



Neurocognitive impairments in chronic pain: Transdiagnostic approach and clinical implications

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ABSTRACT

Chronic pain (CP) affects over 30% of the global population, as leading cause of disability significantly impairs quality of life and daily functioning. Evidence suggest that 20% of people with CP experience neurocognitive impairment. Various CP conditions, including nociplastic, neuropathic, nociceptive (i.e., musculoskeletal, post-surgical pain, among others), demonstrate distinct yet overlapping neurocognitive impairment, underscoring the need for transdiagnostic approaches. Although the problem remains underestimated, the impact of this burden is likely to increase further with the aging population and increasing prevalence of CP. To better understand how a transdiagnostic approach may be helpful in the comprehension of the co-occurrence of neurocognitive impairments and CP, this systematic-narrative hybrid literature review aims to synthesize the state of the art regarding neurocognitive impairments associated with CP, emphasizing clinical implications. A systematic literature search was conducted in PubMed, SCOPUS and EMBASE using keywords related to CP and neurocognitive impairments including peer reviewed articles published from inception to May 2025. Emerging evidence highlights the bidirectional relationship between CP and neurocognitive impairments, particularly in domains such as attention, memory, language, executive function, and perceptual-motor function across diverse populations with CP. A transdiagnostic perspective is needed to bridge the gap between clinical implications and future research. This study highlights the clinical significance of incorporating neurocognitive evaluations and treatments into CP management, advocating a shift towards more personalized and multimodal healthcare approaches. Considering the limitations of this review, further high-quality research is needed to better understand the underlying mechanisms and associated clinical implications.

1. Introduction

Chronic pain (CP) is a complex experience influenced by a myriad of multidimensional factors from a biopsychosocial perspective (Sunzini et al., 2023). According to the latest version of the International Classification of Diseases (ICD-11) (Treede et al., 2019), CP is now

considered a distinct condition that exerts an enormous individual and social burden, affecting more than 30% of the population worldwide (Cohen et al., 2021). Currently, CP is mainly considered by the temporal criterion of pain, which involves any pain lasting longer than 3 months (Nicholas et al., 2019a). As a leading cause of disability, CP interferes with an individual's occupational, social, interpersonal functioning, and

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quality of life (Cohen et al., 2021).

Overall prevalence of neurocognitive impairment is higher in patients with CP than in the general population (Rodríguez-Andreu et al., 2009), and approximately 20% of individuals with CP suffer from neurocognitive impairments (Nahin and DeKosky, 2020). Among the multiple dimensions affected by CP, neurocognitive impairments affect several domains including attention, memory, and executive function, that are present in various CP conditions (Schmidt et al., 2023).

In this line and according to the consensus of the Neurocognitive Working Group of Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM-5), six main domains with subdomains of neurocognitive function can be identified related to CP: (1) Executive functions: function planning, decision-making, working memory, responding to feedback, inhibition, and flexibility; (2) Language: object naming, word finding, fluency, grammar and syntax, and receptive language; (3) Memory and learning: free recall, cued recall, recognition memory, semantic and autobiographical long-term memory, implicit learning, and language; (4) Social cognition: recognition of emotions, theory of mind and insight; (5) Attention: sustained attention, divided attention, selective attention, and processing speed; (6) Perceptual-motor function: visual perception, visuo-constructional reasoning, and perceptual-motor coordination (Sachdev et al., 2014). While the term ‘cognitive’ is widely used to refer to thought and multiple related processes, the term ‘neurocognitive’ has been applied to underscore the disruption of the neural substrates underlying symptoms (Sachdev et al., 2014). Even though there is no consensus on the definition and use of

this term in literature, neurocognitive impairments refer to a decline in previously attained in neurocognitive functioning during behavioral execution (Maldonado and Sher, 2024; Moriarty and Finn, 2014). (Fig. 1)

The interconnectedness of pain and neurocognition suggests that CP may impair neurocognitive functioning, potentially exacerbating the experience of pain (Crowley et al., 2022; Khera and Rangasamy, 2021). A systematic review by Higgins et al. (2018) (Higgins et al., 2018) suggests association across multiple neurocognitive domains with significant implications for clinical management and patient outcomes. In a case-control study, neurocognitive functioning was reported to be significantly worse in individuals with chronic low back pain (CLBP) than in matched controls (Corti et al., 2021). Bell et al. (2022) found that persistent pain was associated with a 21% increase in the likelihood of neurocognitive impairment in community-dwelling older adults (Bell et al., 2022). It has also been highlighted that patients with CLBP with higher pain intensity have greater neurocognitive impairment than those with lower pain intensity (Pereira Nery et al., 2023). Nevertheless, these findings should be interpreted with caution, given the low quality of the studies, the observational nature of many of the studies done and the heterogeneity in the outcome measures used (Berryman et al., 2014).

While the understanding of pain has historically followed a Cartesian model (De Ridder et al., 2022), Loeser and Waddell acknowledged the biopsychosocial nature of pain (Nicholas, 2022). In this vein, given that each person experiences pain uniquely, multidimensional factors interact to creating individual clinical picture. Nowadays, pain is widely

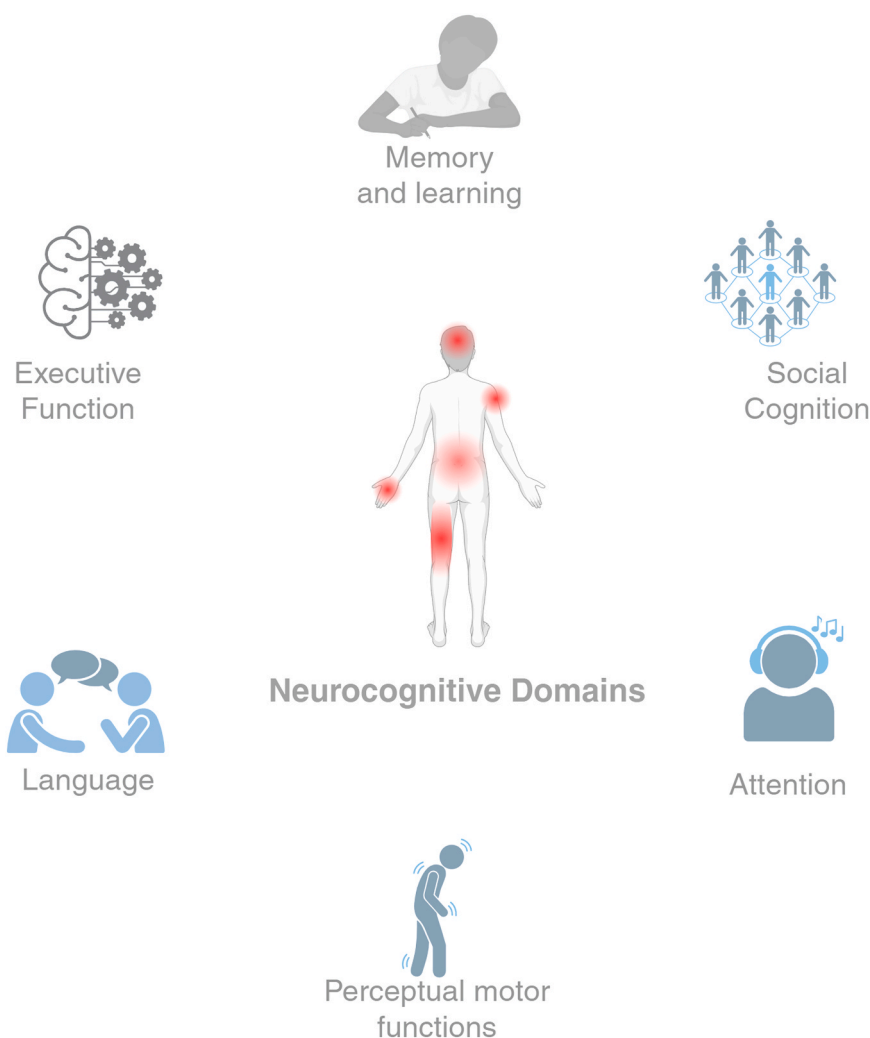


Fig. 1. Neurocognitive domains. The DSM-5 recognizes six key domains of cognitive function, each with its own subdomains. Figure was created using Biorender.

recognized as the result of an integration of sensory, cognitive, and affective components (Raja et al., 2020), leading to a complex dynamic phenomenon (Vlaeyen et al., 2022). Even though CP is not a purely sensory phenomenon, the individual experience of pain requires cognitive evaluation, learning mechanisms, and recall of past experiences and decision-making (Khera and Rangasamy, 2021), as neurocognitive impairments interfere with activities of daily living (ADL) of people suffering from CP (Berginström et al., 2024). These neurocognitive impairments related to CP not only have consequences for quality of life and ADLs (Higgins et al., 2018), but may also affect self-regulation of pain and emotional state (Baker et al., 2018). Within the grades of chronic pain, high-impact chronic pain is defined by the degree of difficulty in functioning and disability in self-care, work participation, and social activities (Eccleston et al., 2023). Because the diagnosis of chronic pain is based solely on a temporal criterion, there has been a growing emphasis on identifying functional impact in chronic pain (Nugraha et al., 2019). Individuals with high-impact chronic pain are three times more likely to experience fatigue (OR = 3.46, 95% CI = 2.76–4.33), as well as memory and concentration problems (OR = 3.18, 95% CI = 2.51–4.02), compared to those with low-impact chronic pain (Pitcher et al., 2019). Consequently, neurocognitive impairments are likely to be a feature that distinguishes between high and low impact on CP. Moreover, common comorbid mental health problems in CP, such as depression, anxiety, sleep disturbance, and analgesic opioid use, may further impact neurocognitive domains (Higgins et al., 2018). Indeed, the likelihood of experiencing functional limitations in ADLs appears to be higher among those experiencing co-occurring symptoms than among those experiencing only CP (De La Rosa et al., 2024).

