of spontaneous (i.e. stimulus-independent) pain/ pain at rest	Arm Sx exceed neck pain
Less likely in case of positive identification of various YFs	
Physical examination	**Physical examination**
Variable findings in active movement assessment	Muscle weakness (not caused by pain inhibition)
Less likely if insufficient posture, or inability to maintain a corrected posture	Less likely in the absence of clear neurological findings
Less likely when reduced muscle power/endurance/impaired NMC	Positive Spurling's test
Intervertebral movement restriction at the impaired segment	Clear neurological findings (function/ provocation tests)
Pain/Sx provocation with repeated movement testing	Pain/Sx provocation in response to palpation of the nerve
Associated with unilateral compression and/or stretch pain	
Less likely in the absence of clear intervertebral movement restriction(s)	
Predominant movement restriction towards extension/rotation	
Diagnostic accuracy	**Diagnostic accuracy**
Interrater reliability (95% CI): κ =.62 (.44 - .79)	Interrater reliability (95% CI): κ =.62 (.44 - .79)
Sensitivity (95% CI): .83 (.36 - 1.00)	Sensitivity (95% CI): .92 (.44 - 1.00)
Specificity (95% CI): .52 (.31 - .72)	Specificity (95% CI): .97 (.93 - .99)
PPV (95% CI): .29 (.10 - .56)	PPV (95% CI): .46 (.18 - .76)
NPV (95% CI): .93 (.66 - 1.00)	NPV (95% CI): 1.00 (.97 - 1.00)
LR+ (95% CI): 1.74 (1.01 - 2.99)	LR+ (95% CI): 26.37 (11.93 - 58.27)
LR- (95% CI): .32 (.05 - 1.99)	LR- (95% CI): .09 (.01 - 1.23)
Overall diagn. accuracy (95% CI): .58 (.39 - .75)	Overall diagn. accuracy (95% CI): .96 (.93 - .99)

Abbreviations YFs, Yellow Flags; Sx, symptoms; CSI, Central Sensitization Inventory; NDI, Neck Disability Index; ROM, range of motion; NMC, neuromuscular control; CI, confidence interval; κ, kappa; PPV, positive predictive value; NPV, negative predictive value; LR+, positive likelihood ratio; LR- negative likelihood ratio; Overall diagn. accuracy, overall diagnostic accuracy.
The criterion descriptions were shortened. Full descriptions are listed in Chapter 3, Table 2. The criteria are ranked in descending order of importance within their respective category, based on the prediction model.

Central dysfunction pattern	Sensorimotor control dysfunction pattern
Subjective examination Widespread pain Positive identification of various YFs	**Subjective examination** Less likely in case of widespread pain Sx are provoked on specific activities/postures that load impaired side Less likely if Sx provocation in response to valsalva maneuvers Less likely in case of unpredictable/disproportionate aggravating & easing factors Less likely if pain is variously described as pins & needles Pain/complaints increase(s) during the day Less likely in case of positive identification of various YFs Less likely in case of lowered immune responses and/or tolerance to activities
Physical examination Hyperalgesia and/or allodynia Inconsistent & ambiguous findings that vary over sessions Disproportionate/abnormal reaction during/after assessment	**Physical examination** Insufficient posture, unable to maintain a corrected posture Less likely if associated with unilateral compression and/or stretch pain Less likely if predominant movement restriction towards extension/rotation Less likely in case of restricted ROM on passive & active movement testing Relaxation of relevant muscles results in increased ROM Mechanical pattern to aggravating & easing factors Less likely in case of variable findings in active movement assessment Muscular imbalance with increased activity of global neck muscles Reduced muscle power/endurance/impaired NMC Less likely in case of intervertebral movement restriction at the impaired segment Absence of clear neurological findings (function/provocation tests) Less likely in case of inconsistent & ambiguous findings
Diagnostic accuracy Interrater reliability (95% CI): κ =.62 (.44 - .79) Sensitivity (95% CI): .69 (.29 - .94) Specificity (95% CI): .98 (.83 - 1.00) PPV (95% CI): .92 (.44 - 1.00) NPV (95% CI): .91 (.73 - .98) LR+ (95% CI): 34.37 (2.13 - 556.00) LR- (95% CI): .32 (.11 - .89) Overall diagn. accuracy (95% CI): .91 (.76 - .98)	**Diagnostic accuracy** Interrater reliability (95% CI): κ =.62 (.44 - .79) Sensitivity (95% CI): .91 (.59 - 1.00) Specificity (95% CI): .80 (.56 - .94) PPV (95% CI): .71 (.42 - .92) NPV (95% CI): .94 (.71 - 1.00) LR+ (95% CI): 4.55 (1.86 - 11.14) LR- (95% CI): .11 (.02 - .75) Overall diagn. accuracy (95% CI): .84 (.66 - .95)

TABLE 3 Clinical criteria associated with nociceptive, peripheral neuropathic and nociplastic pain mechanisms

Nociceptive pain mechanism	Peripheral neuropathic pain mechanism	Nociplastic pain mechanism
Subjective examination	**Subjective examination**	**Subjective examination**
Less likely in case of widespread pain	Arm Sx exceed neck pain	Widespread pain
Less likely when arm Sx exceed neck pain		Positive identification of various YFs
Less likely in case of positive identification of various YFs		
Less likely if pain is variously described as pins & needles		
Physical examination	**Physical examination**	**Physical examination**
Less likely in case of inconsistent & ambiguous findings	Muscle weakness (not caused by pain inhibition)	Inconsistent & ambiguous findings that vary over sessions
Less likely in case of hyperalgesia and/or allodynia	Less likely in the absence of clear neurological findings	Hyperalgesia and/or allodynia
Absence of clear neurological findings (function/ provocation tests)	Positive Spurling's test	Disproportionate/abnormal reaction during/after assessment
Less likely in case of disproportionate/abnormal reaction during/after assessment	Clear neurological findings (function/provocation tests)	
	Pain/Sx provocation in response to palpation of the nerve	
Diagnostic accuracy	**Diagnostic accuracy**	**Diagnostic accuracy**
Interrater reliability (95% CI): κ =.84 (.65 - 1.00)	Interrater reliability (95% CI): κ =.84 (.65 - 1.00)	Interrater reliability (95% CI): κ =.84 (.65 - 1.00)
Sensitivity (95% CI): .75 (.53 - .90)	Sensitivity (95% CI): .92 (.44 - 1.00)	Sensitivity (95% CI): .69 (.29 - .94)
Specificity (95% CI): .86 (.42 - 1.00)	Specificity (95% CI): .97 (.93 - .99)	Specificity (95% CI): .98 (.83 - 1.00)
PPV (95% CI): .95 (.74 - 1.00)	PPV (95% CI): .46 (.18 - .76)	PPV (95% CI): .92 (.44 - 1.00)
NPV (95% CI): .50 (.21 - .79)	NPV (95% CI): 1.00 (.97 - 1.00)	NPV (95% CI): .91 (.73 - .98)
LR+ (95% CI): 5.25 (.84 - 32.70)	LR+ (95% CI): 26.37 (11.93 - 58.27)	LR+ (95% CI): 34.37 (2.13 - 556)
LR- (95% CI): .29 (.14 - .62)	LR- (95% CI): .09 (.01 - 1.23)	LR- (95% CI): .32 (.11 - .89)
Overall diagn. accuracy (95% CI): .77 (.59 - .90)	Overall diagn. accuracy (95% CI): .96 (.93 - .99)	Overall diagn. accuracy (95% CI): .91 (.76 - .98)

Abbreviations: Sx, symptoms; YFs, Yellow Flags; CI, confidence interval; κ, kappa; PPV, positive predictive value; NPV, negative predictive value; LR+, positive likelihood ratio; LR- negative likelihood ratio; Overall diagn. accuracy, overall diagnostic accuracy.

The criterion descriptions were shortened. Full descriptions are listed in Chapter 3, Table 2. The criteria are ranked in descending order of importance within their respective category, based on the prediction model.

EXPLORING THE ARTICULAR DYSFUNCTION PATTERN IN PATIENTS WITH NONSPECIFIC NECK PAIN

The paper included in Chapter 4 proposed a specific reasoning strategy underlying the management of patients with NSNP through the application of mobilizations and manipulations. The clinical algorithm was founded on years of clinical expertise in assessing and treating NSNP patients using standardized procedures, with the intention to increase the specificity and safety in using such particular techniques.[89] The convergence and divergence patterns delineated are to be considered as an example, and more specifically, **a refinement of a part of the pain mechanisms-based reasoning model**. Once the patient's NSNP is appraised as a predominant articular DP, musculoskeletal physiotherapists may direct their decision-making during the assessment and subsequent treatment according to the structured flow detailed in the algorithm. It is admitted that the case studies included in the masterclass on articular DPs in NSNP patients were rather stereotypical and may therefore, not fully capture the complexity of genuine clinical representations. Nonetheless, the context in which the presented reasoning process is situated, was well-defined and confined to a 'predominant input pattern with mechanical nociceptive pain probably arising from articular structures'.[89] Because this manuscript was published before the other studies included in this thesis were undertaken, no stipulations were made regarding the specific criteria resulting from the Delphi- and succeeding studies. The clinical presentations that would suggest an amenity to manipulative therapy described in the original paper,[89] still relate to the nociceptive, input, and articular criteria outlined in Tables 1-3.

