Current Medical Research and Opinion

ISSN: 0300-7995 (Print) 1473-4877 (Online) Journal homepage: http://www.tandfonline.com/loi/icmo20

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To cite this article: Bart Morlion, Flaminia Coluzzi, Dominic Aldington, Magdalena Kocot-Kepska, Joseph Pergolizzi, Ana Cristina Mangas, Karsten Ahlbeck & Eija Kalso (2018) Pain chronification: what should a non-pain medicine specialist know?, Current Medical Research and Opinion, 34:7, 1169-1178, DOI: 10.1080/03007995.2018.1449738

To link to this article: https://doi.org/10.1080/03007995.2018.1449738

Accepted author version posted online: 07 Mar 2018.
Published online: 12 Apr 2018.

CURRENT MEDICAL RESEARCH AND OPINION
2018, VOL. 34, NO. 7, 1169–1178
https://doi.org/10.1080/03007995.2018.1449738
Article ST-0791.R1/1449738

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COMMENTARY

Pain chronification: what should a non-pain medicine specialist know?

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ABSTRACT

Objective: Pain is one of the most common reasons for an individual to consult their primary care physician, with most chronic pain being treated in the primary care setting. However, many primary care physicians/non-pain medicine specialists lack enough awareness, education and skills to manage pain patients appropriately, and there is currently no clear, common consensus/formal definition of "pain chronification".

Methods: This article, based on an international Change Pain Chronic Advisory Board meeting which was held in Wiesbaden, Germany, in October 2016, provides primary care physicians/non-pain medicine specialists with a narrative overview of pain chronification, including underlying physiological and psychosocial processes, predictive factors for pain chronification, a brief summary of preventive strategies, and the role of primary care physicians and non-pain medicine specialists in the holistic management of pain chronification.

Results: Based on currently available evidence, we propose the following consensus-based definition of pain chronification which provides a common framework to raise awareness among non-pain medicine specialists: "Pain chronification describes the process of transient pain progressing into persistent pain; pain processing changes as a result of an imbalance between pain amplification and pain inhibition; genetic, environmental and biopsychosocial factors determine the risk, the degree, and time-course of chronification."

Conclusions: Early intervention plays an important role in preventing pain chronification and, as key influencers in the management of patients with acute pain, it is critical that primary care physicians are equipped with the necessary awareness, education and skills to manage pain patients appropriately.

ARTICLE HISTORY
Received 18 December 2017
Revised 5 March 2018
Accepted 5 March 2018

KEYWORDS
Chronic pain; chronification; pain; non-pain medicine specialist

Introduction

Pain is one of the most common reasons for an individual to consult their primary care physician[1–3], with one in five adults in Europe estimated to be affected by chronic pain[4]. However, one of the challenges of managing pain in the primary care setting is that it is poorly assessed and reported[5–9]. Chronic pain has a major negative impact on quality of life, workforce participation and productivity, and healthcare expenditure[4,10–15]. Indeed, US statistics estimate that total annual costs associated with chronic pain are $US560–635 billion[16] whereas, across Europe, data indicate that 3–10% of gross domestic product is spent on national healthcare and socioeconomic costs associated with chronic pain[17,18].

Pain has been defined by various groups over the years, often categorized according to the terms "acute" and "chronic"[19–21]. A common definition of acute pain is "the normal, predicted physiological response to an adverse chemical, thermal or mechanical stimulus … associated with surgery, trauma, and acute illness"[19]. Traditionally, chronic pain has been defined by the International Association for the Study of Pain (IASP) as "pain without apparent biological value that has persisted beyond the normal tissue healing time (usually about 3 months)"[22]. It is widely accepted that, unlike acute pain, chronic pain has no protective function[20]. Recently, an updated definition of pain has been proposed: "Pain is a distressing experience associated with actual or potential tissue damage with sensory, emotional, cognitive, and social components"[23].

However, the conventional temporal definitions don't account for the complex mechanistic distinctions between acute (physiological) and chronic (pathological) pain and the transition from acute to chronic pain states[20,24]. Indeed, the term "chronic" is derived from "chronos" (Greek) which only indicates the temporal but not the mechanistic aspects, something which is inferred by many physicians but isn't

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part of the specific definition. Furthermore, conventional definitions do not account for the course of pain over time (pain trajectories) associated with different pain types[25]. Evaluating pain trajectories could better describe the course of pain, and the predictors of that course, potentially resulting in the elucidation of the beginnings of common long-term pain conditions[25,26].