Although it seems to be underestimated, the magnitude of this problem is likely to increase further with an aging population and the growing incidence of lifestyle-related disorders. For example, according to the last estimations, in 2030, people aged 65 and over are expected to rise to 20% of the total population (Zimmer and Zajacova, 2020). This data adding to growing trend of chronic pain in older adults, has been highlighted as alarming, potentially reaching epidemic proportions in the coming decades (Katzman and Gallagher, 2024), with significant consequences for the healthcare system and social policies (Jones et al., 2016).

Because chronic pain has been poorly represented in the ICD and DSM, the IASP working group and WHO collaboration endorsed a new classification of chronic pain in 2022, leading to substantial advances in policies, organizational, legal, and clinical management (Barke et al., 2022). Following chronic pain is recognized as a health condition itself, it has led to an update and harmonization of the ICD-11 and DSM-V classifications for CP conditions (Treede et al., 2019; First et al., 2021). This harmonization has also included neurocognitive disorders; whereby major impairments depend on the severity of cognitive decline in only one cognitive domain rather than on a broader range of deficits (First et al., 2021). Nevertheless, those classifications identify distinct patients depending on the diagnostic system used and fail to recognize the overlapping mosaic of clinical symptoms across different conditions under the umbrella term of chronic pain.

While a growing body of evidence suggests that various CP conditions may be considered an impairment of cognition itself (Phelps et al., 2021), an emerging transdiagnostic approach has restarted the debate on the understanding and management of CP (McEvoy et al., 2009). Since traditional diagnostic systems may no longer provide a useful framework for classifying CP disorders and driving novel clinical advances (Ornelas and Moreira, 2024), a transdiagnostic approach has been proposed to understand common factors or symptoms that are shared across diagnoses, as well as the mechanisms underlying the persistence of symptoms in different diseases (Eilenberg and Otis, 2023a).

There is increasing acknowledgement that many, if not most, common chronic conditions are heterogeneous and often exhibit significant

overlap with other prevalent conditions and, are influenced by biopsychosocial factors (Maixner et al., 2016). Previous studies have shown that pain intensity, avoidance, suicidal ideation, itching, fatigue, and sleep disorders share mechanisms that maintain chronicity and commonly occur in various medical conditions (Kirtley et al., 2020; Nadinda et al., 2024; Kim and Day, 2024; Menting et al., 2018; Palagini et al., 2016). The identifiable commonalities between CP and neurocognitive impairment within a transdiagnostic approach provide an opportunity for groundbreaking advances in diagnosis, prevention, and treatment on these conditions. While the multidimensional and transdiagnostic nature of pain calls for multimodal and highly tailored care in CP (Cohen et al., 2021), a systematic review found a lack of evidence on which interventions targeting CP are most appropriate for addressing neurocognitive function in this population (Brennecke et al., 2025). Therefore, a thorough understanding of the current burden of CP is necessary to appropriately implement optimal management strategies in clinical practice.

Addressing neurocognitive impairments in chronic pain is a clinical need; therefore, further research is required to provide evidence-based recommendations for pain management. Considering the under-recognition of neurocognitive impairments as a significant driver of high-impact pain and pain-related disability, along with the lack of standardized neurocognitive assessments in people with chronic pain.

Previous reviews have focused either on a single neurocognitive domain (Berryman et al., 2013; Mazza et al., 2018), methodological analysis of the topic (Schmidt et al., 2023), or have not included a comprehensive review of the neurocognitive impact across different chronic pain conditions (Higgins et al., 2018; Zhang et al., 2021) thereby hindering the translation of these findings into clinical practice. This review expands on previous reviews, incorporating a transdiagnostic lens that captures the multi-domain impact condition-by-condition of chronic pain. To better understand how a transdiagnostic approach may clarify the co-occurrence of neurocognitive impairments and CP, this study aims to synthesize current evidence on neurocognitive impairments associated with CP, identify shared domains across conditions, and explore their clinical relevance within a transdiagnostic perspective.

2. Materials and methods

We provide a broad overview and narrative summary to highlight the clinical conditions and neurocognitive domains affected by CP. This study follows a systematic-narrative hybrid literature review methodology to ensure the quality of the review. This study was organized into six elements of the systematic-narrative hybrid literature review methodology proposed by Turnbull et al. (2023) (Turnbull et al., 2023) are as follows: (1) research questions, (2) justification, (3) literature sources, (4) search parameters, (5) data cleaning, and (6) information synthesis.

2.1. Research question

The following questions were formulated to guide this review:

1. What evidence is available on the impact of neurocognitive impairments in CP?
2. Which clinical conditions of CP are affected by neurocognitive impairments?

2.2. Literature sources

We conducted an electronic search for studies published up to May 2025 in the PubMed, EMBASE, and Scopus electronic databases.

Search parameters

Search strategies were designed around the main concepts of cognition and chronic pain and combined using Boolean operators. The strategy was adapted for each database (including controlled vocabulary

and free-text terms, where applicable). Full search details by database are presented in [Supplementary Materials \(Table S1\)](#). Documents published from inception to May 31st 2025 were considered.

2.3. Data cleaning

Inclusion criteria were: (a) journal articles, (b) in English, (c) published up to May 31st, 2025, (d) in human participants with CP, and (e) related to neurocognitive function or neurocognitive impairments in CP. Exclusion criteria were: (a) participants with acute pain, (b) gray literature (e.g., theses, reports) and conference abstracts, and (c) animal or preclinical studies. After identifying studies that fulfilled the inclusion criteria, titles, abstracts, and citation information obtained through the database search were exported to Mendeley, where duplicates were removed. First, potential articles were screened by title and abstract, and then the full texts of potentially eligible studies were obtained and evaluated for final synthesis by a single author (J.G.), and a second reviewer (A.R.) verified the selection to ensure accuracy. Any disagreements were resolved through discussion, and when necessary, consultation with a third author (J.A.M.M.). Finally, studies that aimed to identify potential clinical conditions of CP affected by neurocognitive impairments were included in the final narrative synthesis.

Information synthesis

Consistent with review recommendations, the main findings were descriptive summarized and presented narratively and visually displayed with figures. All authors discussed and agreed on the final report of the results of the study.

3. Summary of findings

The systematic search initially identified 13,766 studies. Of these, 228 full-text studies were screened, and 38 studies were included in the final summary. Search results are displayed in the PRISMA Flow Diagram ([Fig. 2](#)). Next, a narrative synthesis of the main findings will be provided.

Impaired neurocognitive functioning appears to be common in patients with CP, being associated with how much pain interferes with daily life and represents a major obstacle to pain management. This convergence is reflected in the frequent co-occurrence of neurocognitive impairments, psychosocial factors, and emotional dysregulation in individuals with CP ([De La Rosa et al., 2024](#); [Legrain et al., 2009](#)). Although patients with CP showed impairments across multiple neurocognitive functions, deficits seem to be more pronounced in certain domains than in others ([Higgins et al., 2018](#)). Most of the neurocognitive domains investigated in the CP population relate to attention, learning and memory, perceptual-motor function and executive function ([Moriarty et al., 2011](#)).