METHODOLOGICAL CONSIDERATIONS

The present thesis contributed to a better understanding and recognition of unique characteristics of individuals with NSNP. The designs used for reasoning model development and identification of the clinical criteria were informed by the related literature and were deemed appropriate.[63, 66, 67, 90] Yet, the studies embedded in this thesis were prone to several **shortcomings**. The limitations of these studies have been consistently addressed in the different manuscripts. Nevertheless, particular aspects of the applied methods require some additional consideration and are therefore discussed in this section.

Even though the Delphi-method can be particularly useful for informing clinical decision-making in situations of clinical uncertainty,[91-95] several limitations are related to its use. Since there are no standardized guidelines for defining and selecting experts, the credibility and expertise of participants must be inferred from their professional properties.[63] The clinical criteria were established by a group of expert musculoskeletal physiotherapists meeting the predetermined levels of experience.[44] Consequently, the obtained results might only reflect findings for patients presenting for physiotherapy. This perceived limitation could, however, also be interpreted as a strength: because the proposed reasoning model was originally created with the intention to assist physiotherapists in their clinical reasoning process, the use of clinical experts within the field of physiotherapy is expected to provide clinically meaningful criteria with a high degree of face and content validity.[90, 96] Nonetheless, it is acknowledged that different experts undeniably would have generated different criteria.

Another issue that requires consideration is the wording in terms of dysfunction patterns. The importance of the terminology used, for both the clinician and the patient, is highlighted in the international literature.[29, 38, 97] Indeed, clinicians might find a reference to structural or tissue-related diagnoses. The rationale to preserve the anatomical link for the articular, myofascial, and neural DP was to facilitate translation of old concepts into the proposed reasoning model, even though the experts in the focus group were fully aware that it is usually unhelpful to relate the patient's pain to a pathophysiological source or culprit tissue.[44] Even for the central and sensorimotor control DP this might result in counterproductive reasoning or reinforce abandoned treatment strategies.[28, 41] With regard to the patient, for some this terminology might sound alarming (nocebo).[38, 97] It has been put forward that providing the patient with a pathoanatomical diagnosis, or a label in terms as such (e.g. dysfunction), may be counterproductive via reinforcement of an excessive somatic focus.[97-99] Clearly, this was not intended.

The narrow interpretation of the output pain pattern could also be interpreted as a flaw of the proposed reasoning model. For convenience purposes the output pain pattern was redefined into a sensorimotor DP,[44] although initially conceived as a pattern in which neuroimmune, hormonal, and neuroendocrine systems are at play, in addition to motor systems.[38, 40-42] There is a growing amount of evidence substantiating the importance of these systems underlying pain.[38, 100-104] Nevertheless, this information has difficulties finding its way to the physiotherapy profession, that historically has been oriented towards more tangible operating systems. Translating research findings that exploit the role of these systems in the development and preservation of musculo-skeletal disorders to comprehensible practice guidelines, could offer promising prospects.

With regard to the reliability and validity studies, the included patient samples showed a majority of female patients (72.92% and 71.73%, respectively), which may have repercussions when generalizing the results to the total NSNP population. However, NSNP is more common in women and the gender percentages established in both studies seem to correspond with the prevalence reported in the available literature.[3, 50, 105, 106] Also, the patients were only examined by physio-therapists. It might have been valuable to include a range of clinicians from different disciplines, to allow for generalization of the current findings to other healthcare professions.[107]

Nowadays, physiotherapists are steadily more encouraged to become accustomed to the use of objective outcome measurements during the subjective and physical examination, as well as during treatment.[19, 62] These clinical measurement instruments should also enable the practitioner to better monitor the effectiveness of the provided treatment.[19] Although this could have added to the robustness of our findings, the objective instruments used during the data collection of the clinical trials were limited to the NDI, CSI, and NRS.[108-111] While several other validated and reliable questionnaires and clinical tools are available,[109, 112-116] they are still not routinely used to assess patients with NSNP in private clinical settings.[108] This mindset was transmitted into the clinical studies, partly owing to the belief that the examination procedure had to strongly converge with clinical reality to facilitate implementation of the results into clinical practice. Nevertheless, the assessment procedure used for data collection was performed based on accepted clinical practice.[117-121]

Statistical approaches toward reasoning model development have inherent limitations, logistic regression models just as well. The in- or exclusion of a criterion within a model depends on the statistical variation during the modeling process.[66] Consequently, any statistically derived model is characterized by a degree of uncertainty in which logistic regression will generate a model from a pool of other similar competing models.[66] As a result, regression modeling on a different data set obtained from another patient sample is likely to produce different, though analogue, predictive clusters of clinical criteria.

The high number of clinical criteria identified in the Delphi-study,[44] hampered the application of classical logistic regression models. Therefore, binomial penalized logistic regression analysis was undertaken to identify meaningful criteria associated with the pain mechanism-based categories. This statistical approach is commonly used in domains with high dimensional datasets, i.e. datasets where the number of variables approach or exceed the overall sample size.[122, 123] The fairly small number of patients included in the validity study did, however, result in some methodological restrictions for the univariate descriptive analyses of the identified clinical criteria. It has been indicated that studies with small-to-moderate sample sizes tend to over- or underestimate the ORs, because they do not allow for additional inclusion of covariates. A purposive sampling strategy, resulting in larger numbers of patients within each reference category, may have produced unbiased ORs via the application of unpenalized logistic regression, and may have improved classification accuracy.[66]

In line with the aforementioned, another limitation concerns the lack of an analysis of covariates to test for main and interaction effects of the participants' demographic characteristics on the classification outcome and estimated ORs. For example, the age of the participants might have influenced the predictive capacity of the criteria related to movement restriction (e.g. 'intervertebral movement restriction at the impaired segment'), as the mobility of the cervical spine typically decreases when growing older.[124] In addition, the influence of the interrelation between clinical criteria within their respective category was not established for the univariate OR estimates. This may have inflated the ORs. Consequently, the possible effects of covariates could not be controlled for. The reason for not incorporating this analysis of covariates was justified by the rationale that it was only intended to validate the clinical criteria initially suggested by the Delphi-experts. Besides, statistical analysis alone cannot guarantee that the best model is being used. Good professional judgment is an important component of the reasoning process.

To facilitate this process, scientists are encouraged to translate their findings into accessible, clinically meaningful, and operational information to enable implementation in daily practice.[125] The paper presented in Chapter 4 is a Masterclass (i.e. an expert opinion). From a 'level of evidence' point of view it merely ranks below (Appendix 1), as it is often biased by the authors' experience or opinions and there is no control of confounding factors.[126] Yet, it holds the potential to pitch some clinically meaningful ideas to the international scientific and professional community. The included paper is not to be interpreted as the sole truth, but could fire up the debate of some traditionally accepted concepts regarding mobilizations and manipulations in the treatment of NSNP.[89] Its strengths consists in (1) **educational merit,** by providing students and novice therapists a structured framework on when and how to treat patients with these specific techniques; (2) **clinical usefulness**, by suggesting targeted assessment potentially resulting in more efficient management of patients; and (3) **scientific value**, by raising new hypotheses to be tested for, and acting as a catalyst for communication and discussion on a widely debated topic. The algorithm tolerates the appliance of a broad range of traditional concepts, such as a locking or focus approach, as well as Mulligan techniques.[45, 127-130] To date, the extent to which these articular patterns may benefit clinical practice and patient care has not yet been formally studied. In pursuing an evidence-based mindset,[131] future research underpinning these empirical patterns would obviously increase their scientific resilience.

CLINICAL IMPLICATIONS

Hopefully, the proposed reasoning strategy serves all stakeholders involved in, and troubled with the consequences of NSNP. To emphasize its potential benefits, the clinical implications for healthcare providers and their patients, and students or educational programs are discussed in this section.

What's in it for the patient & clinician?

The accurate identification of the predominant DP and/or pain mechanism underlying the patient's NSNP, by means of the proposed clinical criteria, could assist physiotherapists in **distinguishing distinct profiles** from the heterogeneous group of patients with NSNP.[27, 38, 43, 66, 67, 132] These pain states are not mutually exclusive, and coexistence of more than one is probably the rule rather than the exception.[27, 29] In this respect, the presence of a single finding in the subjective or physical examination is often not diagnostic.[22, 24, 25, 41, 61, 87] While a unique finding might provide a certain probability during the hypothesis formation, it is important to realize that only a **cluster of as much criteria as possible**, from both the subjective and physical examination (outlined in Tables 1-3), indicates the prevailing DP.[24, 47-50, 61, 133, 134] Reassessment at subsequent treatment sessions is necessary to evaluate treatment progression and to confirm or readjust the hypothesis on the dominant DP.[22, 37, 39, 89]

Even though the sets of criteria were established by expert musculoskeletal physiotherapists only, these diagnostic clusters may also prove beneficial to **other healthcare providers**. With the rising healthcare costs and increased exposure to radiation,[135-137] it is critical for general practitioners and medical specialists to identify specific history items and physical examination criteria to aid them in their differential diagnosis without the need for imaging.[61] The suggested reasoning process has the potential to reduce healthcare costs, to decrease the risk of unnecessary exposure to radiation, thus, to improve patient care.[61] These assumptions have yet to be substantiated by future research.