A 2011 Institute of Medicine (IOM) report states that "we believe it is necessary to understand better the link between acute and chronic pain and find ways to break that link"[27]. This article is based on a Change Pain Chronic Advisory Board meeting, consisting of pain specialists from Europe and the US, which was held in Wiesbaden, Germany, in October 2016. The objective of this article is to provide an updated overview of pain chronification, including underlying physiological and psychosocial processes and predictive factors for pain chronification, and the role of non-pain medicine specialists in the holistic management of pain chronification, and to propose a consensus-based definition of pain chronification.

Pain chronification: what is it?

From the mid-1990s, terms such as "chronicity", "persistent pain" and "pain chronification" started to appear in the literature[28–30]. Over time, the terms have been used in various ways in the literature relating to pain conditions. However, there is a need for common semantics, and an urgent requirement for an internationally accepted framework and terminology.

Currently, there are cultural/linguistic differences in the interpretation of the word "chronification". For example, in Germany the term "pain chronification" includes chronic pain as the end point of the process, whereas others consider "pain chronification" to describe only the transition process from acute pain to chronic pain. Moreover, some languages (e.g. British English) do not yet recognize "chronification" as a real word[31].

As part of the Change Pain Chronic Advisory Board meeting of pain specialists, attendees generated and reached consensus agreement on the following overarching definition of "pain chronification":

- Pain chronification describes the process of transient pain progressing into persistent pain.
- Pain processing changes as a result of an imbalance between pain amplification and pain inhibition.
- Genetic, environmental and biopsychosocial factors determine the risk, degree and time-course of chronification.

The following sections discuss aspects of the scientific rationale which support this proposed definition of pain chronification.

Biological and psychosocial processes involved in pain chronification

The biopsychosocial model is now widely accepted as the most heuristic approach to the development and maintenance of chronic pain[32–34]. In addition to neurobiological processes, the overall biopsychosocial model encompasses research on psychological and social factors which can interact with brain processes to influence an individual's well-being[32]. Using the biopsychosocial approach, pain and disability can be described as a multidimensional, dynamic interplay of physiological, psychological and social factors that influence each other in a reciprocal manner, leading to chronic and complex pain syndromes[33].

From the physiological perspective, the standard classification of pain differentiates between nociceptive pain, which originates in tissues in response to a nociceptor stimulation or nociceptive stimulus, and neuropathic pain, which originates in the peripheral or central nervous system (CNS) as a result of nerve fiber damage or inflammation. In both cases, neurotransmitters (e.g. glutamate [excitatory effect, enhances pain] and gamma-aminobutyric acid [GABA; inhibitory effect, reduces pain]) transfer nociceptive impulses via neurons to the spinal cord which are then passed to the brain stem via ascending pathways where they are interpreted within higher centers[35–38]. Descending pathways simultaneously modify pain perception via the noradrenergic pain regulation system[37,39]. Details of the noxious stimuli are transmitted from the limbic system and midbrain structures down through the periaqueductal grey to the brainstem, in particular the rostroventromedial medulla, where the signals are filtered before transferring to the spinal cord dorsal horn at the level of the incoming pain signal[40]. Noradrenaline, which reduces pain, and serotonin (or 5-hydroxytryptamine), which may have both facilitatory and inhibitory functions, are important neurotransmitters in the descending modulatory pathways[41–43]. Although further research is required, there is some promise that it might be possible to measure these modulatory systems clinically and reliably by conditioned pain modulation (CPM)[44].

The development and maintenance of many chronic pain syndromes appears to arise from an imbalance between amplified ascending signals and inadequate activation of the descending inhibitory pathway (Figure 1)[45]. Normally, a robust descending inhibitory system may be engaged to protect against the development of chronic pain and recent clinical findings indicate that diminished descending inhibition is potentially an important factor in determining whether acute pain becomes chronic[40,46,47]. Indeed, when exposed to inflammatory mediators and growth factors in response to activity and after injury, the nociceptive system is capable of undergoing significant changes or plasticity[42,48].