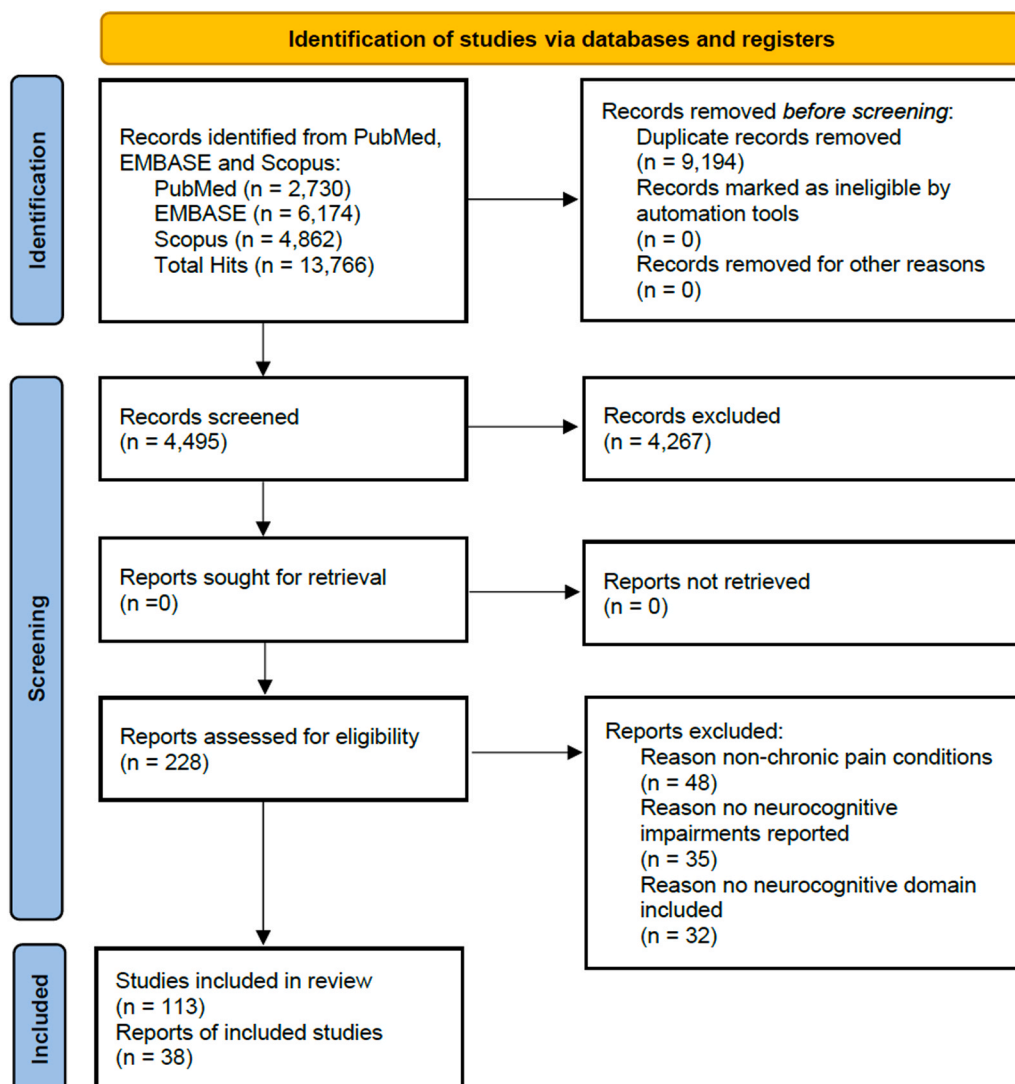


Fig. 2. Flow diagram of the study selection process.

3.1. Neurocognitive domains affected in Chronic Pain

Neurocognitive impairments are frequently reported by individuals with chronic pain and may influence daily functioning, treatment engagement, and long-term outcomes (Zhang et al., 2021). Importantly, these concerns span a continuum ranging from subjective cognitive complaints and reduced mental health to potential risks of clinically defined neurocognitive impairment, underscoring the need to distinguish between functional cognitive deficits and formal neurocognitive disorders in this population.

Quantitative synthesis of the evidence indicates that chronic pain is associated with poorer performance on several measures of global neurocognitive functioning and mental health (Zhang et al., 2021). Large and statistically significant impairments were observed for the SF-36 Mental Component, the Montreal Cognitive Assessment (MOCA), performance validity testing, and working memory capacity assessed with operation span tasks. In contrast, no significant associations were found between chronic pain and clinically defined cognitive decline based on ICD diagnoses. Together, these findings suggest that chronic pain is more consistently associated with deficits in neurocognitive functioning and screening-based cognitive performance than with established neurodegenerative diagnoses.

3.1.1. Attentional deficits

Attentional deficits may represent a fundamental disruption in cognitive processing, including selective and sustained attention processes, and have been suggested to be involved in the development, maintenance, and management of pain (Todd et al., 2015). The attentional burden of CP appears to create a cognitive bias, in which focusing on and maintaining concentration on non-pain tasks becomes increasingly challenging (Crombez et al., 2013).

Across meta-analysis, evidence for attentional biases toward somatosensory stimuli in chronic pain was generally small and heterogeneous (Broadbent et al., 2021a) (see Table 1). The overall between-group meta-analysis did not show a statistically significant attentional bias toward somatosensory stimuli in chronic pain compared with healthy controls; however, sensitivity analyses excluding influential studies revealed a small-to-moderate but significant effect. Subgroup analyses suggested that attentional biases were more consistently observed for non-painful somatosensory stimuli, showing a small and homogeneous effect, whereas findings for painful stimuli were inconsistent and highly heterogeneous. Evidence for somatosensory attentional bias in fibromyalgia and across different task paradigms was similarly mixed and characterized by substantial heterogeneity. In contrast, spatial attentional bias to somatosensory stimuli showed large effect sizes but was based on few studies, with significance emerging only after sensitivity analyses, highlighting the limited and unstable evidence base for spatial attentional deficits in chronic pain.

3.1.2. Working memory

Likewise, it has been highlighted that working memory represents another domain consistently affected in CP populations (Berryman et al., 2013), with many patients with CP report poor memory, recall, and concentration in their ADL (Berryman et al., 2013). According to a review by Mazza et al. (2018) (Mazza et al., 2018), the results showed a moderate decline in both working memory and long-term memory performance in patients with CP. Both memory deficits may reflect encoding difficulties during the initial learning and retrieval problems when attempting to access previously learned information (Mazza et al., 2018). Since conditioned learning has been suggested to play a key role in predicting potential threats that trigger pain-related memory (Zhang et al., 2021; Harvie et al., 2017) and working memory activity (Lenaert et al., 2016; Smith and Ayres, 2014), an increased vulnerability to the development of CP in some populations may be due to reduced extinction and increased resilience of pain memory has been suggested (Timmers et al., 2019).

Studies have shown that individuals with CP exhibit specific deficits in updating their working memory, which limits their capacity to screen incoming information and replace outdated or irrelevant information with newer and more relevant data (Dick and Rashiq, 2007). This updating function represents a crucial executive process for complex cognitive tasks, as it is necessary for guiding behavior, decision-making, language acquisition, reasoning, and planning (Postle, 2006). Given that executive functions, which encompass higher-order cognitive processes, such as inhibition, planning, and cognitive flexibility, are consistently impaired in CP conditions (Zhang et al., 2021), people with chronic pain face challenges in problem-solving, abstract reasoning, and resistance to interference (Higgins et al., 2018). Indeed, such impairments lead to increased response latency for cognitively demanding tasks, including sequential thinking goal-oriented behavior¹⁷, spatial learning and recognition (Hu et al., 2010). Functional overlap in brain pathways responsible for executive functioning and pain experience has been identified as an important factor in neurocognitive impairments in CP (McCarberg and Peppin, 2019).

Meta-analytic evidence indicates that memory impairments in chronic pain vary as a function of pain subtype and cognitive domain (Kelly et al., 2025) (see Table 1). Large and statistically significant deficits in short-term memory were observed in individuals with nociceptive and nociplastic pain compared with healthy controls, whereas short-term memory performance in neuropathic pain did not differ significantly from controls despite moderate effect sizes. Similarly, working memory deficits were evident in nociplastic pain but not in neuropathic pain. In contrast, individuals with nociceptive pain exhibited moderate and robust impairments in verbal long-term memory. Across domains, heterogeneity was consistently high, highlighting substantial variability across studies and suggesting that cognitive deficits in chronic pain are not uniform but depend on both pain mechanism and memory system assessed.

3.1.3. Social cognition

People suffering from CP also struggle with social relationship (Philpot et al., 2020), including loneliness (Petitte et al., 2015), perceived injustice (Penn et al., 2020) and stigma (Hickling et al., 2024). Despite wide endorsement of a biopsychosocial framework for pain, social aspects of pain remain rarely addressed (Kapos et al., 2024). While conflicting evidence has been found in people with CP in the social cognition domain, especially in the absence of psychiatric comorbidities (Telesca et al., 2024; Luque-Reca et al., 2021; Ayhan et al., 2023; Gunnarsson and Agerström, 2020), scarce evidence exists addressing specific social cognition impairments in chronic pain.

From a clinical perspective, stigma represents a salient psychosocial factor in chronic pain that may shape patients' experiences, healthcare interactions, and symptom trajectories (Hickling et al., 2024). Perceived stigmatization by healthcare professionals and others can influence help-seeking behavior, exacerbate emotional distress, and contribute to greater pain burden, particularly in individuals with comorbid psychological symptoms. Stigma may also interact with pain severity, reinforcing maladaptive coping strategies and amplifying pain-related disability. Quantitative evidence indicates a complex relationship between stigma and pain outcomes. Cross-sectional studies provide mixed findings regarding differences in overall stigma between individuals with and without chronic pain; however, individuals with pain are more likely to perceive stigmatization from doctors and others, and weight-related self-stigma is associated with increased odds of chronic pain. Both prospective and cross-sectional data demonstrate a positive association between stigma and pain intensity, with a small but significant pooled correlation and stronger associations observed among individuals reporting moderate to high levels of stigma. Comparisons across pain conditions suggest generally small differences in stigma, although higher stigma is consistently observed in individuals with multiple co-occurring pain conditions. Together, these findings highlight stigma as a clinically relevant factor associated with pain severity

Table 1

Summary of meta-analysis evidence of neurocognitive impairments associated with chronic pain.