Complex pain states (e.g. NSNP) require an **interdisciplinary approach**.[138] If we pursue a better-quality patient management, we must embrace the contributions of other healthcare disciplines. Knowing where the physiotherapist's competences end, and when the patient's condition requires referral to another healthcare professional, seems crucial for a safe, holistic, and sound patient management.[138, 139] To avoid communication failures and facilitate efficient patient management, all disciplines involved need a common language and profound understanding of each other's reference frames. Furthermore, understanding one another's reasoning models might bridge the gaps between healthcare professionals working with the same patients. Comprehension of how the 'diagnostic labels' specific to the various disciplines overlap, allows for more efficient communication. As a result, multidisciplinary transforms into interdisciplinary.[138] Obviously, this implies an active involvement and regular coordination of all disciplines' services.[138] When considering NSNP as a spectrum that ranges from less complex to highly complex clinical representations, not all patients with NSNP demand an equally intensive collaboration. Hence, it should become clear that the more complex, the greater the need for effective interdisciplinary communication and monitoring.

It goes without saying, but in order to benefit from this reasoning model, it implies the understanding and recognition of its limits. Clinicians need to consider carefully the reasons for using this reasoning model.[140] The reasoning in terms of neurophysiological pain mechanisms alone, will not meet the requirements to obtain an operable diagnosis. As mentioned in the general introduction, this reasoning strategy is only one of the **several rounds of thought** that contribute to the diagnostic process.[37, 141]

Apart from the diagnostic advantages, the suggested reasoning model and clinical algorithm may have **implications for treatment** as well. Currently, the way forward seems to be in favor of (secondary) prevention of NSNP, to avoid the condition from becoming chronic.[142-145] Given its professional identity, that is a challenge tailored to physiotherapy.[146, 147] Accordingly, through proficient early pain management, patient-specific pain education, and progressive increase in activities, further worsening of the **(sub)acute pain** could be prevented.[143, 148-150] The clinical algorithm included in Chapter 4 serves as an example of how to think and act when encountering patients with (sub)acute NSNP that is presumed to be predominantly articular in nature. By describing clear clinical features and recommending a stepwise management strategy, novice and experienced musculoskeletal physiotherapists can bring this mechanisms-based approach promptly into play.[89, 151]

Still, the offered reasoning model could also yield benefits for patients with ongoing symptoms. Through the application of the reasoning model, if necessary supplemented with other algorithms,[65, 87, 88] **chronic NSNP** patients can be reliably identified as well. This distinction is vital to prevent poor therapy outcomes from treatments merely focusing on input-related patterns, that would otherwise result in frustrations of the patient and/or therapist, snowballing medical costs, etc.[35, 38, 64, 65] In other words, maintaining instead of improving the patient's condition. Indeed, in line with recently developed and evaluated treatment strategies, it is suggested that patients' chronic pain conditions can improve as a result of a specific management strategy that is better attuned to their specific needs.[152-155] However, research investigating the cost-effectiveness in large clinical trials with long-term follow-up is desired to provide clinicians and policymakers with robust evidence, before its general implementation into clinical practice is recommended.[154]

What's in it for students & educational programs?

From a teaching perspective, the usefulness of the proposed reasoning model system is ultimately dependent on the extent to which it fulfills the **clinical and didactical purposes** for which it was designed.[66] If the designations into the articular, myofascial, neural, central, and sensorimotor control DP can be shown to help students (1) make sense of a patient's pain presentation, (2) facilitate an appropriate assessment, (3) predict an outcome regarding the natural course of the pain or predict treatment results, and (4) facilitate the selection of appropriate interventions and/or discourage the selection of inappropriate ones, then arguably the reasoning model has fulfilled its educational function.[66]

Research on the differences between experts' and novices' conceptualization of a problem, indicates that experts possess superior organization of knowledge and chunk information into recognizable patterns, whereas novices make more verbatim recall of superficial features of the problem and have less developed and fewer variations of patterns stored in their memory.[22] It is aimed and hoped for that the proposed clinical (dysfunction) patterns serve as valuable additions to students' and (novice) therapists' **collection of clinical patterns** discernable in patients with NSNP. However, a word of caution regarding excessive attention to clinical patterns is needed. Clinical patterns are at risk of becoming rigidly established when the patterns themselves control the therapist's focus.[22] Consequently, this may lead to limited hypotheses generation, so that anything that resembles the most obvious pattern will be seen as that pattern.[22] Fundamental to the proposed reasoning strategy is the pursuit of additional **supporting or negating evidence** to confirm or reject the most plausible hypothesis, in order to appreciate the full spectrum of clinical manifestations of NSNP.

The dynamic character of the suggested reasoning model was intended to reflect clinical reality.[19, 41, 138] It is accepted though, that the relationships and shared features across the different DPs may create difficulties for the apprentice, when confronted with patient presentations containing overlapping, multifactorial or non-textbook variations. Treating patients does require a sense of awareness for **subtle distinctions**, where reconsideration, adaptation or perhaps elaboration of examination findings may entail successful decision-making.[89]

The formation of 'critical thinking' physiotherapists requires attention to and facilitation of clinical reasoning skills, and has presumably always been inherent to physiotherapy education.[22] Focus should not be restricted to the students' acquisition of new knowledge. Knowledge that is acquired in the context for which it will be used, becomes more accessible.[22, 46] Accordingly, the integration of pain physiology in this reasoning model has the potential for future therapists to acquire **accessible organization of knowledge**, fostering clinically valuable reasoning skills. In a changing health climate, the skills expected of physiotherapists require an increasing amount of independence and accountability in decision-making.[46] Musculoskeletal physiotherapists may be required to engage in continuing education in order to develop the breadth and depth of their knowledge of applied pain neurophysiology.[39] The findings from this study may encourage physiotherapy clinicians and educators to reflect consciously upon the extent to which mechanisms-based reasoning of pain underlies and informs their practice and teaching.

FUTURE PERSPECTIVES

In an ideal world, healthcare practitioners are gifted with the indispensable knowledge and insight in the patients' NSNP, provide their patients with the best possible care available, and adapt their management strategy to the capricious nature of the patient's condition in accordance with the state-of-the-art research findings. As a result, people perform better in their daily activities, overall quality of life improves, the available healthcare resources are used more efficiently, and so on and so forth.

Bearing in mind the increasing burden associated with spinal pain conditions,[2, 105, 136, 137, 158] it is clear that there is still a long way ahead before such an ideal situation is achieved. Identifying effective treatment is therefore a high research priority.[159, 160] In the meantime, recognizing distinct patient profiles in a timely manner, and providing patients with earlyon matched interventions, is expected to yield superior results.[10, 143, 148-150] Accordingly, the first step should be the **replication of the current findings** through additional studies in well-defined patient samples with NSNP that relate to the suggested categories. A subsequent step could be **to elucidate whether, and to what extent, this reasoning strategy contributes to reducing the burden of NSNP**. For example, exploring the possible advantages of translating our findings into a self-reporting questionnaire and its associated diagnostic value may prove beneficial in a more efficient and less costly clinical diagnosis in an ever-changing healthcare environment.[61, 161]

Although appealing, the idea of potentially **improving treatment efficiency and effectiveness by matching patients with optimal treatments** might be a challenging task. Although we are well-placed as physiotherapists to manage the care of patients with spinal problems,[162-164] we may overestimate the likely effectiveness of our interventions by expecting moderate to large differences when in reality, the true picture is one of small and often short-term differences between treatment groups.[165] This does not imply one should discount techniques or treatments that may be beneficial to some patients, purely because of failure to identify appropriate patient subgroups.[165, 166] Then again, just because pain can be altered or relieved by a technique directed to a particular structure does not necessarily indicate that this structure is the source of the problem. That the technique can have a significant impact on pain processing is not questionned.[38] Future clinical trials addressing these hurdles, should therefore consider concentrating on the predominant pain mechanism underlying the patient's NSNP, rather than targeting specific structures.

It has been repeatedly suggested that research and healthcare efforts on prevention and therapy must be implemented more widely if we hope to constrict disability from neck pain.[137] Hence, i**nvestigating the assumed benefits of a preventative strategy** could therefore reinforce a patient-tailored physiotherapy approach in educational programs and clinical practice.