Peripheral and central sensitization

Peripheral or central sensitization may result in increased nociceptive input to the brain and can also change the processing of nociceptive information within the brain[48–50]. As a result of inflammation or lesion, alterations in the nociceptive system occur in nociceptors, with their peripheral terminals becoming sensitized (peripheral sensitization). This process is characterized by hyperexcitability and an increased sensitivity to chemical, thermal and mechanical stimuli and

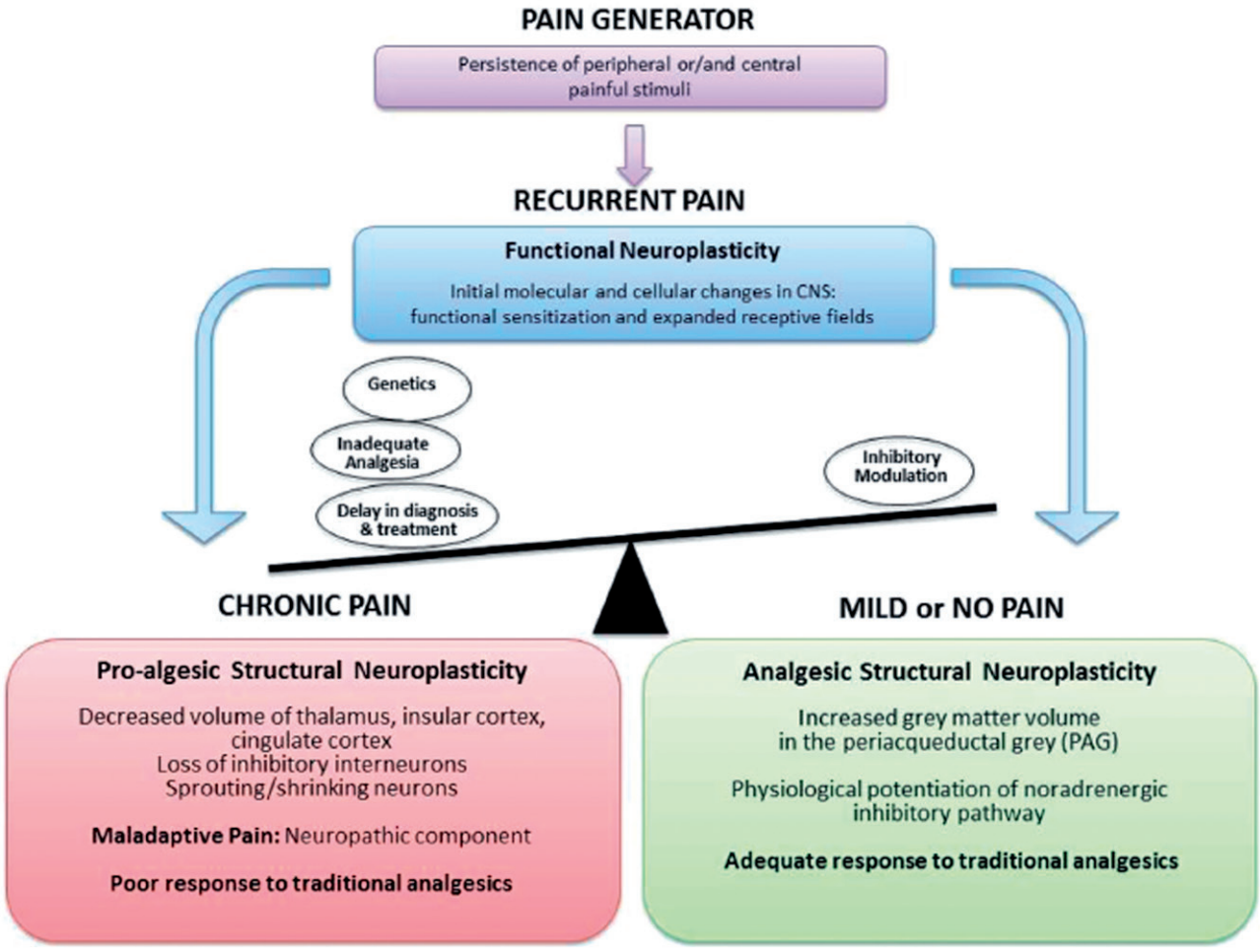

Figure 1. From the physiological perspective, an imbalance between enhanced ascending nociceptive inputs and inadequate inhibitory descending pathways is responsible for pain chronification[45]. Reproduced with permission from Coluzzi *et al.*[45].

spontaneous activity of the neuron. Indeed, axons can also become sufficiently hyperexcitable to generate spontaneous action potentials, cell bodies can undergo dramatic alterations in protein expression and trafficking, and changes can occur in the strength and structural organization of spinal cord synapses. Similar functional and structural changes take place in the spinal cord and brain, involving central neurons and non-neuronal cells (e.g. glial cells[51]), and these changes (central sensitization) are responsible for facilitating the responses to peripheral inputs so that the threshold for generating pain decreases and the duration, amplitude and spatial distribution of pain increase[52,53]. Clinically, innocuous tactile stimuli can become painful (allodynia) or nociceptive stimuli can evoke more intense painful sensations (hyperalgesia).

