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Examining the Effects of Chronic Pain on Memory Processes within the Framework of the Biopsychosocial Model

Kronik Ağrının Bellek Süreçleri Üzerindeki Etkilerinin Biyopsikososyal Model Çerçevesinde İncelenmesi

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Abstract: Chronic pain, one of the most common types of pain, has been linked to impaired cognitive abilities such as memory difficulties. The current article aims to provide a review of studies examining how the biological, psychological, and social components affect memory in patients with chronic pain. Studies have found that chronic pain patients mostly complain about memory deficits, and the biopsychosocial model is widely used to better understand why these patients have such deficits. The biopsychosocial model also enables each patient to cope with cognitive and behavioral difficulties by developing a unique intervention model. First, the biological component of model argues that chronic pain causes biological changes in patients and negatively affects cognitive processes, such as attention and memory. Second, the psychological component discusses the comorbidities such as depression and anxiety disorder caused by chronic pain and investigates how they influence memory performance. Third, the social component suggests that patients experience adverse impacts of chronic pain due to several impairments, such as increased healthcare costs, and insufficient sleep. The review concludes that memory performance in patients with chronic pain is affected by the biological, psychological, and social components, and these components interact with each other and cause impairments in memory.

Keywords: Chronic Pain, Memory, Models, Biopsychosocial

Öz: En yaygın ağrı türlerinden biri olan kronik ağrı, bellek güçlükleri gibi bilişsel becerilerde bozulma ile ilişkilendirilmektedir. Mevcut makale, kronik ağrısı olan hastaların belleğini biyolojik, psikolojik ve sosyal bileşenlerin nasıl etkilediğini inceleyen çalışmaların derlenmesini amaçlamaktadır. Araştırmalar, kronik ağrı hastalarının çoğunlukla bellek bozulmalarından şikâyet ettiğini ve biyopsikososyal modelin bu hastaların neden bellek şikayetleri yaşadıklarını daha iyi anlamak için yaygın olarak kullanıldığını göstermiştir. Biyopsikososyal model aynı zamanda her hastaya özgü müdahale modeli geliştirerek hastaların bilişsel ve davranışsal zorluklarla baş etmelerini sağlamaktadır. Birincisi, modelin biyolojik bileşeni, kronik ağrının hastalarda biyolojik değişikliklere neden olduğunu, dikkat ve bellek gibi bilişsel süreçleri olumsuz etkilediğini savunmaktadır. İkinci olarak, psikolojik bileşen, kronik ağrının neden olduğu depresyon ve anksiyete bozukluğu gibi komorbiditeleri tartışmakta ve bunların bellek performansını nasıl etkilediğini araştırmaktadır. Üçüncüsü, sosyal bileşen, hastaların artan sağlık hizmeti maliyetleri ve yetersiz uyku gibi çeşitli bozukluklara bağlı olarak kronik ağrının olumsuz etkilerini deneyimlediklerini öne sürmektedir. Çalışma, kronik ağrısı olan hastaların bellek performansının biyolojik, psikolojik, sosyal bileşenlerden etkilendiği ve bu bileşenlerin birbirleriyle etkileşime girerek bellekte bozulmalara neden olduğu sonucuna varmaktadır.