Author, year	Type of chronic pain	Type of studies	Results from Meta-Analysis
Attention (Broadbent et al., 2021a)	Migraine, fibromyalgia, low back, CRPS, Abdominal pain, tension headache, Somatoform pain, orofacial pain	Observational (n = 18): case-control, single group	1-Attentional bias (AB) to the somatosensory modality Chronic pain vs healthy controls: Small-to-moderate attentional bias toward somatosensory stimuli, but not statistically significant overall ($g = 0.27$; 95% CI -0.04–0.58), with substantial heterogeneity ($I^2 = 66.7\%$). Sensitivity analysis: Significant small-to-moderate attentional bias toward somatosensory stimuli in chronic pain patients compared to controls ($g = 0.34$; 95% CI 0.05–0.64), with moderate heterogeneity ($I^2 = 62.1\%$). 2-Subgroup analyses by stimulus type Painful somatosensory stimuli: No significant attentional bias toward painful somatosensory stimuli ($g = 0.28$; 95% CI -0.28–0.84), with high heterogeneity ($I^2 = 78.1\%$). Painful stimuli: Moderate effect size but non-significant, suggesting a possible attentional bias toward painful stimuli ($g = 0.45$; 95% CI -0.10–1.00), with high heterogeneity ($I^2 = 74.2\%$). Non-painful somatosensory stimuli: Significant small attentional bias toward non-painful somatosensory stimuli in chronic pain patients ($g = 0.26$; 95% CI 0.03–0.48), with no heterogeneity ($I^2 = 0\%$). 3-Subgroup analyses by pain condition Fibromyalgia: Small-to-moderate attentional bias toward somatosensory stimuli, but not statistically significant ($g = 0.32$; 95% CI -0.06–0.71), with substantial heterogeneity ($I^2 = 72.2\%$). 4-Subgroup analyses by task paradigm Common task paradigm: No evidence of attentional bias toward somatosensory stimuli ($g = 0.17$; 95% CI -0.39–0.72), with moderate heterogeneity ($I^2 = 60.8\%$). Common task paradigm: Non-significant moderate effect, suggesting a possible attentional bias ($g = 0.36$; 95% CI -0.10–0.83), with low-to-moderate heterogeneity ($I^2 = 34.9\%$). Primary task paradigm: No significant attentional bias detected, despite a moderate effect size ($g = 0.34$; 95% CI -0.48–1.17), with very high heterogeneity ($I^2 = 86.3\%$). 5-Spatial attentional bias to somatosensory stimuli Chronic pain vs healthy controls: No significant spatial attentional bias, with a large but imprecise effect size ($g = 0.60$; 95% CI -0.63–1.83) and very high heterogeneity ($I^2 = 85.1\%$). Sensitivity analysis: Large and statistically significant spatial attentional bias to somatosensory stimuli in chronic pain patients ($g = 1.20$; 95% CI 0.55–1.86), with no heterogeneity ($I^2 = 0\%$).
Memory (Kelly et al., 2025)	Fibromyalgia, Traumatic brain injury, Diabetic peripheral neuropathy with pain, Peripheral neuropathic pain, Chronic pancreatitis, Chronic lower back pain, Chronic neuropathic pain, Postherpetic pain, Multiple sclerosis,	Observational (n = 15): case-control,	1- Short-term memory Nociceptive pain vs healthy controls: Significant large deficit in short-term memory in individuals with nociceptive pain compared with healthy controls ($g = -0.95$; 95% CI -2.26 to -0.06; $p = 0.04$), with very high heterogeneity and evidence of publication bias, although findings were robust to Fail-Safe N analysis. Neuropathic pain vs healthy controls: No significant short-term memory deficits in individuals with neuropathic pain compared with controls, despite a moderate negative effect size ($g = -0.41$; 95% CI -0.83 to -0.00; $p = 0.06$) and high heterogeneity. Nociplastic pain vs healthy controls: Significant large short-term memory deficits in individuals with nociplastic pain compared with healthy controls ($g = -0.80$; 95% CI -1.40 to -0.20; $p = 0.01$), with very high heterogeneity and strong robustness according to Fail-Safe N. 2- Working memory Neuropathic pain vs healthy controls: No significant working memory deficits were observed in individuals with neuropathic pain compared with healthy controls ($g = -0.15$; 95% CI -0.40–0.10; $p = 0.23$), despite high heterogeneity across studies. Nociplastic pain vs healthy controls: Significant moderate working memory deficits in individuals with nociplastic pain compared with healthy controls ($g = -0.46$; 95% CI -0.88 to

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Table 1 (continued)

Author, year	Type of chronic pain	Type of studies	Results from Meta-Analysis
			–0.05; $p = 0.03$), with very high heterogeneity and robust findings based on Fail-Safe N. 3-Long-term memory Nociceptive pain vs healthy controls: Significant moderate deficits in verbal long-term memory in individuals with nociceptive pain compared with healthy controls ($g = -0.48$; 95% CI -0.69 to -0.27; $p < 0.001$), with high heterogeneity but no evidence of publication bias.
Social cognition (Hickling et al., 2024)	Lower back pain, fibromyalgia, rheumatoid arthritis, chronic temporomandibular pain, chronic pelvic pain,	Observational (n = 19)	Stigma Mixed evidence regarding differences in stigma between individuals with and without chronic pain. No significant differences in total stigma were observed between individuals with chronic pain and those without pain or depression; however, higher stigma was reported in individuals with comorbid chronic pain and depression. Individuals with pain were more likely to perceive stigmatization from doctors (RR = 1.44; 95% CI 1.36–1.52) and from others (RR = 1.58; 95% CI 1.46–1.70) compared with those without pain. Weight-related self-stigma was associated with increased odds of having chronic pain unrelated to arthritis (OR = 1.50; 95% CI 1.20–1.87). Stigma and pain intensity Prospective evidence indicated a moderate positive association between baseline stigma and subsequent pain intensity ($r = 0.41$; $p < 0.001$). Cross-sectional meta-analysis demonstrated a small but significant positive association between stigma and pain intensity (Fisher's Z = 0.24; 95% CI 0.14–0.34; $p < 0.001$), with high heterogeneity ($I^2 = 61.2\%$). Higher pain intensity was associated with moderate and high stigma classes compared with low stigma (OR range = 1.54–1.80). Stigma across different chronic pain conditions Small differences in stigma levels across pain conditions were observed. Daily stigma levels did not differ significantly between fibromyalgia and rheumatoid arthritis, but were higher in individuals with comorbid fibromyalgia and rheumatoid arthritis compared with rheumatoid arthritis alone ($g = 0.39$). Cross-sectional comparisons showed no significant differences in stigma between fibromyalgia and rheumatoid arthritis. Women with multiple co-occurring pain conditions were more likely to report perceived stigmatization by doctors (RR = 1.69; 95% CI 1.46–1.97) and by others (RR = 2.35; 95% CI 1.83–3.02) compared with women with nonsyndromic pain only.
Perceptual-motor function (Martinez-Calderon et al., 2019)	Chronic musculoskeletal pain	Observational (n = 70)	1-Fear of pain: Moderate positive association between fear of pain and pain intensity in mixed chronic musculoskeletal samples (standardized $b = 0.34$; $P < .0005$). 2-Pain-related anxiety: Weak but significant association between pain-related anxiety and pain intensity across chronic pain conditions (pooled standardized $b = 0.29$; 95% CI 0.23–0.36; $P < .01$), with low heterogeneity ($I^2 = 35.9\%$). Associations were observed in rheumatoid arthritis, chronic widespread pain, and mixed chronic musculoskeletal, while findings were inconsistent in chronic low back pain. No moderating effects of sex or risk of bias were identified; publication bias was suspected. 3-Fear-avoidance beliefs – Work subscale: Weak but significant association between fear-avoidance beliefs related to work and pain intensity (pooled standardized $b = 0.23$; 95% CI 0.15–0.30; $P < .01$), with high heterogeneity ($I^2 = 87.4\%$). Sensitivity analyses showed reduced heterogeneity in chronic neck pain and mixed chronic chronic musculoskeletal samples, while heterogeneity remained high in chronic low back pain. Sex and risk of bias did not moderate the association; publication bias was suspected. 4-Fear-avoidance beliefs – Physical activity subscale (motor function-relevant): Weak but significant association between fear-avoidance beliefs related to physical activity and pain intensity (pooled standardized $b = 0.22$; 95% CI 0.16–0.28; $P < .01$), with high heterogeneity ($I^2 = 69.9\%$). Stronger and

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Table 1 (continued)