Due to the fact that central sensitization results from changes in the properties of neurons in the CNS, pain associated with the chronification process is no longer linked, as in acute nociceptive pain, to the presence, intensity or duration of noxious peripheral stimuli. On the contrary, central sensitization produces pain hypersensitivity by changing the sensory response elicited by normal inputs, including inputs that usually evoke innocuous sensations[52].

Multiple mechanisms contribute to these changes, with each one being subject to, or an expression of, neural plasticity (the capacity of neurons to change their function, chemical profile, or structure)[54]. In some pain syndromes, such as fibromyalgia and irritable bowel syndrome, no identifiable noxious stimulus nor lesion or disease of the somatosensory nervous system is present. Some authors classify these pain syndromes under the term central sensitivity syndromes, indicating the presence of central sensitization as the predominant mechanism[55,56].

Functional and structural neuroplasticity

Increasing evidence reveals structural and functional maladaptive neuroplastic changes within the central and peripheral nervous system of individuals with chronic pain disorders that appear to play a prominent role in the pathophysiology of these disorders[48,57,58].

Molecules may become functionally sensitized, synaptic transmission may become potentiated by presynaptic mechanisms or by postsynaptic plasticity, cells may respond to noxious stimuli with increased activity and expanded receptive fields after injury and network function may change so that more cell ensembles respond to noxious stimuli, collectively leading to a higher net spinal output after injury or inflammation[54].

Among the structural changes, synaptic spines may increase in size and density, axons may sprout or degenerate, and cells may atrophy (e.g. loss of inhibitory interneurons) or proliferate (e.g. microglia and astrocytes)[54]. For example, gray matter density was reduced in the bilateral dorsolateral prefrontal cortex and right thalamus of patients with chronic back pain, and this reduction was strongly correlated with pain characteristics[59]. These findings imply that chronic back pain is accompanied by brain atrophy and suggest that the pathophysiology of chronic pain includes thalamocortical processes[59]. A subsequent study has shown that chronic low back pain is associated with decreased cortical thickness in multiple brain areas and abnormal cognitive task-related activity; moreover, effective treatment resulted in increased cortical thickness in the left dorsolateral prefrontal cortex[60].

Recent advances in the neuroimaging, electrophysiological and genetic aspects of neuroplasticity have also demonstrated the key role that brain atrophy/reduced brain gray matter volumes play in a range of chronic pain conditions[61], including fibromyalgia[62], pelvic pain (CPP)[63] and common forms of chronic headaches[64]. Women with or without endometriosis-associated CPP displayed decreased gray matter volume in brain regions involved in pain perception[63]; in contrast, increased periaqueductal gray matter volume was observed in women with endometriosis who had no CPP, indicating a possible protective role of the descending inhibitory system in these indivivduals[63].

In the peripheral nervous system, maladaptive neuroplastic changes have been demonstrated in, for example, the expression of new receptors (e.g. embryonal Na_v 1.8) after nerve injury. Dysfunction of C-fibers is assumed to underlie negative symptoms in neuropathic pain and is accompanied by long-lasting downregulation of Na_v 1.8 sodium channel and μ-opioid receptors in the dorsal root ganglion[65]. Nerve injury has been shown to upregulate the expression of neuron-restrictive silencer factor in dorsal root ganglion neurons, mediated through epigenetic mechanisms, suggesting that this gene silencer causes pathological and pharmacological dysfunction of C-fibers, which underlies the negative symptoms in neuropathic pain[65].

In a mouse model of a painful arthritic joint, ectopic sprouting of sensory and sympathetic nerve fibers was shown to occur in the painful arthritic joint, indicating that they may be involved in the generation and maintenance of arthritic pain[66]. It has also been postulated that a distinct subgroup of individuals with osteoarthritis experience widespread pain with neuropathic features[67]. Sustained pain referral in these patients is considered to be mediated by central sensitization, resulting from nociceptors continuously firing (ectopically) in and around the affected joint[67], indicating the potential for widespread, disproportionate and neuroanatomically illogical pain in these patients.

Psychosocial aspects of pain chronification

In patients with subacute back pain, the persistence of chronic pain was shown to be predetermined by corticolimbic neuroanatomical factors[68,69]. Indeed, the chronification of back pain shifts brain representation from nociceptive to emotional learning circuits. Brain representation for a constant percept, back pain, can undergo large-scale shifts in brain activity with the transition to chronic pain. These observations challenge long-standing theoretical concepts regarding brain and mind relationships, in addition to providing important novel insights regarding definitions and mechanisms of chronic pain[70,71]. This shift from nociceptive to emotional circuits help to provide an underlying explanation for the psychosocial mechanisms involved in pain chronification.