***Anahtar sözcükler*:** Kronik Ağrı, Bellek, Modeller, Biyopsikososyal

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Pain is defined as "*an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage"* by the International Association for the Study of Pain (Merskey & Bogduk 1994). Loeser and Melzack, (1999) suggest that pain has many different causes, so there are different types of pain: transient pain (TP), acute pain (AP), and chronic pain (CP). TP might be defined as pain that occurs with the enactment of nociceptive transducers in the skin or different tissues of the body with no tissue harm. This pain type is common in daily life and is generally not a reason to seek health care (Loeser & Melzack 1999). AP might be defined as a physiological response seen as a sign of significant body tissue injury, trauma, surgery, or an acute illness. Recovery from this type of pain can take place without health care, but occasional medical help may be required for acute pain after trauma, surgical interventions, and some diseases (Loeser & Melzack 1999). Finally, CP is usually triggered by an injury or illness but continues after the recovery phase (Apkarian *et al.* 2009). A study conducted using the National Health Interview Survey of the National Center for Health Statistics shows that the prevalence of CP among US adults is 20.4% and the prevalence of high-impact CP is 7.4% (Zelaya *et al.* 2020). CP typically lasts more than six months and is more difficult to treat than other types of pain. One of the explanations is that as long as the pain is permanent, it causes continuous effects on the patient's life and the patient may have to shape his or her life according to this pain (Russo & Brose 1998). Considering the secondary effects of CP on the life of the patient, studies show that treatment with a multidisciplinary approach, which consists of various medications, psychological support, and rehabilitation combined, might give more successful results (Russo & Brose 1998; Gatchel *et al.* 2007; WHO 1990; Adams & Turk 2018). Moreover, since this pain is long-lasting and affects the patient's life to a great extent, many studies have proven that CP patients have impaired cognitive abilities such as concentration and memory difficulties (Jamison *et al.* 1989; Mazza *et al*. 2018). Furthermore, CP patients with memory complaints also mentioned that they suffer from emotional distress such as depression and anxiety (Edwards *et al.* 1992). In addition, CP patients with memory deficits encounter social difficulties, such as not receiving the expected support from their families and not enjoying social activities and sex (Jamison *et al.* 1989). For this reason, most studies showed that the best treatment for CP requires effective medication as well as education and rehabilitation (Bevers *et al.* 2016). According to the findings of some previous studies, CP patients suffer from both working memory (WM) and long-term memory (LTM) deficits (Berryman *et al.* 2013). WM can be defined as a system deemed important for remembering things while performing complicated tasks like reasoning, understanding, and learning (Baddeley 2010). In this sense, WM is crucial in terms of managing behavior, settling on choices, judgments, and arranging (Walteros *et al.* 2011). For instance, in a study conducted with 40 nonmalignant CP patients, the continuous reaction time test was used to measure attention, the finger tapping test was used to measure psychomotor speed, and the paced auditory serial addition test (PASAT) was applied to measure WM (Sjøgren *et al.* 2000). The results showed major deficits in attention, psychomotor speed, and WM in the participants with chronic nonmalignant pain. Although the researchers did not aim to find the components affecting results, they suggested that pain had a stimulating effect on WM. Furthermore, Nicholson and Verma (2004) argue that CP patients might experience many other psychological comorbidities such as insomnia, depression, and anxiety affecting memory. A study involving 1204 complex CP patients aimed to assess the pervasiveness and impact of depression (Rayner *et al.* 2016). The participants first completed a questionnaire that assessed mental and physical health, functionality, and service use. Then a 9-item patient health questionnaire was used to measure depression levels. The results showed that a large proportion of the participants (60.8%)

experienced depression and 55.6% of these participants had severe depression symptoms.

Additionally, some studies show that persistent harmful stimuli, such as CP, lead to molecular changes in the hippocampus, which plays a central role in memory formation and emotion-based disorders such as depression, mediating the emotional cognitive component of pain (Maletic *et al.* 2007). These cognitive components can be pain management strategies, mood changes due to pain, and the arrangement of recollections of painful stimuli (Fasick *et al.* 2015). Besides these, more of the participants meeting the criteria for depression reported being unable to work due to their health compared to the participants who did not. Studies show that depression, anxiety, and insomnia comorbidity in CP patients negatively affect their work life, relationships, and hobbies (Nicholson & Verma 2004). These comorbidities reduce patients' quality of life and prevent them from enjoying life.

Ray (2004) found that there is a strong relationship between mind and body. He argues that beliefs affect the way of thinking, and they change behavioral and social factors that influence the brain mechanism and physical health. Thus, the leading cause of memory problems in CP patients may arise not only from biological factors but also from other psychological or social factors (Andrasik *et al.* 2005). The evaluation of physical disorders such as pain, primarily due to dynamic interactions between physiological, psychological, and social factors, can be achieved with the biopsychosocial model (Gatchel 2004).

In the light of the research, it can be inferred that while evaluating memory in CP patients each of the biological, psychological, and social components has a separate effect, but they are also related to each other. Therefore, since the biopsychosocial model might be the most suitable one for examining memory in CP patients, the relationship between CP and memory is discussed according to that model in this review study. The biopsychosocial model might be defined as one in which diseases and well-being are affected by the interactions between biological, psychological, and social components (Alonso 2004). The biological component includes factors like physiology, genetics, tissue health, and biochemistry; the psychological component includes factors like emotions, mood, and behavior; and the social component includes factors such as socioeconomic status, social support, and social learning (Gatchel *et al.* 2007). The biopsychosocial model plays an essential role in understanding the causes of CP and intervening because a unique intervention method can be developed for each CP patient through understanding how biological, psychological, and social factors interact with each other (Gatchel *et al.* 2007). Therefore, the present review aims to examine how the biological, psychological, and social components affect memory in CP patients, discuss the effects of interactions among the components on memory, and suggest effective interventions for CP patients by considering these effects using the biopsychosocial model.

The Biopsychosocial Model of CP

The biomedical model has been the model used predominantly in the diagnosis and treatment of diseases since the middle of the 19th century. In this model, psychological, social, and environmental factors are not considered in evaluating diseases; instead, the model just considers physical and biological processes (McLaren 1998). Engel (1977) proposed the biopsychosocial model as an alternative in which these limitations were eliminated, and patients were treated considering biological, psychological, and social factors together. This model is critical in evaluating the relationship between CP and memory and appropriate interventions for CP patients. Since each patient with CP has uniquely experienced pain, each pain assessment and treatment method should be specific to the patient (Esmaeilzadeh *et al.* 2015). This model

allows experts to establish the predominant pain mechanism and evaluate the factors that cause this pain to persist (Gatchel 2004).