Author, year	Type of chronic pain	Type of studies	Results from Meta-Analysis
			more consistent associations were observed in chronic neck pain and osteoarthritis, with reduced heterogeneity. Associations remained significant but heterogeneous in chronic low back pain and mixed chronic musculoskeletal samples. Neither sex nor risk of bias moderated the association; publication bias was suspected. 5-Fear-avoidance beliefs – Longitudinal evidence: Inconsistent longitudinal evidence regarding the predictive value of baseline fear-avoidance beliefs for future pain intensity in chronic low back pain, with one study showing significant prediction and another reporting null findings.
Cognitive function (Pereira Nery et al., 2023)	Low back	Observational (n = 11)	Low Back Pain (LBP) vs asymptomatic controls 1-Problem-solving: Small-to-moderate impairment in problem-solving abilities in individuals with LBP compared with asymptomatic controls (k = 5; d = 0.33; 95% CI 0.16–0.50; p < 0.001), based on very low-quality evidence. 2- Speed of information processing: Small-to-moderate reduction in processing speed in individuals with LBP compared with asymptomatic controls (k = 5; d = 0.44; 95% CI 0.22–0.65; p < 0.001), supported by very low-quality evidence. 3- Working memory: Moderate impairment in working memory performance in individuals with LBP compared with asymptomatic controls (k = 6; d = 0.50; 95% CI 0.34–0.66; p < 0.001), based on very low-quality evidence. 4- Delayed memory: Small impairment in delayed memory in individuals with LBP compared with asymptomatic controls (k = 3; d = 0.34; 95% CI 0.07–0.60; p = 0.02), supported by low-quality evidence.
Executive function (Berryman et al., 2014)	Chronic low back pain, Fibromyalgia, Chronic pancreatitis, Chronic widespread pain, Rheumatoid arthritis, Osteoarthritis, Chronic temporomandibular disorder	Observational (n = 15)	Behavioural outcomes (number/sum of correct responses) 1- Executive function-response inhibition No overall impairment in response inhibition in chronic pain compared with healthy controls (ES = –0.12; 95% CI –0.44–0.20). Sensitivity analyses excluding accuracy-derived outcomes suggested a moderate impairment, indicating instability of findings. No significant deficits observed in either chronic non-fibromyalgia pain (ES = –0.33; 95% CI –0.86–0.20) or fibromyalgia (ES = –0.07; 95% CI –0.24–0.39). 2-Complex executive function Small but significant impairment in complex executive function in individuals with chronic pain compared with controls (ES = –0.49; 95% CI –0.81 to –0.17), with substantial heterogeneity. Significant moderate impairment in fibromyalgia (ES = –0.57; 95% CI –0.94 to –0.20), whereas no significant deficits were observed in chronic non-fibromyalgia pain (ES = –0.38; 95% CI –0.83–0.07). 3-Set shifting Small but significant impairment in set shifting in chronic pain compared with healthy controls (ES = –0.25; 95% CI –0.41 to –0.09). Significant impairment in chronic non-fibromyalgia pain (ES = –0.32; 95% CI –0.53 to –0.11), while no significant deficits were observed in fibromyalgia (ES = –0.14; 95% CI –0.40–0.13). Behavioral outcomes (response time) 1-Executive function-Response inhibition Small but significant impairment in response inhibition in individuals with chronic pain compared with healthy controls (ES = 0.31; 95% CI 0.08–0.55), with low-to-moderate heterogeneity. Significant impairment in chronic non-fibromyalgia pain (ES = 0.43; 95% CI 0.15–0.70), whereas no significant deficits were observed in fibromyalgia (ES = –0.05; 95% CI –0.45–0.34). 2- Complex executive function Small but significant impairment in complex executive function based on response time measures in chronic pain compared with controls (ES = 0.34; 95% CI 0.03–0.66), supported by converging evidence from sustained attention and reaction time paradigms. 3-Set shifting Moderate and significant impairment in set shifting in

(continued on next page)

Table 1 (continued)

Author, year	Type of chronic pain	Type of studies	Results from Meta-Analysis
			individuals with chronic pain compared with healthy controls (ES = 0.57; 95% CI 0.32–0.82). Moderate impairments in both chronic non-fibromyalgia pain (ES = 0.59; 95% CI 0.26–0.92) and fibromyalgia (ES = 0.57; 95% CI 0.18–0.96), indicating consistent deficits across pain subtypes. Physiological outcomes (BOLD activation) 1-Executive function – Response inhibition (Go/No-Go task) Altered task-related brain activation during response inhibition in chronic pain compared with healthy controls. Healthy controls showed greater activation in fronto-parietal and motor control regions (right precentral gyrus, inferior parietal lobe, supplementary motor area, midcingulate gyrus, left middle frontal gyrus, and putamen), whereas individuals with chronic pain exhibited greater activation in the right inferior temporal/fusiform gyrus. 2-Functional connectivity Increased functional connectivity in fibromyalgia during inhibition tasks, with greater coupling between the right inferior temporal/fusiform gyrus and bilateral medial/superior frontal regions and the supplementary motor area, compared with healthy controls.
Cognitive decline (Zhang et al., 2021)	Fibromyalgia, Low back pain, Cancer pain, Knee pain, Neuropathic pain, Musculoskeletal pain	Observational (n = 37)	1-SF-36 Mental Component: Large and significant association with cognitive/mental health decline in individuals with chronic pain (SMD = –1.50; 95% CI –2.19 to –0.81). 2-Montreal Cognitive Assessment (MoCA): Large and significant cognitive decline in individuals with chronic pain, reflected by lower MoCA scores (SMD = –1.11; 95% CI –1.60 to –0.61). 3-Performance Validity Testing (PVT): Very large impairment in cognitive performance, particularly sustained attention, alertness, and reaction time, in individuals with chronic pain (SMD = 3.05; 95% CI 1.74–4.37). 4-Operation Span (working memory): Large and significant impairment in working memory capacity in individuals with chronic pain (SMD = –1.83; 95% CI –2.98 to –0.68). 5-ICD-defined cognitive decline (dementia / Alzheimer's disease): No significant association between chronic pain and clinically diagnosed cognitive decline (OR = 1.58; 95% CI 0.97–2.56). 6-Mini-Mental State Examination (MMSE): No significant association between chronic pain and global cognitive decline when analysed as continuous scores (SMD = –0.42; 95% CI –0.94–0.10). No significant association when cognitive impairment was analysed categorically (OR = 1.14; 95% CI 0.91–1.42). 7-RBANS – memory component: No significant association between chronic pain and memory impairment assessed with RBANS (SMD = –0.06; 95% CI –0.37–0.25).

Note= Positive effect sizes indicate poorer performance or greater impairment in the chronic pain group unless otherwise specified. Heterogeneity is reported using the I^2 statistic. When available, sensitivity and subgroup analyses are summarized to highlight the robustness of findings across pain subtypes, task paradigms, and outcome measures.

AB, attentional bias; BOLD, blood oxygen level-dependent; CI, confidence interval; CP, chronic pain; CRPS, complex regional pain syndrome; ES, effect size; g, Hedges' g; ICD, International Classification of Diseases and Related Health Problems; I^2 , heterogeneity index; LBP, low back pain; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; OR, odds ratio; PVT, Performance Validity Testing; RBANS, Repeatable Battery for the Assessment of Neuropsychological Status; SMD, standardized mean difference.

and patient experience rather than a uniform marker distinguishing the presence or absence of chronic pain.

3.1.4. Perceptual-motor function

Finally, perceptual-motor function is also altered, and CP has been associated with lower physical function, disability (Martinez-Calderon et al., 2020, 2019) and sensorimotor changes, such as slower reaction times, delayed peak velocity, increased movement variability, sensitivity to exteroceptive stimuli (Wang et al., 2021), decreased proprioception (Tsay et al., 2015) and body awareness (Tsakiris et al., 2010), deficits in higher-order cognitive processes (Higgins et al., 2018; Attridge et al., 2019) and motor strategies (Nzamba et al., 2024). Such perceptual-motor impairments can occur at multiple levels, including task planning, movement execution and feedback mechanisms (Kantak

et al., 2022; Vittersø et al., 2022). While contemporary theories hold that perception is not based solely on sensory evidence, but also on brain inferences, which are continuously refined from sensorimotor feedback (Pinto et al., 2021; Chen and Wang, 2023), the underlying mechanism that explains perceptual-motor deficits in CP remains largely unknown.

From a clinical perspective, fear-related constructs play a central role in motor function by shaping movement behavior, activity engagement, and pain-related avoidance in individuals with chronic musculoskeletal pain. Elevated fear of pain, pain-related anxiety, and fear-avoidance beliefs—particularly those related to physical activity—can limit willingness to move, reinforce protective motor strategies, and contribute to reduced physical functioning, irrespective of structural pathology. These processes are especially relevant for rehabilitation, as they may perpetuate movement avoidance and interfere with graded exposure

and exercise-based interventions. Quantitative evidence supports a consistent, albeit weak, association between fear-related constructs and pain intensity (Martinez-Calderon et al., 2019). Meta-analytic findings indicate small but significant positive associations between pain-related anxiety and pain intensity, as well as between fear-avoidance beliefs—both work- and physical activity-related—and pain intensity, with substantial heterogeneity across conditions (see Table 1). Associations were more stable in chronic neck pain and osteoarthritis, while findings in chronic low back pain were more heterogeneous. Cross-sectional evidence also showed moderate associations between fear of pain and pain intensity. Longitudinal findings regarding the predictive value of fear-avoidance beliefs for future pain intensity were inconsistent. Overall, these results suggest that fear-related factors are clinically relevant correlates of pain intensity and motor behavior, reinforcing their importance as modifiable targets in interventions aimed at restoring movement and functional capacity.