There is also increasing recognition that many, if not most, common chronic pain conditions are heterogeneous with a high degree of overlap, or coprevalence, with other common pain conditions, along with influences from biopsychosocial factors[72]. The likely determinants that contribute to the risk of onset and maintenance of common chronic overlapping pain conditions (COPCs) are highlighted in Figure 2.

Consequently, it is important to acknowledge that, rather than being considered simply as secondary reactions to persistent pain, psychosocial factors play a key role and are intricately involved in a complex mixture of overall biopsychosocial processes that characterize chronic pain. In this regard, it is also important to consider lifespan – ideally, whilst taking into account developmental, biological, psychological and socioenvironmental aging changes, pain chronification taxonomy would apply to individuals of all ages rather than considering pediatric, adult and geriatric populations separately[73].

Factors which can influence pain chronification

Table 1 summarizes some of the key factors which may influence the pain chronification process. The timing (i.e. starting very early) of the various processes and factors which can contribute to pain chronification require rapid diagnostic identification and adequate pain management. Therefore, primary care physicians and other non-pain medicine specialists have a crucial role to play in avoiding diagnostic and therapeutic delays.

Predictive factors associated with pain chronification include patient demographics (e.g. level of education, female gender, older age, poor health status)[74–79], epigenetics (phenotypic trait variations which result from developmental or environmental cues rather than from alterations to the genomic DNA sequence itself)[80–82], acute pain characteristics (e.g. acute pain intensity/severity, duration, cumulative trauma exposure) and psychosocial factors (e.g. high baseline fear, anxiety, negative beliefs on chronic pain severity, depression, catastrophizing, pain vulnerability/resilience)[33,83,84].

With regard to acute pain characteristics, an analysis of data from 254 patients receiving total hip replacement and 239 patients receiving total knee replacement in a US cohort study suggested that, although preoperative widespread pressure pain sensitivity was associated with pain severity before and after joint replacement, it was not a predictor of the amount of pain relief that patients gain from joint