Biological Factors Affecting Memory in CP Patients

The biological components include the body's physical factors that influence and determine well-being, such as physiology, genetics, tissue health, and biochemical processes (Gatchel *et al.* 2007; Lehman *et al.* 2017). The biological functions of each system, organ, and cell depend on genetic expression to produce peptides or proteins that participate in metabolism through various enzymes, so overexpression or elimination of a gene can result in functional changes. Changes in gene expression may occur in CP patients due to the fact that the neuronal activity involved in pain transmission can be affected by immediate early gene activity as well as transcriptional factors (Gatchel *et al.* 2007). Therefore, it has been reported that CP such as migraine and fibromyalgia is genetically inherited (Buskila & Sarzi-Puttini 2006). There is much evidence indicating that people who suffer from CP might experience memory deficits (Berryman *et al.* 2013). There are different views regarding the causes of memory deficits, and the widely accepted one was developed by Legrain and his colleagues. (2009). They developed a model of neurocognitive attention that includes bottom-up capture of attention and top-down modulation of attention. The bottom-up capture can be defined as pain and involuntary attention that interrupts continuous actions and spontaneously demands attention (Legrain *et al*. 2009). For example, someone who puts his or her hand on a hot stove will automatically pull it away before damage is done; however, in such a case, it has been observed that the messages going to or coming from the brain are interrupted in CP patients. One of the essential features of the pain alarm system is involuntary pain capture because it can prevent us from performing other actions and causing injury by focusing on pain messages. Moreover, some studies show that attention is impaired, and performance may be lower in tasks requiring cognitive effort in patients with CP, depending on the pain intensity (Torta *et al*. 2017).

For instance, in a study with 15 fibromyalgia patients and 15 healthy controls, participants were given the Iowa Gambling Task and a conditional associative learning task. The results indicated that patients with fibromyalgia performed worse on both tasks. Furthermore, the fibromyalgia patients exhibited more errors in the learning task and made more inconvenient choices in the gambling task (Walteros *et al.* 2011). According to the other component of the neurocognitive model, which is called top-down modulation of attention, pain decreases when attention is removed from the nociceptive stimulus (Van Damme *et al.* 2008). It has been argued that it is possible for CP patients to focus on pain information or increase attention depending on the stimulus and activity expectations by means of the pain reduction ability of top-down modulation. Moreover, studies claim that meditation using this model can be successful in reducing pain (Legrain *et al*. 2009).

Sources of attention that can be reduced by impairment of the ability to maintain a memory track may be an important cause of the decrease in memory performance in CP patients (Mazza *et al*. 2018). The current literature shows that diminished attention has a significant effect on both WM and LTM (Moore *et al*. 2012). CP patients frequently show impaired WM or cognitive functioning and mostly tend to show poor performance on cognitively demanding tasks (Walteros *et al*. 2011). For example, Dick and his colleagues (2002) assessed attentional functions in 60 patients suffering from CP for longer than six months by using the Test of Everyday Attention (TEA). The TEA gives information about four different aspects of cognitive functioning: selective attention, sustained attention, attention switching, and auditory-verbal WM. In addition to the TEA, a 10-cm visual analogue scale (VAS), the Hospital Anxiety and

Depression Scale (HAD), Pain Disability Index, Modified Somatic Perception Questionnaire, and Pain Catastrophizing Scale (PCS) were used. The results showed that there were significant results in selective and sustained attention and auditory-verbal WM tasks. When the results are evaluated in general, it is seen that CP patients' concentration and memory problems greatly affect their mood and cognitive functions and, consequently, their psychological states. Furthermore, Luerding and his colleagues (2008) conducted a study to measure verbal and nonverbal LTM in fibromyalgia patients and used a series of tests. The California Verbal Learning Test (CVLT) and Rey Visual Design Learning Test were used to measure nonverbal LTM, the digit span backward task was used to measure verbal WM, and the Corsi block span task was used to measure nonverbal WM. The results indicated that the fibromyalgia patients' cognitive performance was impaired in nonverbal LTM and nonverbal WM in free recall. They also had impaired verbal WM compared with verbal LTM. Furthermore, in another study, the relationships between physical and psychological factors and cognitive functions were examined by measuring the pain intensity, trait anxiety, and depression levels of 30 patients with fibromyalgia and a control group (Grace *et al*. 1999). The Wechsler Memory Scale was given to measure the visual, verbal, and delayed short-term memory (STM) performance; the PASAT was given to measure concentration sensitivity; and the Symbol Modalities Test was given to measure attention. The results showed that the fibromyalgia patients performed worse in immediate and delayed recall tests than the controls. In addition, there were significant correlations between concentration and memory performance measures and scores on trait anxiety and pain intensity questionnaires. In another study, researchers investigated whether memory functions were impaired in patients with chronic low back pain (LBP) and patients with rheumatoid arthritis (RA) (Jorge *et* al. 2009). The participants were matched in terms of age, gender, and anxiety score; they then were given the Wechsler Memory Scale III to measure memory functions. The results showed that while chronic LBP and RA patients generally had lower memory performance in all memory subtypes compared to the normative data of historical controls, memory performances did not differ significantly between the participants with chronic LBP and those with RA. In another study conducted with 25 CP patients and 32 controls, a total of 57 participants who underwent arthroscopic surgery, the relationship between preoperative CP and postoperative cognitive dysfunction was investigated (Gu *et al*. 2019).