3.1.5. Executive function

From a clinical standpoint, growing evidence indicates that chronic pain is accompanied by meaningful alterations in executive functioning that extend beyond sensory symptoms and directly affect patients' ability to regulate behavior, sustain goal-directed actions, and adapt to changing task demands. Difficulties in response inhibition, cognitive flexibility, and processing efficiency may compromise everyday activities that require planning, self-control, and rapid decision-making, such as adhering to rehabilitation programs, pacing physical activity, or managing pain-related avoidance behaviors. Importantly, these executive alterations appear to reflect inefficiencies in cognitive control rather than global cognitive failure, suggesting that patients may rely on compensatory strategies that increase mental effort during demanding tasks. Recognizing executive dysfunction as a clinically relevant component of chronic pain has implications for assessment and intervention, underscoring the potential value of integrating cognitive and behavioral strategies into pain management and rehabilitation.

Across behavioral and physiological outcome measures, converging evidence indicates that executive functioning is altered in individuals with chronic pain, although the pattern of deficits varies by cognitive component, pain subtype, and outcome metric (Berryman et al., 2014) (Table 1). Behavioral measures based on accuracy revealed small but significant impairments in complex executive function and set shifting, with more consistent deficits observed in fibromyalgia for complex

executive demands and in non-fibromyalgia pain for set shifting, while findings for response inhibition were unstable and sensitive to analytic decisions. In contrast, response time measures showed more robust and consistent impairments, particularly for response inhibition and set shifting, suggesting reduced processing efficiency and increased cognitive effort during executive control tasks. Neurophysiological evidence further supports these behavioral findings, demonstrating altered task-related BOLD activation during response inhibition, with reduced engagement of fronto-parietal and motor control regions and increased activation and connectivity in temporal regions in chronic pain, particularly in fibromyalgia. Taken together, these results suggest that executive deficits in chronic pain are better characterized as inefficiencies and compensatory neural reorganization within control networks rather than uniform losses of executive capacity.

3.2. Chronic pain conditions showing neurocognitive impairment

While diagnostic categories are useful for classifying and reporting clinical patterns, there is an increasing emphasis on assessing the underlying core domains that share commonalities across multiple CP conditions (Eilenberg and Otis, 2023b). Given the common impairments reported in CP across a range of conditions, implications for the transdiagnostic approach have been advocated (Crowe et al., 2017). Hence, neurocognitive impairments have been reported in several conditions including CP (Fig. 3).

3.2.1. Chronic Nociceptive pain or Chronic widespread pain

Nociceptive pain refers to a mechanism-based category that is particularly applicable to chronic primary pain conditions outlined in the ICD-11 (Nicholas et al., 2019b). Nociceptive pain is often accompanied by other pain-related symptoms, such as fatigue, sleep disturbances, cognitive decline, hypersensitivity to external stimuli, and mood disturbances (Fitzcharles et al., 2021). Neurocognitive impairments have been identified as a clinical predictor of the future severity of key symptoms such as pain and fatigue in patients with fibromyalgia (Ranum et al., 2022). Impaired neurocognitive domains in chronic nociceptive pain have been described, including memory (Kelly et al., 2025; Galvez-Sánchez et al., 2024), attention (Wu et al., 2018), language (Bell et al., 2018), perceptual-motor (Wu et al., 2018; Waller et al., 2024) and executive functions (Tesio et al., 2015; Kelleher et al., 2025).

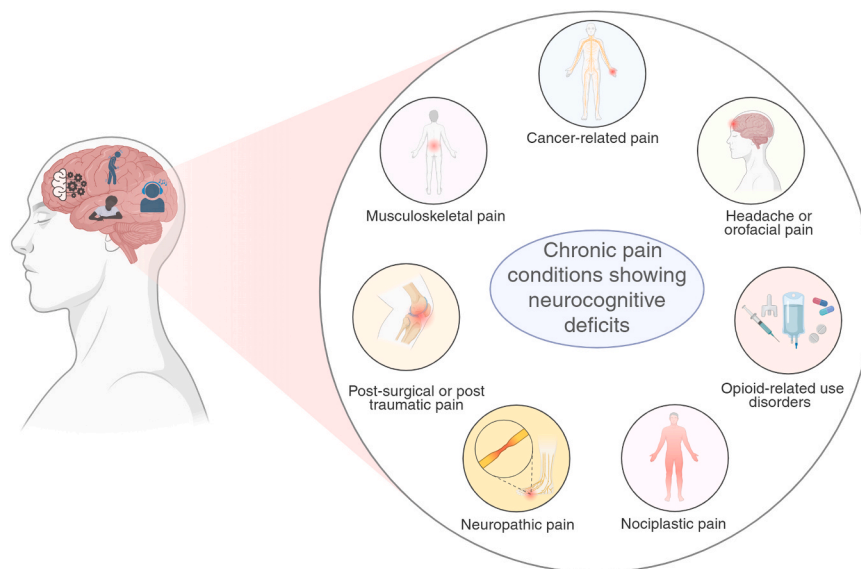


Fig. 3. Transdiagnostic approach to neurocognitive impairments in chronic pain. Neurocognitive domains investigated in several chronic pain conditions suggest deficits in attention, learning and memory, perceptual-motor function and executive function. Figure was created using Biorender.

3.2.2. Chronic Neuropathic pain

Apart from negative and positive neurological symptoms or signs, such as decreased sensation or allodynia and hyperalgesia, respectively (Scholz et al., 2019), people with neuropathic pain may present with other features that indicate neurocognitive impairment (Ojeda et al., 2018), including impaired memory, attention (Moriarty et al., 2017), executive function, language (Povedano et al., 2007) or perceptual-motor (Ryan et al., 1992).

3.2.3. Chronic secondary musculoskeletal pain

As a chronic secondary pain condition is highlighted in the ICD-11 (Perrot et al., 2019), chronic musculoskeletal pain is characterized by significant emotional distress and functional disability (Blyth et al., 2019). Likewise, chronic musculoskeletal pain may also present with neurocognitive impairment, such as decreased executive function (Ojeda et al., 2018), memory (Simon et al., 2016), attention (Oosterman et al., 2012), perceptual-motor functions and language (Söderfjell et al., 2006). Evidence suggests that chronic low back pain is associated with subtle but clinically relevant alterations in cognitive functioning, particularly in domains that support everyday decision-making, attention, and memory (Pereira Nery et al., 2023).

3.2.4. Chronic secondary visceral pain

In ICD-11, chronic secondary visceral pain is another diagnosis considered a chronic primary pain condition (Organization, 2022). Although a recent systematic review found that impairments in executive functioning, memory, intelligence, or attention biases do not appear to be consistently present in this condition (Arévalo-Martínez et al., 2022), some neurocognitive impairments have been reported, such as impaired memory (Kilkens et al., 2005), language (Dancey et al., 2009), attention (Chapman and Martin, 2011) and executive function (Kennedy et al., 2012).

3.2.5. Chronic primary headache or orofacial pain

Chronic headache or orofacial pain is a primary CP condition associated with poorer cognitive performance, including impairments in attention, executive function, language, perceptual-motor functions and memory, which has been closely examined in migraine sufferers (Begasse de Dhaem and Robbins, 2022). Similarly, neurocognitive impairments, such as vigilance-avoidance attentional bias when visualizing painful expressions, have also been reported in orofacial pain (Mazidi et al., 2019).

3.2.6. Chronic cancer-related pain

As a chronic primary pain condition included in the ICD-11 (Organization, 2022), cancer-related pain is a prevalent and debilitating symptom of cancer, often exacerbated by both the disease itself and its treatments, which can cause pain to become chronic (Bennett et al., 2019). In addition, cancer survivors may present with non-pain-related symptoms, such as fatigue, depression, anxiety, oral dysfunction and body image (Tan et al., 2022). Moreover, individuals with chronic cancer-related pain may experience perceived neurocognitive impairments (Boscher et al., 2020; Von Ah et al., 2018) such: memory, attention, executive function, and perceptual-motor function

3.2.7. Chronic post-surgical or post traumatic pain

Chronic post-surgical or post traumatic pain is classified as a distinct diagnosis within chronic primary pain conditions (Organization, 2022). This population often presents with pain-related distress, functional impairment, and diminished quality of life (Schug et al., 2019). In addition, neurocognitive domains are impaired, thereby significantly impacting patient health (Wang et al., 2014). These include memory, language, attention, perceptual-motor and executive function (Zhao et al., 2024; Steinmetz et al., 2009).

3.2.8. Chronic central poststroke pain

While post-stroke pain is included within chronic neuropathic pain according to ICD-11, experiencing CP after a stroke may occur in up to 50% of these patients (Naess et al., 2012), affecting up to 70% of them in ADL (Klit et al., 2011). Pain is often associated with depression, neurocognitive impairment, and a poor quality of life (Paolucci et al., 2016). Stroke survivors with CP exhibit a high utilization of pain treatments, notwithstanding their perception that treatment is often ineffective. This underscores the need to develop effective pain interventions in stroke survivors (Haslam et al., 2021). Regarding cognitive function, a high proportion of stroke survivors can encounter cognitive impairments within three months after stroke (Pendlebury et al., 2010), which may even lead to the development of dementia (Nys et al., 2005). Such impairments includes executive function, attention, memory, and perceptual-motor function (Donnellan and Werring, 2020).