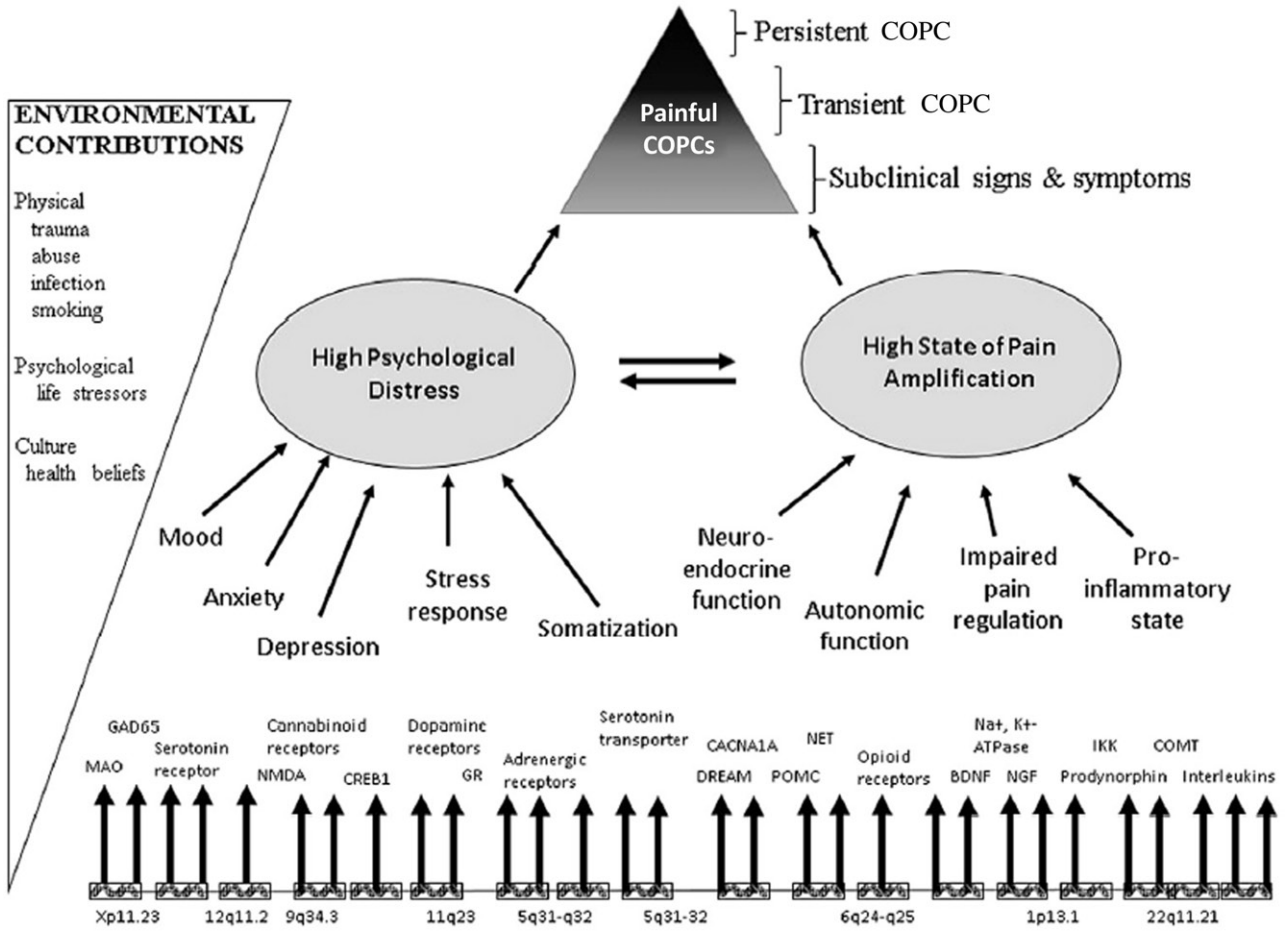

Figure 2. This model depicts likely determinants that contribute to the risk of onset and maintenance of common chronic overlapping pain conditions (CPPCs). These factors are determined by genetic variability and environmental events that determine an individual's psychological profile and pain amplification status. These two primary domains are interactive and influence the risk of pain onset and persistence. Likely modifiers of the interaction between genetic and environmental factors include sex and ethnicity[72]. Abbreviations. MAO, monoamine oxidase; GAD65, glutamate decarboxylase; NMDA, N-methyl-D-aspartic acid; CREB1, CAMP responsive element binding protein 1; GR, glucocorticoid receptor; CACNA1A, calcium voltage-gated channel subunit alpha1A; POMC, proopiomelanocortin; NET, norepinephrine transporter; BDNF, brain-derived neurotrophic factor; NGF, nerve growth factor; IKK, IkB kinase; COMT, catechol-O-methyl transferase.

Table 1. Main factors influencing the pain chronification process.

Positive factors	Negative factors
Social support (marriage/family)	Poor health status
High level of education	Type (e.g. neuropathic) and severity of pain
Coping strategies	Depression
Work satisfaction	Stress
Appropriate communication with HCPs	Litigation
Adequate self-recognition	Fear avoidance
	Perceived injustice
	Catastrophizing

Abbreviation. HCPs, health care professionals.

replacement surgery, independent of preoperative pain severity[85].

As noted previously, psychosocial factors play a crucial role in the diagnosis and trajectory of chronic pain. Psychosocial factors can include general variables such as negative affect, social support and childhood trauma, in addition to variables which are pain-specific, including pain-related catastrophizing and/or coping, and self-efficacy for managing pain[33]. A model based on literature relating to the progression of acute neck and back pain to chronic pain and disability showed that greater exposure to past traumatic life events and depressed mood were most predictive of chronic pain; depressed mood and negative pain beliefs were most predictive of chronic disability[83]. More cumulative traumatic life events, higher levels of depression in the early stages of a new pain episode, and early beliefs that pain may be permanent, all contribute significantly to increased severity of subsequent pain and disability[83]. Borsook and colleagues[86] recently proposed the Combined Reward deficiency and Anti-reward Model (CReAM) to describe how biopsychosocial variables which modulate brain reward, motivation and stress functions can interact in a "downward spiral" fashion to exacerbate the intensity, chronicity and comorbidities of chronic pain syndromes (i.e. pain chronification).

From the psychosocial perspective, the development of chronic pain is considered to represent a complex interplay of multiple factors which represents a balance between vulnerability and resilience to pain[87,88]. Research in this area is currently limited but it is anticipated that an improved understanding of the balance between pain vulnerability and resilience may help to identify at-risk individuals and may lead to the development of novel therapeutic options which target new pathways.

Pain chronification: options for its prevention/management

Any painful condition can lead to the chronification of pain. It is particularly common with trauma, low back pain and osteoarthritis. Consequently, treatment options need to be tailored according to the individual patient and their specific conditions. This section aims to briefly overview the general approach to the prevention and management of pain chronification.