As the body of pain science literature seems infinite and is often presented at a level of neuro-physiological detail, it may be difficult for clinicians to assimilate the information into clinical practice.[41] Furthermore, it has been suggested that the basic sciences, including pathophysiology, do not swiftly inform and influence clinical decision-making.[39] Therefore, efforts were made to translate the pain mechanisms and their related clinical criteria in accessible and recognizable patterns, to facilitate implementation into clinical practice. Nevertheless, for students or clinicians unfamiliar to this field of study, it may still be confusing that the specific terminology from the different original concepts is being used interchangeably to explain partially overlapping topics.[29] From a didactical point of view, it might be worth the effort **to investigate the effect of rewording some of these labels** on its perceived level of difficulty, and its capacity to enhance interdisciplinary communication. Appendix 12 displays a proposition for rewording some of the key terminology used, based on the recent literature from different disciplines.[29, 38, 43-45, 66]

Physiotherapy has evolved considerably over the past decades. Although prone to trending ideas, it appears that the ever-skeptical science that nourishes and supports the profession protects it from wandering off too far. This intertwined relation between science and clinical practice should be well-preserved, to ensure that physiotherapy remains a profession that endeavors qualitative and holistic care for the patient, and that allows to closely work together with other disciplines, without renouncing its origin.

GENERAL CONCLUSION

Nonspecific neck pain has a serious impact on patients, care practitioners, society, and policy makers that govern the provision of healthcare. Even though its course is most commonly favorable, the onset, progression, and consequences are affected by a full spectrum of personal and environmental factors, especially in the case of ongoing neck complaints.

Physiotherapists are challenged with the thought-provoking task to unravel the complex processes underneath the patients' NSNP. In order to succeed, it seems imperative to understand that the most plausible hypothesis can only result from a well-structured and comprehensive subjective and physical examination. The blueprint of the ICF conceptual framework may facilitate this process, along with a well-argued clinical reasoning process. The introduction of EBP, and bio-psychosocial models of pain and disability have undeniably led to a shift from an overexcited search for a causative structure towards a focus on pain mechanisms underlying the patient's NSNP.

The results from this dissertation contribute to the increasing understanding of the distinctive features that characterize individuals with NSNP, by providing the clinician, the research community, and educational programs with a reliable and validated reasoning model that relates to clinical practice. It is hoped for that these findings enable physiotherapists, together with all other healthcare professionals, to manage NSNP more effectively, and thus help to reduce the personal and societal burden of neck pain.

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There remains plenty of tunnel at the end of the light.

Jerry Fodor

ENGLISH SUMMARY

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The current thesis identified characteristic features that define distinct clinical subgroups in patients with nonspecific neck pain (NSNP), with the aim to improve our understanding on how these attributes could direct clinical reasoning during the physiotherapeutic assessment of this prevalent and challenging condition. Based on a well-structured and comprehensive subjective and physical examination, the clinician can collect the information required to substantiate the clinical reasoning process. This diagnostic work-up comprises several parallel rounds of thought, which eventually generate the most plausible hypothesis concerning the patient's neck pain. From a biopsychosocial perspective, physiotherapists are encouraged to embrace a pain mechanisms-based reasoning strategy, as this can assist and contribute to the practitioners' understanding of complex and unpredictable clinical presentations of pain and movement dysfunction.

In line with these recommendations, this dissertation proposed a reasoning strategy founded on the pain mechanisms driving the patient's NSNP. To investigate the clinical value of such a mechanistic approach, the body of the current dissertation was based on four studies, divided in three parts:

PART I CLINICAL CRITERIA FOR NONSPECIFIC NECK PAIN

The first study introduced a novel reasoning model, incorporating five clinical dysfunction patterns (DPs) (i.e. articular DP, myofascial DP, neural DP, central DP, and sensorimotor control DP), together with a set of pertinent consensus-derived criteria to inform healthcare professionals on distinct classes within patients suffering from NSNP. This reasoning model was modified from the 'Mature Organism Model', including the input, processing, and output pain patterns, as originally proposed by Gifford. The results from the included expert consensus study showed notable correspondence with the results of a similar Delphi-study on nonspecific low back pain (NSLBP) with regard to the obtained clinical criteria and revealed a reoccurring interrelation between input and output related criteria. Inherent to the Delphi-technique, it is acknowledged that these criteria reflect the reasoning of the included Delphi-experts, and that different expert panels may have generated different sets of clinical criteria.

PART II PSYCHOMETRIC PROPERTIES OF THE PROPOSED REASONING MODEL

The main objective of Part II was to examine the psychometric properties of the proposed mechanism-based reasoning model for NSNP. Accepting reliability as a prerequisite for validity, the second study assessed the interrater reliability and agreement of the clinical judgements associated with the pain mechanisms, pain patterns, and DPs driving the patients' NSNP. These three stratification levels showed acceptable clinical reliability. Subsequently, a cross-sectional diagnostic accuracy study was carried out and identified several discriminatory clusters of subjective and physical examination criteria as predictive of the proposed classification categories, and revealed overall high levels of diagnostic accuracy. As a result of the statistical model used, it is highlighted that the proposed clinical criteria should not be used as stand-alone

criteria. Hence, their diagnostic value will only remain when a multitude of clustered criteria are identified in the clinical representation of the patients' NSNP. Screening for these clusters may help clinicians to recognize clinical patterns that hold the possibility to assist judgements regarding prognosis and reasoned management procedures. Future studies should elaborate on the present preliminary findings.

PART III EXPLORING THE ARTICULAR DYSFUNCTION PATTERN IN PATIENTS WITH NONSPECIFIC NECK PAIN

The third and final part of this dissertation extracted the articular DP from the proposed reasoning model and elaborated on its characteristic clinical decision-making underlying the patient examination and treatment. This pragmatic approach serves as an example on how a mechanisms-based reasoning strategy can inform the assessment and guide appropriate technique selection in the event of a prevailing articular DP in patients with NSNP. The (novice) therapist is provided with a clinical algorithm in order to identify patients who are likely to respond to mobilizations and/or manipulations, and to increase safety in applying these specific techniques to NSNP patients.

Given the methodological considerations raised, future studies are needed to confirm and refine the findings of the included studies before general implementation into clinical practice is recommended. The results from this doctoral dissertation provide the clinician, the research community, and educational programs with a reliable and validated reasoning model that relates to clinical practice. It is hoped for that these findings enable physiotherapists, together with all other healthcare professionals, to manage NSNP more effectively, and thus help to reduce the personal and societal burden of neck pain.

NEDERLANDSTALIGE SAMENVATTING

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Het doel van dit doctoraal proefschrift bestond erin meer inzicht te verwerven in hoe kinesitherapeuten bepaalde patiënten profielen kunnen herkennen in de heterogene groep van patiënten met niet-specifieke nekpijn (NSNP). Op basis van kenmerkende klinische criteria konden verschillende subgroepen van elkaar onderscheiden worden. Voorgaand onderzoek heeft reeds aangetoond dat clinici de nodige informatie voor het diagnostisch redeneerproces verzamelen aan de hand van een grondige en gestructureerde anamnese en klinisch onderzoek. Dit klinisch redeneren bestaat uit meerdere parallelle denkpistes, dewelke uiteindelijk resulteren in de meest plausibele hypothese aangaande de nekklacht van de patiënt. Vanuit een biopsychosociaal referentiekader worden kinesitherapeuten gestimuleerd om een pijnmechanisme-gestuurd redeneermodel te gebruiken. Dit heeft immers als voordeel dat het zorgverstrekkers kan helpen om complexe en onvoorspelbare klinische presentaties beter te begrijpen en efficiënter aan te pakken.

In overeenstemming met deze aanbevelingen uit de wetenschappelijke literatuur, werd in dit proefschrift een voorstel gedaan om patiënten met niet-specifieke nekklachten te classificeren op basis van de pijnmechanismen die de nekpijn van de patiënt aansturen. Om de klinische relevantie van dit redeneermodel na te gaan, werden vier studies opgenomen in dit doctoraat, onderverdeeld in drie delen:

DEEL I KLINISCHE CRITERIA VOOR NIET-SPECIFIEKE NEKKLACHTEN

De eerste studie introduceerde een nieuw redeneermodel met vijf klinische disfunctie-patronen (DPn) (articulair DP, myofasciaal DP, neurogeen DP, centraal DP en sensorimotorische controle DP), met telkens een bijhorende set van klinische criteria. Dit model is geïnspireerd op eerder werk van Gifford, die het proces van ontstaan en in stand houden van pijnklachten initieel ordende in input (invoer), processing (verwerking) en output (reactie) systemen. De criteria voor de huidige indeling werden verkregen door klinische experten met ervaring in het onderzoeken en behandelen van patiënten met nekklachten te bevragen in een Delphi-onderzoek. De resultaten van deze studie vertoonden heel wat overeenkomsten met een analoge Delphi-studie over de klinische criteria voor patiënten met niet-specifieke lage rugpijn. Zo werden er gelijkenissen gevonden in de verkregen klinische criteria en werd er een sterke overlap vastgesteld tussen de input- en output-gerelateerde criteria. Als gevolg van de aangewende Delphi-methodiek moeten de bekomen klinische criteria geïnterpreteerd worden als een weerspiegeling van de gedachtegang van de deelnemende kinesitherapeuten. Het lijkt evident dat andere experten panels alternatieve, weliswaar gelijkaardige, criteria zouden opgeleverd hebben.