3.2.9. Complex regional pain syndrome

Complex regional pain syndrome (CRPS) is a chronic primary pain disorder that is most frequently triggered by trauma, such as surgery or fracture (Ferraro et al., 2024). CRPS is characterized by heightened sensitivity, including hyperalgesia and allodynia, primarily affecting the extremities (Taylor et al., 2021). It severely affects the quality of life of patients, implying a poor prognosis despite treatment. A significant percentage of people with CRPS report constant pain that interfered with sleep, mobility, and ADLs (Sharma et al., 2009) and shows signs of altered body perception and neuropathic pain (Arcos-Holzinger et al., 2023; Shafiee et al., 2023; Harvie et al., 2022). Such CRPS symptoms are not limited to the affected limb (Halicka et al., 2024), which may impact on neurocognitive resources given the attentional bias to somatosensory stimuli reported in CRPS (Broadbent et al., 2021b). Impaired neurocognitive domains in CRPS such as attention, perceptual-motor and executive functions, have been reported (Bultitude et al., 2017; Lee et al., 2015; Wittayer et al., 2018).

3.2.10. Chronic pain and opioid-related use disorders

The increase in opioid prescriptions that began the 1990s to manage CP was associated with an increase in opioid-related use disorders (OUD) and opioid-related deaths (Dowell et al., 2016; Kolodny et al., 2015). Opioid-dependent patients often present with a range of comorbidities that could cause or influence their pain experience, with a reported prevalence of 55% for OUD (Latif et al., 2021). In this context, OUD leads to cognitive impairment (Mintzer et al., 2005), such as attention, memory, language and executive functions (Sofuoglu et al., 2016). Neurocognitive impairment has been consistently observed with the use of opioids, cannabis, and methadone, and this effect is exacerbated when combined with antidepressants and/or anticonvulsants (Baldacchino et al., 2017; Zhang et al., 2018; Polles et al., 2020; Allegrì et al., 2019).

3.2.11. Chronic pain in elderly population

CP is highly prevalent in the elderly population and is associated with substantial suffering, social isolation, disability, and increased healthcare burden (Patel et al., 2013). The impact of CP on the elderly is especially relevant (Domenichiello and Ramsden, 2019). This is associated with an increased risk of early death and faster cognitive deterioration (Whitlock et al., 2017; Macfarlane et al., 2017). As previously mentioned, neurocognitive decline is highly prevalent in older adults with CP (Baker et al., 2016), with up to 45.8% of those with dementia experiencing CP (van Kooten et al., 2016). Attention, memory and executive functions are habitually impaired neurocognitive domains in the elderly (van der Leeuw et al., 2018; Rouch et al., 2021a). Moreover, a significant relationship was observed between CP and poorer 15-year prognosis on neurocognitive performance has been reported (Rouch et al., 2021b) highlighting this bi-directional relationship.

3.3. Transdiagnostic approach in neurocognitive impairments in chronic pain

There is a growing recognition that CP and neurocognitive disorders often do not occur in isolation but share overlapping mechanisms and clinical features. Understanding the transdiagnostic relationship between these conditions remains a key priority for optimizing pain management. A transdiagnostic construct comprises symptoms cutting across diagnostic boundaries or categories (Eadeh et al., 2021). In this manner, neurocognitive functioning, including bottom-up and top-down processes, may serve as a transdiagnostic core domain relevant to numerous CP conditions. Recognizing these shared neurocognitive impairments provides a valuable lens for understanding how CP intersects with disability and interference, and yields common targets for intervention in tackling disabling CP. (Table 2)

A unified approach that targets the underlying, shared mechanisms that are significant to the maintenance of both CP and neurocognitive impairments would have several advantages (McGorry and Nelson, 2016): (1) transdiagnostic multimodal approach for patients with CP may help provide more holistic care and lead to a more appropriate relief of the symptoms present in CP; (2) using a transdiagnostic multimodal approach that focuses on a set of core therapeutic principles rather than several diverse protocols would simplify decision-making in CP disorders; and (3) including this approach in pain treatment and neurocognitive deficit management would potentially result in much more cost-effective interventions, facilitating the implementation of evidence-based treatments and extending the reach of precision medicine to those who need it the most.

As previously noted, recent evidence advocates the use of a transdiagnostic framework that emphasizes common neurocognitive impairments across various CP conditions rather than relying solely on traditional categorizations. This shift aligns with the National Institute of Mental Health's Research Domain Criteria (RDoC) (Cuthbert, 2022; Boersma et al., 2019), which promotes a dimensional approach to understanding brain-behavior relationships, acknowledging that neurocognitive deficits may transcend different pain syndromes (Zhang et al., 2021). Currently, frameworks such as RDoC and IMMPACT incorporate a multidimensional, non-linear, dynamic, contextual-environment-dependent, and highly interactive perspective beyond diagnostic labels, in line with transdiagnostic science (Turk et al., 2003; Hajcak and Patrick, 2015). These initiatives reflect a paradigm shift in research leading to a neuroscience-based pain science, incorporating outcome domains and measures to better identify individual-level improvements and differences between groups.

We argue that this approach is essential in the field of CP for generating new scientific hypotheses, probing physiological mechanisms, developing therapeutic strategies, and transferring findings across disciplines. Given the large variability in clinical responses, even for the most effective pain treatments, a call for a more personalized and tailored approach to managing people with CP is encouraged (Edwards

et al., 2023). Methodologically, research is increasingly aiming to map the shared and distinct pathways that underlie comorbid symptoms, which may offer translational value in clinical settings, where assessment and treatment should prioritize identifying and targeting of transdiagnostic features (Linton, 2013). Thus, addressing both pain-specific and non-pain-related symptoms may be crucial for improving clinical effectiveness in individuals with CP and comorbid neurocognitive disorders.

3.4. Clinical implications and future research

Although significant advances have been made in the last two decades in understanding the underlying processes in both the peripheral and central nervous systems, the burden of CP continues to grow. The transdiagnostic nature of neurocognitive impairments in CP requires a fundamental shift in clinical practices. As diagnostic categories are useful for the classification of symptom clusters, in the field of pain, there is an expanding emphasis on evaluating core domains that share commonalities across multiple disorders (Eilenberg and Otis, 2023a). Traditional approaches that focus solely on pain intensity or physical dysfunction have failed to address the profound impact of cognitive deficits on ADLs interference and quality of life. Emerging evidence underscores that neurocognitive impairments are not merely a comorbidity, but a core feature of CP pathophysiology, necessitating systematic assessment and targeted intervention (Moriarty et al., 2011). High-impact chronic pain refers to pain that lasts three months or longer and is associated with significant social, personal, or functional limitations (Eccleston et al., 2023), whereby neurocognitive alterations being a relevant marker. An important consequence of these findings is that clinicians and researchers are likely to benefit from assessing both pain and neurocognitive impairments when conducting research or providing treatment for either condition.

Another challenge that requires further attention is the lack of consensus regarding methods for evaluating neurocognition, which hinders standardization in both research and clinical setting. Since most clinical studies assess self-reported measures, such as the Montreal Cognitive Assessment (MOCA) or the Short-Form 36 Health Survey Questionnaire Mental Component, it has been pointed out that most studies have found small correlations between standardized tests and self-reported measures (Friedman and Gustavson, 2022). Current clinical evaluations often overlook neurocognitive screening, despite data linking these deficits to poorer treatment adherence (Fleck et al., 2023). While multidimensional assessment of patients with chronic pain has been proposed, which incorporate screening of neurocognitive impairments as a critical component (Montero-Cuadrado et al., 2025), there are no neurocognitive assessment tools with a functional emphasis specifically developed for people with chronic pain. Today, neurocognitive assessments incorporating digital technology are available to capture the patient's condition efficiently, in a standardized manner, and intensively (Libon et al., 2025). Digital tools have been shown to be valid

Table 2
Summary of neurocognitive domains affected in chronic pain conditions.

	Attention	Memory	Language	Executive function	Perceptual-motor function
Chronic Nociplastic pain	X	X	X	X	X
Chronic Neuropathic pain	X	X	X	X	X
Chronic secondary musculoskeletal pain	X	X	X	X	X
Chronic secondary visceral pain	X	X	X	X	
Chronic primary headache or orofacial pain	X	X	X	X	X
Chronic cancer-related pain	X	X		X	X
Chronic post-surgical or post traumatic pain	X	X	X	X	X
Chronic central poststroke pain	X	X		X	X
Complex regional pain syndrome	X			X	X
Opioid-related use disorders	X	X	X	X	
Elderly Chronic pain	X	X		X	

Note: X = neurocognitive impairment present.

and reliable test for assessing neurocognitive domains in people with mild neurocognitive impairments, such as those experienced in chronic pain (Siddi et al., 2021; Bonvino et al., 2025). Neurocognitive impairments may further complicate pain management by affecting treatment adherence, self-reported accuracy, and rehabilitation engagement (Schmidt et al., 2023). Difficulties in attention, working memory, and mental efficiency can affect patients' ability to follow complex instructions, sustain effort during rehabilitation, and cope with the cognitive demands of pain self-management. In this context, emerging evidence such as computerized cognitive training has shown promising effects in improving working memory, executive function, and processing speed in individuals with CP (Baker et al., 2018), supporting the growing role of technology-supported cognitive interventions in CP management.