Patient management should follow a logical process which can be outlined broadly as:

- initial patient assessment (history, examination)
- immediate (preventative) treatment (reassurance, non-pharmacological and/or pharmacological interventions)
- early treatment (days to weeks), which should aim to build on previous management options and should consider psychosocial factors/interventions)
- late treatment (weeks to months).

Monotherapy often leads to insufficient therapeutic response; hence, wherever possible, it is important to identify the distinct factors causing acute pain and treat them properly via a multimodal therapeutic approach[89,90]. If possible, all acute post-operative pain should be prevented or, at the very least, diagnosed accurately and then treated promptly and effectively to improve patient comfort, avoid complications and reduce the economic burden on society[91,92]. Based on a 2013 Cochrane review, the available evidence for pharmacological prevention of chronic pain is limited and additional evidence from well designed, large-scale trials is required in order to rigorously evaluate pharmacological interventions for the prevention of chronic pain after surgery in adults[93].

Acknowledging the multidimensional factors which can contribute to the development of chronic pain, Müller-Schwefe and colleagues recently highlighted the need to change the focus of treatment for chronic low back pain to individually tailored multimodal management (i.e. integrated multidisciplinary therapy with coordinated somatic and psychotherapeutic options) that reflects the underlying pain mechanisms[94]. A multimodal approach for chronic low back pain may potentially include the use of pharmacotherapy (including nonsteroidal anti-inflammatory drugs, cyclooxygenase-2 inhibitors, tricyclic antidepressants, opioids and anticonvulsants)[95], in combination with appropriate non-pharmacological options (including exercise programs, manual therapies, behavioral therapies, interventional pain management, physical therapies and traction), and recognizing that, in carefully selected individuals, surgery may be an appropriate option[94]. This comprehensive, multidisciplinary team-driven approach to the prevention or management of chronic pain, involving all stakeholders, has been endorsed elsewhere; however, despite acknowledgement that comprehensive multidisciplinary management based on the biopsychosocial model of pain has been shown to be clinically effective and cost-efficient, it is still not available widely[96].

Importantly, with ongoing pain, the role of the peripheral neuroanatomical structures becomes less important and more central mechanisms will take over gradually. Therefore, the focus for management strategies should be directed more towards the CNS[50]. Future directions in the management of pain chronification include the development of novel pharmacological interventions in the epigenetic processes which are involved in chronic pain, stem cell research and improved diagnoses in patients (e.g. via imaging methods of peripheral nociceptors)[97,98].

The role of non-pain medicine specialists in the multidisciplinary management of pain chronification

The majority of chronic pain is treated in the primary care setting[5–9]. Unfortunately, as is the case with the majority of clinicians, primary care physicians and non-pain medicine specialists are time-poor and confronted with a wide variety of complex acute and chronic pain conditions that rival the complexity of those seen in specialized tertiary care pain management facilities[99]. In general practice, management can encompass causal and symptomatic therapy in addition to the identification of patients who require specialist treatment. Therefore, general practitioners have a key role to play in the prevention of pain chronification and in the continuation of processes that have been initiated in pain management programs.

However, in order for primary care physicians and other non-pain medicine specialists to play a key role in the prevention of pain chronification, there needs to be awareness of the problem (i.e. that acute pain can become chronic), and simple, interdisciplinary education regarding pain management (including pain chronification)[89]. There is also an ethical imperative to orient students, the public, medical care providers and mental health professionals to the important role of psychological factors in the experience of pain[100]. In addition to improving pain education and awareness for primary care physicians, pain education is also needed at all levels of psychology training[100].

Moreover, few primary care physicians and non-pain medicine specialists are formally trained in effectively managing pain[3,89], and there is considerable scope for improvements in healthcare literacy relating to the pain chronification process. Surveys have demonstrated that many physicians do not feel comfortable managing patients with chronic pain[6,101–103]. A large UK survey demonstrated a diversity of attitudes and self-reported practice behaviors among primary care practitioners (GPs and physiotherapists) with regard to patients with nonspecific lower back pain[104]. Education is a key comfort factor among primary care physicians and non-pain medicine specialists, and education/pain management training has been shown to increase primary care physicians' comfort in managing patients with chronic pain[101].