DEEL II PSYCHOMETRISCHE EIGENSCHAPPEN VAN HET VOORGESTELDE REDENEERMODEL

Het doel van Deel II bestond uit het toetsen van de psychometrische eigenschappen van het voorgestelde redeneermodel voor NSNP. Met betrouwbaarheid als voorwaarde voor validiteit, werd eerst de interbeoordelaarsbetrouwbaarheid en de overeenstemming in inschatting van het dominant pijnmechanisme (nociceptief / perifeer neuropathisch / nociplastisch), pijn-patroon (input / processing / output) en DP (articulair / myofasciaal / neurogeen / centraal / sensori-motorische controle DP) bij patiënten met NSNP nagegaan. Alle drie niveaus vertoonden klinisch aanvaardbare betrouwbaarheid. Vervolgens werd een cross-sectionele studie uitgevoerd die de validiteit en accuraatheid van dit redeneermodel aantoonde. Verschillende clusters van anamnestische en klinische criteria werden geïdentificeerd als zijnde voorspellend voor de aparte DPn, dewelke over het algemeen een goede diagnostische nauwkeurigheid vertoonden. Het gebruikte statische model impliceert dat de klinische criteria niet als unieke criteria gebruikt kunnen worden om besluiten te nemen. Het is correcter om op basis van zoveel mogelijk criteria een inschatting te maken van het dominant DP. De identificatie van deze clusters in het verhaal en onderzoek van de patiënt zou kinesitherapeuten kunnen helpen om een betere inschatting te maken van de prognose en om tot een onderbouwde behandelstrategie te komen. Verder onderzoek is nodig om de resultaten van de huidige studies te bevestigen en verfijnen.

DEEL III VERFIJNING VAN HET ARTICULAR DISFUNCTIEPATROON IN PATIËNTEN MET NIETSPECIFIEKE NEKKLACHTEN

Het derde en laatste deel van dit proefschrift nam het articulair DP uit het voorgestelde redeneer-model onder de loep. Van zodra de musculoskeletale kinesitherapeut een dominant articulair DP vermoedt, lijkt het immers zinvol om het patroon verder te verfijnen met het oog op een efficiëntere behandeling. In het laatste hoofdstuk werd een algoritme–voorgesteld die de (beginnende) therapeut kan aanwenden om de patiënten met niet-specifieke nekklachten die in aanmerking komen voor specifieke mobilisaties en/of manipulaties te identificeren. Een nauwere omschrijving van het toepassingsgebied voor dergelijke technieken zou een veiliger gebruik ervan in de hand moeten werken. Deze pragmatische benadering kan als voorbeeld dienen van hoe een op pijn-mechanismen gebaseerde redeneerwijze het onderzoek en handelen van kinesitherapeuten kan ondersteunen tijdens hun behandeling van patiënten met NSNP.

De resultaten van de geïncludeerde studies zijn onderhevig aan enkele methodologische restricties, dewelke beschreven werden in de discussie. Bijkomend onderzoek lijkt dan ook noodzakelijk om de huidige bevindingen te verfijnen en bij te sturen, alvorens ze ondubbelzinnig geadviseerd kunnen worden voor dagdagelijkse praktijkvoering. In afwachting kunnen clinici, onderzoekers en opleidingen aan de slag met een betrouwbaar en gevalideerd redeneermodel dat overeenstemt met de klinische werkelijkheid. Hopelijk draagt dit proefschrift bij tot een efficiëntere aanpak van NSNP door kinesitherapeuten en andere zorgverstrekkers.

APPENDICES

APPENDICES

APPENDIX 1 Levels of evidence according to the criteria described by the Center for Evidence-Based Medicine, Oxford, UK*

I	High-quality SR† containing consistent findings from multiple high-quality primary sources‡
II	High- or acceptable-quality SR containing mostly consistent findings from generally high-quality primary sources, or Consistent findings from at least 1 high quality large (n >100 in each arm) RCT, or Consistent findings from more than 1 small, high-quality RCT
III	High- or acceptable-quality SR containing mostly consistent findings from moderate primary sources, or Mostly consistent findings from 1 high quality RCT or more than 1 moderate quality RCT
IV	High- or acceptable-quality SR where higher-quality primary sources tend to favor a clear direction, or Inconsistent findings from case-control studies or retrospective studies, or inconsistent findings from RCTs where the higher-quality trials tend to favor a clear direction (even when lower-quality trials favor the opposite), or Consensus statements from content experts
V	Inconsistent evidence drawn from a low rated SR that may indicate the balance of evidence favoring one direction but with very low confidence, regardless of the quality of the primary sources, or Case series or individual expert opinion, or direct or indirect evidence from physiology, bench research, or theoretical constructs

Abbreviations: UK, United Kingdom; SR, systematic review; RCT, randomized clinical trial; AMSTAR, assessment of multiple systematic reviews; SIGN, Scottish Intercollegiate Guidelines Network.

* Adapted from Blanpied et al.[37]

† SRs were rated using AMSTAR or SIGN criteria, where 8 or higher received a "high," 6 to 7 received an "acceptable," 4 to 5 received a "low," and below 4 received a "very low" score. Very low–quality reviews were not used.

‡ Quality of the primary sources was calibrated to "high," "moderate," "low," and "very low" levels. Results from very low–quality primary sources were not used.

APPENDIX 2 The overall strength of the evidence supporting the APTA recommendations*

Grade	Strength of evidence	Basis of strength assignment
A	Strong	One or more level I SR support the recommendation, providing evidence for a strong magnitude of effect
B	Moderate	One or more level II SR or a majority of level III SR or studies support the recommendation, providing evidence for a mild to moderate magnitude of effect
C	Weak	One or more level III SR or a majority of level IV evidence supports the recommendation, providing minimal evidence of effect
D	Conflicting	Higher-quality studies conducted on this topic disagree with respect to their conclusions and effect. The recommendation is based on these conflicting studies
E	Theoretical/foundational evidence	A multitude of evidence from animal or cadaver studies, from conceptual models or principles, or from basic science or bench research supports the recommendation, providing theoretical/foundational evidence of effect
F	Expert opinion	Best practice to achieve a beneficial effect and/or minimize a harmful effect, based on the clinical experience of the guidelines development team

Abbreviations: APTA, American Physical Therapy Association; SR, systematic review. Levels refer to the levels of evidence outlined in Appendix 1.

* Adapted from Blanpied et al.[37]

APPENDIX 3 Clinical criteria associated with a predominant input, processing & output pain pattern*

Input pain pattern
Clinical representation is dominated by the peripheral somatosensory dimension of the pain (i.e. tissue/functional status)
Pain/symptoms localized to a neuro-anatomically plausible area of injury/dysfunction (with/without somatic referral)
Clinical representation in proportion to the damage done and stage of tissue healing
Patient functions within boundaries of the dysfunction or pathology
Pain or symptoms can usually be explained by 'simple' clinical (biomechanical/mechanical) models
Processing pain pattern
Clinical representation is dominated by the cognitive-emotional dimension of the pain
Pain experience and behavior are out of proportion
Pain is not conform or persisting beyond expected tissue healing/pathology recovery times
Patient does not function within the boundaries of the dysfunction or pathology
Strong association with maladaptive psychosocial factors
Pain or symptoms cannot be readily explained by 'simple' clinical (biomechanical/mechanical) models
Output pain pattern
Clinical representation is dominated by other relevant body systems (i.e. motor, neuroendocrine, immune and/or sympathetic systems)
Maladaptive motor strategies, i.e. the movement pattern explains the patients' symptoms
Changing or optimizing movement patterns alters and usually improves the symptoms
Signs or symptoms of a maladaptive neuroendocrine system (e.g. fatigue or weakness)
Signs or symptoms of a maladaptive immune system (e.g. frequent and/or recurrent respiratory infections, delayed healing, failure to gain weight, poor nutritional status)
Signs or symptoms of a maladaptive sympathetic system (e.g. altered vigilance, sweating, energy-levels, skin changes)

* Amended from the available literature.[25, 26, 39, 60, 62]

APPENDIX 4 Clinical criteria associated with a predominant nociceptive, peripheral neuropathic & central (or nociplastic) pain mechanism*

Nociceptive pain mechanism

Subjective examination criteria

NOC ▶ Clear, proportionate mechanical/anatomical nature to aggravating/easing factors

NOC ▶ Pain localized to the area of injury/dysfunction (with/without somatic referral)

NOC ▶ Usually intermittent & sharp with mechanical provocation; may be more constant dull ache or throb at rest

Pain associated with & in proportion to trauma or pathological process (INFLAM) or movement/postural dysfunction (ISCHEM)

Usually rapidly resolving or resolving in accordance with expected tissue healing recovery times

Responsive to simple analgesia/NSAIDs

Pain in association with other symptoms of inflammation (i.e. swelling, redness, heat) (INFLAM)

Pain of recent onset

Physical examination criteria

NOC ▶ Antalgic (i.e. pain relieving) postures/movement patterns

Clear, consistent & proportionate mechanical/anatomical pattern of pain reproduction on movement/mechanical testing of target tissues