In addition, it may also be relevant to consider assessments that account for state-dependent fluctuations, as neurocognitive functioning in patients with CP may decline during pain exacerbations. Future

longitudinal studies, ideally including mediation analysis, are needed to unravel the causal mechanisms underlying neurocognitive impairments and to determine their prognostic value in chronic pain persistence. We hope that by underscoring the neurocognitive deficits that substantially drive the maintenance of a persistent problem, we can also highlight the 'whys' and 'whom' so that clinicians can apply this knowledge in practice. Shifting both research and clinical paradigms by integrating neurocognitive assessments and treatment may be imperative in this regard. Implementing new digital health technologies can further enhance patient management, but it is even more urgent to consider this transdiagnostic approach that will allow clinicians to reach a comprehensive diagnosis and understanding of the patient (Fig. 4).

Our review showed that neurocognitive alterations occur across different pain phenotypes and are not exclusive to nociplastic pain. These results resemble those found by Kelly et al (Kelly et al., 2025), who reported that individuals with nociceptive and nociplastic pain had impaired short- and long-term memory performance compared to

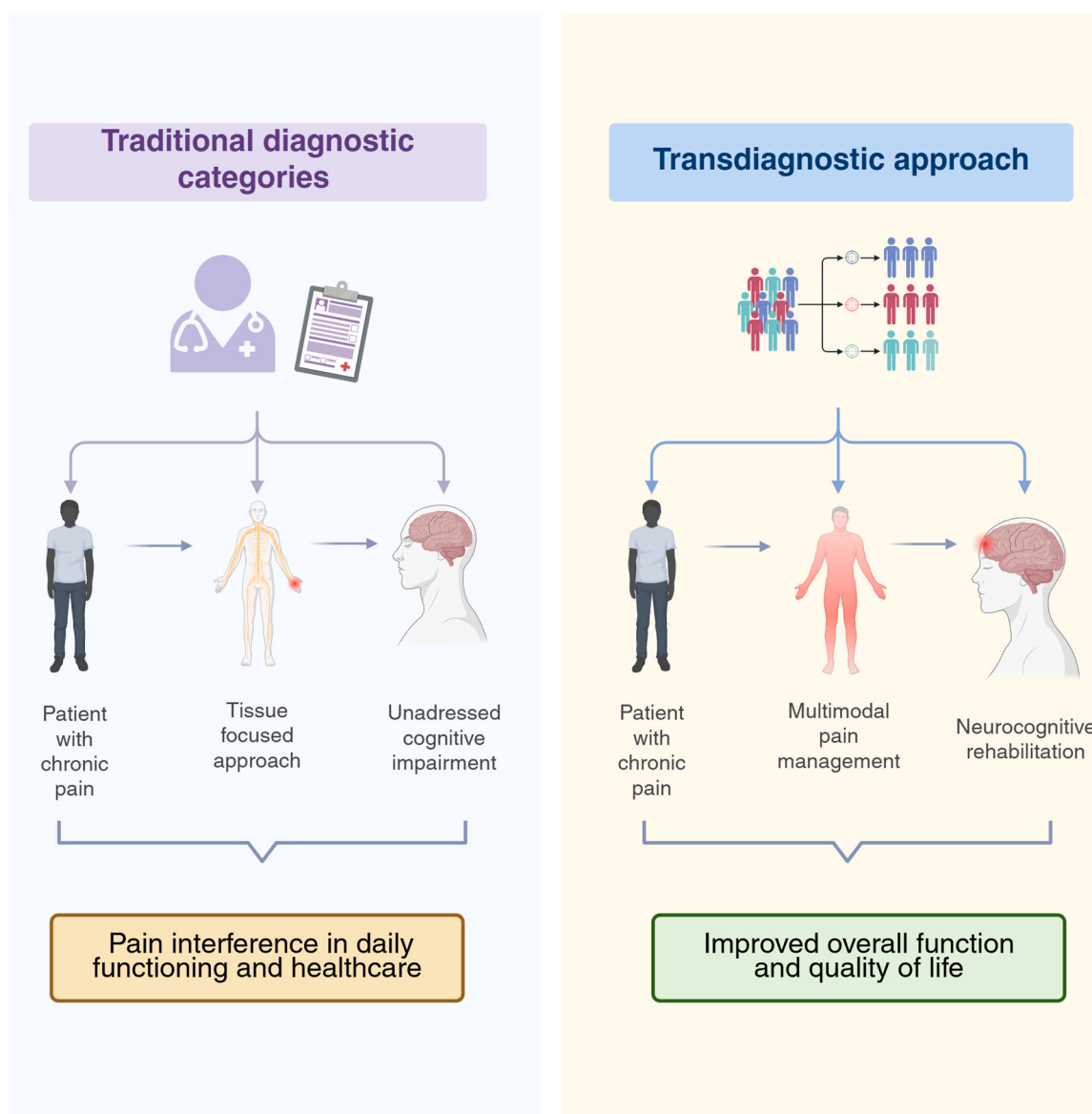


Fig. 4. Comparison between traditional diagnostic categories and transdiagnostic approach in chronic pain management. Traditional diagnostic approaches primarily focus on tissue-based mechanisms, often overlooking concomitant neurocognitive impairments, which may contribute to pain-related disability and sub-optimal healthcare outcomes. In contrast, a transdiagnostic approach integrates multimodal pain management and neurocognitive rehabilitation, aiming to address shared mechanisms underlying chronic pain and neurocognitive impairments, ultimately improving overall functioning and quality of life. Figure was created using Biorender.

healthy controls, although they found no differences in memory performance in individuals with neuropathic pain. Accordingly, both the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) (Edwards et al., 2021) and the Back Pain Phenotyping Consortium (BACPAP) (Nijs et al., 2024) have recommended phenotyping CP as a necessary initial step in determining whether personalized medicine can be used to treat CP. The BACPAC Biobehavioral Research Working Group (BWG) identified key domains for harmonization and identified well-validated Patient Reported Outcome Measures (PROMS) to represent the domains to guide clinical practice (Greco et al., 2023). However, neurocognitive impairments have not been included in any recent international consensus on the core domains of CP.

Finally, a formal meta-analysis was not conducted due to the substantial heterogeneity across included studies, including variability in study designs, outcome definitions, and the cognitive and neurobiological measures used to assess impairments. Additionally, recent and robust meta-analyses are already available for all impairments covered in this review, although not consistently across all chronic pain conditions. This combination of methodological heterogeneity and partial overlap with existing quantitative syntheses limited the appropriateness and added value of conducting a new pooled meta-analysis within the scope of the present review. Neurocognitive rehabilitation is gaining attention as a viable adjunct to traditional pain management approaches. Nonetheless, we do not have standardized neurocognitive training programs specifically tailored for individuals with CP, as variability in neurocognitive profiles and pain phenotypes require further research. This includes exploring the optimal timing, intensity, and modality of interventions, and determining whether improvements in cognitive function translate into better pain outcomes and functional enhancements. Hence, high-quality experimental studies are recommended to evaluate the efficacy of neurocognitive rehabilitation as an adjunctive pain treatment.

4. Conclusions

This review outline the multidimensional interference on neurocognitive domains, such as attention, language, memory and learning, executive and perceptual-motor function, and highlights the current understanding of the intertwined relationship between CP and neurocognition. The domains and constellations of clinical conditions affected by neurocognitive impairments in CP illustrate the potential of the transdiagnostic approach and its clinical and research implications. Our review highlights that neurocognitive impairments are a transdiagnostic feature of CP, rather than being confined to any single disorder. Such deficits represent a critical yet under-recognized dimension of CP experience with direct implications for treatment outcomes and daily functioning (Higgins et al., 2018). There is growing literature in this field addressing CP and neurocognitive impairment, underscoring the importance of multimodal and highly tailored pain management. In this sense, viewing CP through a dual lens, targeting both pain and neurocognition, could lead to more cost-effective and comprehensive care. Nevertheless, we encourage further research to better understand the potential mechanisms, standardize the evaluation, and explore new therapeutic opportunities.

CRedit authorship contribution statement

Conceptualization, J.G-A. and A.R-R.; methodology, J.G.; validation and investigation, A.R-R., J.A.M-M. and J.G-A.; writing—original draft preparation, J.G-A.; writing—review and editing, A.R-R., G.C-B, F.M.C, J.A.M-M. and J.G-A.; visualization, J.G-A. project administration, J.G-A. All authors have read and agreed to the published version of this manuscript.

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Declaration of Competing Interest

The authors declare no conflicts of interest.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.neubiorev.2026.106711.

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