Although there is a need to assess and address the continuum of pain, there is currently a lack of awareness and clarity for primary care physicians to assist them in clearly understanding the warning signs and non-resolving

functions, and when to address the situation (e.g. after 2 weeks of unsuccessful therapy, or over a shorter or longer time period?). The use of properly administered early interventions, including cognitive–behavioral therapy, potentially decreases sick leave and prevents chronic problems in patients with acute pain[105,106]. Moreover, since psychological factors are central in the development of chronic problems, the early administration of a cognitive–behavioral intervention which focuses on the psychological aspects of pain appears to be feasible for identifying high-risk patients[107]. Another recent example of a predictive approach has been proposed for the management of persistent pain after breast cancer surgery, using validated prediction models and an online risk calculator to provide clinicians with a simple tool to identify patients at high risk of developing persistent pain and preventive interventions[108]. However, despite this promising research and that of others, including the development of a validated tool to predict the risk of chronic disease in patients with acute low back pain in an orthopedic practice setting[109,110], there are currently no simple, easy-to-use, evidence-based assessment tools/questionnaires for primary care physicians, specifically relating to the transition from acute to chronic pain. It is anticipated that the availability of such a tool would allow non-pain medicine specialists to readily identify patients at risk of pain chronification, to better understand when to refer to a pain specialist, what to do in the case of persistent pain, distress, disability and comorbidities, and to help identify risk factors/predictors which can influence the pain chronification process. This represents an unmet need in the management of pain chronification in the primary care setting.

A simple, easy-to-use screening tool for neuropathic pain and localized neuropathic pain, designed for use in general practice, has previously been shown to have realistic diagnostic accuracy[111]. The screening tool, based on IASP criteria, focuses on medical history and the distribution of painful symptoms and sensory signs[111]. Using currently available information, is it feasible that a simple, easy-to-use screening tool could also be developed for use by primary care physicians and non-pain medicine specialists in patients at risk for pain chronification?

Conclusions

Although there are many good reviews of acute and chronic pain in the medical literature, there is scope to provide primary care physicians/non-pain medicine specialists with greater understanding and awareness of pain chronification, and to address the unmet need for a formal definition of "pain chronification". This article attempts to address some of those issues. Indeed, the current lack of a universal understanding and formal definition of "pain chronification" resulted in the Change Pain Chronic Advisory Board proposing the following definition:

- Pain chronification describes the process of transient pain progressing into persistent pain.
- Pain processing changes as a result of an imbalance between pain amplification and pain inhibition.
- Genetic, environmental and biopsychosocial factors determine the risk, degree and time-course of chronification.

It is our hope that, through the proposed definition, primary care physicians and non-pain medicine specialists will gain a broader understanding and appreciation of pain chronification. Early intervention plays an important role in preventing pain chronification (the transition from acute to chronic pain) and, as key influencers in the management of patients with acute pain, it is critical that primary care physicians are equipped with the necessary awareness, education and skills to manage pain patients appropriately. There is a need for improved education and knowledge-sharing among health care practitioners involved in the management of pain patients, particularly primary care physicians, including increased awareness of how and where non-pain medicine specialists can find appropriate education opportunities. The future development of a simple, easy-to-use screening tool would also benefit primary care physicians in the early diagnosis of patients at risk of pain chronification.

Transparency

Declaration of funding

This manuscript was funded by Grünenthal GmbH, Aachen, Germany.

Declaration of financial/other relationships

B.M. has disclosed that he has received speaker and/or consultancy fees from Astellas, Grünenthal, Boehringer-Ingelheim, Mundipharma, Pfizer, Zambon and TEVA. F.C. has disclosed that she has received speaker and/or consultancy fees from Grünenthal. D.A. has disclosed that he has received lecture fees from Grünenthal. M.K.-K. has disclosed that she has acted as a consultant/advisor for Mundipharma and STADA Arzneimittel AG. J.P. has disclosed that he has acted as a lecturer, consultant and/or received research fees from Depomed, Grünenthal, BDSI, DSI, Purdue Pharma, Mundipharma and Astra Zeneca. A.C.M. has disclosed that she has acted as a consultant/advisor for Grünenthal. K.A. has disclosed that he has acted as a consultant/advisor for Grünenthal. E.K. has disclosed that she has no significant relationships with or financial interests in any commercial companies related to this study or article.

CMRO peer reviewers on this manuscript have no relevant financial or other relationships to disclose.

Acknowledgements

Medical writing support was provided by David P. Figgitt PhD, Content Ed Net, with funding from Grünenthal GmbH, Aachen, Germany. This article is based on an international Change Pain Chronic Advisory Board meeting held in Wiesbaden, Germany, October 2016, which was supported by an unrestricted educational grant from Grünenthal GmbH, Aachen, Germany.

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