Localized pain on palpation

Absence of or expected/proportionate findings of (primary and/or secondary) hyperalgesia and/or allodynia

Peripheral neuropathic pain mechanism

Subjective examination criteria

PNP ▶ History of nerve injury, pathology or mechanical compromise

PNP ▶ Pain referred in a dermatomal or cutaneous distribution

NOC ▶ Pain variously described as burning, shooting, sharp, aching or electric-shock-like

NOC ▶ Pain in association with other dysesthesias (e.g. crawling, electrical, heaviness)

Pain in association with other neurological symptoms (e.g. pins & needles, numbness, weakness)

Less responsive to simple analgesia/NSAIDs and/or more responsive to anti-epileptics/anti-depressants

Pain of high severity & irritability (i.e. easily provoked, taking longer to settle)

Mechanical pattern to aggravating & easing factors involving activities/postures associated with movement, loading or compression of neural tissue

Reports of spontaneous (i.e. stimulus-independent) pain and/or paroxysmal pain (i.e. sudden recurrences & intensification of pain)

Physical examination criteria

PNP ▶ Pain/symptom provocation with mechanical/movement tests (e.g. active/passive, neurodynamic tests) that move/load/compress neural tissue

Antalgic posturing of the affected limb/body part

Pain/symptom provocation on palpation of relevant neural tissues

continued

APPENDIX 4 Continued

Peripheral neuropathic pain mechanism
Physical examination criteria
Positive neurological findings (including altered reflexes, sensation & muscle power in a dermatomal/myotomal or cutaneous nerve distribution)
Positive findings of hyperalgesia (primary or secondary) and/or allodynia and/or hyperpathia within the distribution of pain
Central or nociplastic pain mechanism
Subjective examination criteria
CP ▶ Disproportionate, non-mechanical, unpredictable pattern of pain provocation in response to multiple/nonspecific aggravating/easing factors
CP ▶ Pain disproportionate to the nature & extent of injury or pathology
CP ▶ Strong association with maladaptive psychosocial factors (e.g. negative emotions, poor self-efficacy, maladaptive beliefs & pain behaviors, altered family/work/social life, medical conflict)
NOC ▶ Night pain/disturbed sleep
Pain persisting beyond expected tissue healing/pathology recovery times
Widespread, non-anatomical distribution of pain
History of failed interventions (medical/surgical/therapeutic)
Unresponsive to NSAIDs and/or more responsive to anti-epileptics/anti-depressants
Reports of spontaneous (i.e. stimulus-independent) pain and/or paroxysmal pain (i.e. sudden recurrences & intensification of pain)
Pain in association with high levels of functional disability
More constant/unremitting pain
Pain in association with other dysesthesias (e.g. burning, coldness, crawling)
Pain of high severity and irritability (i.e. easily provoked, taking a long time to settle)
Physical examination criteria
CP ▶ Diffuse/non-anatomic areas of pain/tenderness on palpation
Disproportionate, inconsistent, non-mechanical/non-anatomical pattern of pain provocation in response to movement/mechanical testing
Positive findings of hyperalgesia (primary, secondary) and/or allodynia and/or hyperpathia within the distribution of pain
Positive identification of various psychosocial factors (e.g. catastrophisation, fear-avoidance behavior, distress)

Abbreviations: INFLAM, inflammatory nociceptive; ISCHEM, ischemic nociceptive; NSAIDs, non-steroidal anti-inflammatory drugs.
* Amended from Smart et al.[112, 123-125, 127] Criteria are displayed per category as identified in the Delphi-study of Smart et al.[112]
NOC ▶ Indicates the 7 criteria that were retained in the final predictive model for nociceptive pain.[125, 127]
PNP ▶ Indicates the 3 criteria that were retained in the final predictive model for peripheral neuropathic pain.[124, 127]
CP ▶ Indicates the 4 criteria that were retained in the final predictive model for central/nociplastic pain.[123, 127]

APPENDIX 5 Characteristics of the subjects included in the validity study, by pain mechanism classification (n=191)

Variable	Nociceptive pain mechanism n =145 (75.9%)	Peripheral neuropathic pain mechanism n =5 (2.6%)	Nociplastic pain mechanism n =41 (21.5%)
Sex (Female)	100.0 (69.0%)	1.0 (20%)	36.0 (87.8%)
Age (y), Mean (SD, Range)	39.6 (14.7, 20-75)	40.0 (14.3, 25-63)	41.3 (13.5, 20–67)
Predominant pain location			
Neck	19.0 (13.1%)	0.0 (0.0%)	0.0 (0.0%)
Neck/Uni Prox Arm (AE)	19.0 (13.1%)	5.0 (100.0%)	6.0 (14.6%)
Neck/Uni Dist Arm (BE)	11.0 (7.6%)	5.0 (100.0%)	8.0 (19.5%)
Neck/Bi Prox Arm (AE)	9.0 (6.2%)	0.0 (0.0%)	10.0 (24.4%)
Neck/Bi Dist Arm (BE)	4.0 (2.7%)	0.0 (0.0%)	5.0 (12.2%)
Neck/Other (TMJ, Tx, abdom)	62.0 (42.8%)	0.0 (0.0%)	32.0 (78.0%)
Head	100.0 (69.0%)	1.0 (20.0%)	39.0 (95.1%)
Wide spread	4.0 (2.8%)	0.0 (0.0%)	23.0 (56.1%)
Work status			
Full-time	125.0 (86.2%)	4.0 (80.0%)	28.0 (68.3%)
Part-time	5.0 (3.4%)	0.0 (0.0%)	5.0 (12.2%)
Unemployed	0.0 (0.0%)	1.0 (20.0%)	6.0 (14.6%)
Retired	15.0 (10.3%)	0.0 (0.0%)	2.0 (4.9%)
Average Sx intensity (NRS) over previous 7d, Mean (SD, Range)	3.9 (1.9, 1-8)	3.2 (1.8, 0-4)	4.9 (1.8, 1-8)
Worst Sx intensity (NRS) over previous 7d, Mean (SD, Range)	5.9 (2.0, 1-10)	5.2 (3.0, 0-7)	6.9 (1.92, 1-10)
NDI score, Mean (SD, Range)	9.9 (4.6, 0-24)	12.6 (6.9, 7-24)	16.9 (7.18, 2-33)
CSI score, Mean (SD, Range)	32.6 (10.5, 8-66)	29.8 (14.2, 15-52)	45.0 (11.5, 12-68)
Duration of current episode (weeks), Mean (SD, Range)	250.0 (413.0, 0.14-2080)	194.0 (273.0, 3-624)	513.0 (526.0, 0.1-2080)
<4 weeks	45.0 (31.0%)	1.0 (20.0%)	3.0 (7.3%)
4-12 weeks	5.0 (3.5%)	0.0 (0.0%)	1.0 (2.4%)
>12 weeks	95.0 (65.5%)	4.0 (80.0%)	37.0 (90.2%)

Abbreviations: Neck/Uni Prox Arm (AE), neck pain with unilateral proximal arm pain above elbow; Neck/Uni Dist Arm (BE), neck pain with unilateral distal arm pain below elbow; Neck/Bi Prox Arm (AE), neck pain with bilateral proximal arm pain above elbow; Neck/Bi Dist Arm (BE), neck pain with bilateral distal arm pain below elbow; Neck/Other (TMJ, Tx, abdom), neck pain associated with temporomandibular joint complaints, musculoskeletal thoracic complaints or abdominal complaints; Sx, symptom; NRS, numeric pain rating scale; NDI, Neck Disability Index; CSI, Central Sensitization Inventory.

APPENDIX 6 Descriptive odds ratios for criteria in the pain mechanism classification models

Criteria	OR	95% CI Lower	95% CI Upper	P-value
Nociceptive pain mechanism				
6 Arm symptoms exceed neck pain	.160	.033	.667	.005
8 Widespread pain	.029	.007	.096	<.001
21 Pain variously described as pins and needles	.156	.061	.388	<.001
28 Positive identification of various YFs	.087	.037	.197	<.001
38 Hyperalgesia and/or allodynia	.020	.001	.145	<.001
58 Absence of clear neurological findings (function/ provocation tests)	10.889	3.004	49.778	<.001
62 Inconsistent and ambiguous findings	.017	.003	.062	<.001
63 Disproportionate/abnormal reaction	.036	.004	.172	<.001
Peripheral neuropathic pain mechanism				
6 Arm symptoms exceed neck pain	92.568	7.955	4857.556	<.001
22 Muscle weakness (not caused by pain inhibition)	126.459	10.421	6732.219	<.001
48 Positive Spurling's test	81.478	7.103	4253.610	<.001
58 Absence of clear neurological findings (function/ provocation tests)	.017	.001	.187	<.001
59 Clear neurological findings	106.977	9.029	5649.428	<.001
60 Pain/symptom provocation in response to palpation of the nerve	37.043	2.330	490.327	.005
Nociplastic pain mechanism				
8 Widespread pain	44.932	13.387	199.483	<.001
28 Positive identification of various YFs	14.526	6.124	36.646	<.001
38 Hyperalgesia and/or allodynia	59.855	8.289	2611.318	<.001
62 Inconsistent and ambiguous findings	80.821	21.361	464.438	<.001
63 Disproportionate/abnormal reaction	33.414	7.006	320.430	<.001

Abbreviations: OR, odds ratio; CI, confidence interval; YFs, Yellow Flags; Cx, cervical; subj. exam, subjective examination; Sx, symptom; VAS, Visual Analogue Scale; NRS, Numeric Rating Scale; CSI, Central Sensitization Inventory; NDI, Neck Disability Index; ROM, range of motion; phys. exam, physical examination.
The criterion descriptions were shortened. Full descriptions are listed in TABLE 2 in Chapter 3.
In case of zero cell counts, an adjustment by adding .5 to each of the cells (known as Haldane-Anscombe correction) was performed.[39]

APPENDIX 7 Classification accuracy of the nociceptive pain mechanism model

	Reference standard positive	Reference standard negative	Total
Cluster positive	18 patients	1	19
Cluster negative	6	6	12
Total	24	7	31

APPENDIX 8 Classification accuracy of the peripheral neuropathic pain mechanism model

	Reference standard positive	Reference standard negative	Total
Cluster positive	5 patients	6	11
Cluster negative	0	180	180
Total	5	186	191

APPENDIX 9 Classification accuracy of the nociplastic pain mechanism model

	Reference standard positive	Reference standard negative	Total
Cluster positive	5 patients	0	5
Cluster negative	2	24	26
Total	7	24	31

APPENDIX 10 Diagnostic accuracy measures for the pain mechanism classification model

	Nociceptive pain mechanism	**Peripheral neuropathic pain mechanism**	**Nociplastic pain mechanism**
Sensitivity (95% CI)	.75 (.53 - .90)	.92 (.44 - 1.00)	.69 (.29 -0.94)
Specificity (95% CI)	.86 (.42 - 1.00)	.97 (.93 - .99)	.98 (.83 - 1.00)
PPV (95% CI)	.95 (.74 - 1.00)	.46 (.18 - .76)	.92 (.44 - 1.00)
NPV (95% CI)	.50 (.21 - .79)	1.00 (.97 - 1.00)	.91 (.73 - .98)
LR+ (95% CI)	5.25 (.84 - 32.70)	26.37 (11.93 - 58.27)	34.37 (2.13 – 556.00)
LR- (95% CI)	.29 (.14 - .62)	.09 (.01 - 1.23)	.32 (.11 - .89)
Overall diagnostic accuracy (95% CI)	.77 (.59 - .90)	.96 (.93 - .99)	.91 (.76 - .98)

Abbreviations: CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value; LR+, positive likelihood ratio; LR- negative likelihood ratio.
In case of zero cell counts, an adjustment by adding .5 to each of the cells (known as Haldane-Anscombe correction) was performed.[39]

APPENDIX 11 The continuum of pain patterns & dysfunction patterns (DP), including their respective clinical criteria identified by the final predictive model

APPENDIX 12 Proposal for rewording key terminology to enhance clarity*

New terminology	Former terminology
Pain states	Pain mechanisms
Nociceptive pain state	
Inflammatory	
Mechanical	
Ischemic	
Neuropathic pain state	
Peripheral neuropathic	
Central neuropathic	
Nociplastic pain state	
Pain mechanisms	Pain mechanisms
Nociceptive transmission	
Peripheral sensitization	
Ectopic activity	
Central sensitization/central disinhibition	
Patterns of pain & disability	Pain mechanisms
Input pain pattern	
Processing pain pattern	
Output pain pattern	
Clinical patterns	Dysfunction patterns
Articular pattern	
Articular convergence pattern	
Articular divergence pattern	
Articular mixed pattern	
Myofascial pattern	
Neural pattern	
Central/Nociplastic pattern	
Sensorimotor control pattern	

* Based on literature from different disciplines.[29, 38, 43-45, 66]

List of abbreviations

APTA	American Physical Therapy Association
CI	Confidence interval
CNS	Central nervous system
CSI	Central Sensitization Inventory
DP	Dysfunction pattern
IASP	International Association for the Study of Pain
ICF	International Classification of Functioning, Disability and Health
KCE	Belgian Health Care Knowledge Centre (Federaal Kenniscentrum voor de gezondheidszorg)
LBP	Low back pain
LR-	Negative likelihood ratio
LR+	Positive likelihood ratio
NDI	Neck Disability Index
NPV	Negative predictive value
NSLBP	Nonspecific low back pain
NSNP	Nonspecific neck pain
OR	Odds ratio
PNP	Peripheral neuropathic pain
PPV	Positive predictive value
ROM	Range of motion
SNAG	Sustained natural apophyseal glide
STARD	Standards for Reporting of Diagnostic Accuracy
VAS	Visual analogue scale

List of publications

Publications in international journals with peer review

Dewitte V*, De Pauw R*, De Meulemeester K, Danneels L, Bouche K, Roets A, Cagnie B. Diagnostic accuracy of a pain mechanisms-based classification for nonspecific neck pain. Submitted in Clinical Journal of Pain, 2018.
(* shared first author)

Dewitte V*, De Pauw R*, Danneels L, Bouche K, Roets A, Cagnie B. The interrater reliability of a pain mechanisms-based classification for patients with nonspecific neck pain. Braz J Phys Ther 2018 (October 29); (Epub ahead of print)
(* shared first author)

Dewitte V, De Pauw R, De Meulemeester K, Peersman W, Danneels L, Bouche K, Roets A, Cagnie B. Clinical classification criteria for nonspecific low back pain: a Delphi-survey of clinical experts. Musculoskeletal science & practice 2018; 34:66-76.

De Meulemeester K, Calders P, **Dewitte V**, Barbe T, Danneels L, Cagnie B. Surface electromyographic activity of the upper Trapezius before and after a single dry needling session in female office workers with Trapezius myalgia. Am J Phys Med Rehabil 2017; 96:861-868.

Dewitte V, Peersman W, Danneels L, Bouche K, Roets A, Cagnie B. Subjective and clinical assessment criteria suggestive for five clinical patterns discernible in nonspecific neck pain patients. A Delphi-survey of clinical experts. Man Ther 2016; 26:87-96.

Dewitte V, Cagnie B, Barbe T, Beernaert A, Vanthillo B, Danneels L. Articular dysfunction patterns in patients with mechanical low back pain: A clinical algorithm to guide specific mobilization and manipulation techniques. Man Ther 2015; 20:499-502.

Dewitte V, Beernaert A, Vanthillo B, Barbe T, Danneels L, Cagnie B. Articular dysfunction patterns in patients with mechanical neck pain: a clinical algorithm to guide specific mobilization and manipulation techniques. Man Ther 2014; 19:2-9.

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Other Publications

Dewitte V, De Pauw R, De Meulemeester K, Peersman W, Danneels L, Bouche K, Roets A, Cagnie B. Clinical classification criteria for nonspecific low back pain: a Delphi-survey of clinical experts. Fysiopraxis maart 2018; 27(2).

Cagnie B, Barbe T, Beernaert A, Bouche K, Descheemaeker, De Corte K, De Ridder R, **Dewitte V**, Leten K, Maere B, Parlevliet T, Vanden Borre K, Van Eeckhoven T, Vanthillo B. Klinisch Onderzoek van de Cervicale Wervelkolom. Wommelgem: Van In - De Boeck, 2017.

Beernaert A, Cagnie B , Vanthillo B, Barbe T, **Dewitte V**. Mobilisaties en manipulaties van de wervelkolom. Wommelgem: Van In - De Boeck, 2016.

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CURRICULUM VITAE

VINCENT DEWITTE

—

Physiotherapist
Manual therapist

CONTACT ME @WORK

Department of Rehabilitation Sciences
Ghent University Hospital Campus
Corneel Heymanslaan 10, B3, B-9000 Ghent
Vincent.Dewitte@UGent.be
+32 9 332 12 17
www.ugent.be/ge/revaki
www.mtghent.ugent.be

ABOUT ME

Born on September 19, 1983 in Ghent, Belgium
Happily married to Sofie Bode
Proud father of Ella Noa & César

Broad knowledge base in rehabilitation & musculoskeletal physiotherapy, supplemented with 13 years of clinical experience as an independent physiotherapist & teaching assistant at Ghent University.

GENERAL INTERESTS

Sports — Music — Family & Friends

Scandinavian Design — Traveling/ Italy — Good Food

EDUCATION PROGRESS

PhD in Health Sciences (in view) — **2013 / 2018**
Department of Rehabilitation Sciences, Faculty of Medicine & Health Sciences, Ghent University

Postgraduate Degree in Musculoskeletal Physiotherapy (Manual Therapy) — **2006 / 2007**
Department of Rehabilitation Sciences, Faculty of Medicine & Health Sciences, Ghent University

MSc in Health Science Rehabilitation & Physiotherapy — **2001 / 2006**
Department of Rehabilitation Sciences, Faculty of Medicine & Health Sciences, Ghent University

_Additional Courses, Training & Conferences

Public speaking for researchers — **2018**
H. Van de Water, The Floor is Yours

Search Engine Optimization – Basic Course — **2018**
S. Verhaegen, Google

Knowledge 2 Connect Seminars of The Knowledge Centre Ghent — **2016 / 2018**
S. Van der Burght, Research integrity
H. Helsmoortel, How to get your message across effectively: the science of storytelling
C. Surridge, How can I turn my manuscripts into an article
R. Sankey, EMBASE as source for biomedical literature

NASM Certified Personal Trainer 2017
Physical Coaching Academy, EQF level 6 in The European Register of Exercise Professionals

Plunge into your own business plan – Summer school 2017
B. Sas, X. Gellynck, I. Sioen, H. De Steur, Ph. Jacobs, Food2Know, Ghent University

European Congress Manual Therapy 2017 2017
I. Baert, C. Cook, B. Dingenen, A. Grimaldi, J. Lewis, F. Struyf, Manual Therapy Association, Brussels (Belgium)

Dry Needling Course – Basic & Advanced Module Lower Quadrant 2016 / 2017
Dry Needling Gent

Journées de Thérapie Manuelle Orthopédique 2016
P. O'Sullivan, F. Grondin, J. Nijs, OMT France, Lille (France)

IFOMPT 2016 – Expanding Horizons 2016
Various international speakers, IFOMPT, Glasgow (The United Kingdom)

Journées de Thérapie Manuelle Orthopédique 2015
B. Hidalgo, B. Cagnie, L. Danneels, OMT France, Lille (France)

Direct Access Physiotherapy 2014
J. A. Simons, University of Leuven

IFOMPT Teachers Meeting 2014 2014
Various international speakers, IFOMPT Teachers Meeting, Utrecht (The Netherlands)

Belgian Back Society – Neck Complaints: a 360° View 2014
Various international speakers, BBS, Ghent (Belgium)

Statistical Parametric Mapping – Basic course 2014
T. Pataky, M. Robinson, J. Vanrenterghem

Statistics – Introduction to SPSS 2013
E. Goetghebuer, IPVW

Craniocervical & Craniomandibular dysfunctions 2010
M. Rocabado, Institute for Permanent Education, Ghent University

Clinical Neurodynamics – Upper + Lower Quadrant Module 2009
M. Shacklock, Institute for Permanent Education, Ghent University

Muscle Energy Techniques – Lower back & Pelvis + Cervical & Thoracic Spine Module 2008
B. Hungerford, Institute for Permanent Education, Ghent University

PROFESSIONAL EXPERIENCE

_Clinical Experience

Independent Physiotherapist – Manual therapist 2006 / present
Private Physiotherapy Clinic (Ghent) 2013 / present
Flanders Athletics League (Topsportschool Atletiek – Ghent) 2011 / 2013
Private Physiotherapy Clinic (Deurle) 2007 / 2012
Private Physiotherapy Clinic (Mariakerke) 2006 / 2007

_Teaching Experience

Bachelor & Master in Rehabilitation & Physiotherapy Program	**2008 / present**
Department of Rehabilitation Sciences, Faculty of Medicine & Health Sciences, Ghent University	
Teacher	2013 / present
Assistant Teacher	2008 / 2012
Musculoskeletal Physiotherapy Postgraduate Program	**2008 / present**
Department of Rehabilitation Sciences, Faculty of Medicine & Health Sciences, Ghent University	
Teacher	2013 / present
Assistant Teacher	2008 / 2012
Department of Rehabilitation Sciences, Faculty of Kinesiology & Rehabilitation Sciences, University of Leuven	
Invited Teacher	2016 / present

_National & International Publications

Dewitte V*, De Pauw R*, De Meulemeester K, Danneels L, Bouche K, Roets A, Cagnie B. Diagnostic accuracy of a pain mechanisms-based classification for nonspecific neck pain. Submitted (July 2018)
(* shared first author)

Dewitte V*, De Pauw R*, Danneels L, Bouche K, Roets A, Cagnie B. The interrater reliability of a pain mechanisms-based classification for patients with nonspecific neck pain. Braz J Phys Ther 2018; doi: 10.1016/j.bjpt.2018.10.008. [Epub ahead of print]
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Dewitte V, De Pauw R, De Meulemeester K, Peersman W, Danneels L, Bouche K, Roets A, Cagnie B. Clinical classification criteria for nonspecific low back pain: a Delphi-survey of clinical experts. Musculoskeletal science & practice 2018; 34:66-76.

Cagnie B, Barbe T, Beernaert A, Bouche K, Descheemaeker, De Corte K, De Ridder R, **Dewitte V**, Leten K, Maere B, Parlevliet T, Vanden Borre K, Van Eeckhoven T, Vanthillo B. Klinisch Onderzoek van de Cervicale Wervelkolom. Wommelgem: Van In - De Boeck, 2017.

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Cagnie B, **Dewitte V**, Coppieters I, Van Oosterwijck J, Cools A, Danneels L. Effect of ischemic compression on trigger points in the neck and shoulder muscles in office workers: a cohort study. J Manipulative Physiol Ther 2013; 36:482-9.

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Cools A, **Dewitte V**, Lanszweert F, Notebaert D, Roets A, Soetens B, Cagnie B, Witvrouw E. Rehabilitation of scapular muscle balance: which exercises to prescribe? Am J Sports Med 2007; 35:1744-51.

_ National & International Presentations & Workshops

Subjective & Clinical Assessment Criteria Suggestive for 5 Clinical Patterns Discernible in Nonspecific Neck Pain Patients. A Delphi-Survey of Clinical Experts **2016**

Oral presentation, IFOMPT 2016 - Expanding Horizons, Glasgow (The United Kingdom)

Un Algorithme Clinique pour l'Application de Mobilisations & Manipulations Selon la Douleur

Oral presentation & workshop, Journées de Thérapie Manuelle Orthopédique, OMT France, Lille (France) 2016

Oral presentation & workshop, Journées de Thérapie Manuelle Orthopédique, OMT France, Lille (France) 2015

Low Back Pain from a Manual Therapist's Perspective **2015**

Oral presentation, LOKK Kinekring Aalst, Aalst (Belgium)

Articular Dysfunction Patterns in Patients with Mechanical Neck Pain: a Clinical Algorithm to Guide Specific Mobilization & Manipulation Techniques

Oral presentation, Belgian Back Society – Neck Complaints: a 360° View, Ghent (Belgium) 2014

Oral presentation, IFOMPT Teachers Meeting, Utrecht (The Netherlands) 2014

Physiological Effects of Dry Needling 2014

Oral presentation, Dry Needling Conference, Houten, (The Netherlands)

Physiological Effects of Mobilizations & Manipulations

Oral presentation, LOKK Kinekring Oudenaarde, Ronse (Belgium) 2016

Oral presentation, MATHERA, Vilvoorde (Belgium) 2014

Oral presentation, KineClub, Department of Rehabilitation Sciences, Ghent University 2013

_Memberships

Member of the Musculoskeletal Physiotherapy Postgraduate Steering Committee	2013 / present
Member of the Spine Research Unit Ghent	2014 / present

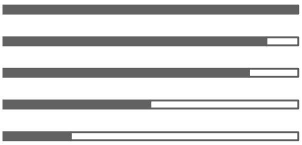
PROFESSIONAL SKILLS

_Software skills

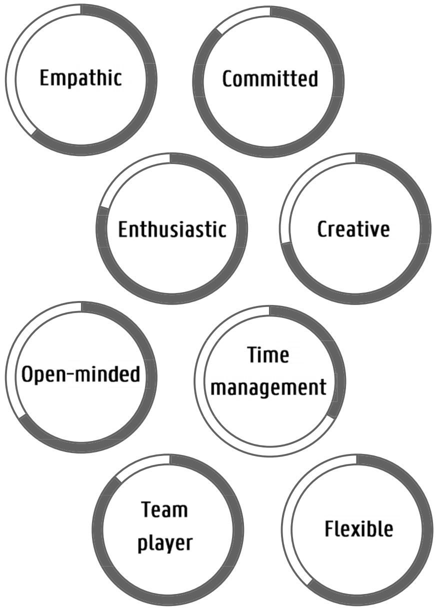
Word
Excel
PowerPoint
Prezi
Mimics

_Knowledge of languages

Dutch
English
French
German
Italian



PERSONAL SKILLS



CONTACT ME @Home

Hemingplein 19, 9051 Sint-Denijs-Westrem
+32 479 60 52 68
vincent_dewitte@hotmail.com
@vincent_dewitte
Vincent Dewitte

Gratitude turns what we have into enough.

Melody Beattie

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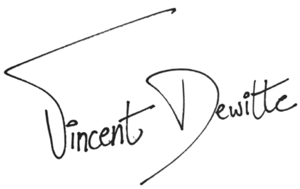

Ghent, December 2018.

DANKWOORD

DANKWOORD

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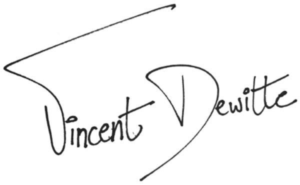

Gent, december 2018.