Arthroscopic surgery is performed to diagnose and treat joint problems; after the operation, symptomatic relief was observed in patients' pain complaints (Moseley *et al*. 2002). In the same study, a VAS was used to measure the pain intensity of the participants. After that, the Syndrome Kurz Test was used to measure the cognitive functions of the participants. These tests were administered to all participants before and after the surgery. The findings revealed that memory and attention abilities developed slowly after the surgery in the control group, while numerical ability was impaired. However, the cognitive functions including memory and attention improved faster in the group of CP patients after the surgery, indicating that arthroscopic surgery was effective in enhancing cognitive abilities (Gu *et al.* 2019).

As mentioned above, findings have indicated that CP patients suffer from poor memory, and memory performance in these patients might decrease due to many biological reasons, such as the pain messages interfering with other messages (Berryman *et al*. 2013; Mazza *et al*. 2018). As a result, it has been documented that people with CP showed poorer performance on attention and memory tasks with an increase in pain. Considering all these studies, it might be concluded that CP has a large impact on different cognitive processes, particularly attention and memory.

Psychological Factors Affecting Memory in CP Patients

The psychological component of the biopsychosocial model includes emotional, cognitive, behavioral, attitudinal, and motivational systems that affect health (Lehman *et al*. 2017). In this part, some psychological factors causing CP patients to suffer memory problems are introduced. First, it is noteworthy that in most of the studies that measure the relationship between CP and memory, patients are usually given depression and anxiety tests. It has been noted that CP patients also suffer from emotional distress such as depression, anxiety, and insomnia (Muñoz & Esteve 2005). For instance, in a study conducted with 149 CP patients, the HAD was used to measure their levels of depression and anxiety (Muñoz & Esteve 2005). The PCS was given to measure rumination, magnification, and helplessness levels. The results proved that depression and anxiety play an essential role in memory complaints for CP patients. In particular, depression has been found to be largely responsible for memory complaints (Muñoz & Esteve 2005). Moreover, researchers have inferred that as depressed individuals often negatively assess themselves and their abilities, their memory complaints may be uniquely explained by depression.

Some studies show that depression and anxiety disorders might have adverse effects on memory directly, independent of CP. In other words, CP triggers emotional distress such as depression and anxiety, and depression might trigger deficits in memory performance (Mazza *et al.* 2018). In a study conducted with 3999 participants selected from among American Vietnam veterans, the depression and anxiety levels of the participants were measured (Kizilbash *et al*. 2002). The CVLT was used to measure memory performance. According to the findings, only depression symptoms had a negative effect on immediate recall, but this was not the case for anxiety symptoms. However, when anxiety and depression levels were examined together, they had a negative effect on both immediate recall and retrieval performance (Kizilbash *et al*. 2002). In another study conducted with 25 fibromyalgia patients, 22 depressed controls, and 18 healthy controls, the participants were subjected to laborious memory tests, including the Randt Memory Test and the Code Memory Test (Sletvold *et al*. 1995). The results showed that the fibromyalgia and depression patients performed poorly on these memory tests compared to the healthy control participants. Additionally, when the fibromyalgia patients were examined in terms of past depression, it was found that those who had experienced depression before performed worse than the control group. Many studies show that emotional and cognitive factors greatly influence the chronicity of pain (Malfliet *et al*. 2017). Moreover, it was reported that patients with depression and anxiety disorders showed more physical symptoms, and the probability or severity of depression and anxiety symptoms increased as physical symptoms increased (Kroenke *et al*. 1994).

Another factor that affects CP patients' memory performance might be the mood-congruity effect, which refers to the inclination to recall and learn information more effectively when the affective valence of information is congruent with the individual's emotional state (Drace 2013). In a study with 35 migraineurs and 31 control participants, the participants were shown pain-related, negative, and neutral words in a pseudo-randomized order (Tomé-Pires & Miro 2014). They were then asked to remember the words shown and their skin conductance responses (SCRs) were recorded during the experiment. The results showed that the SCRs given to pain-related words and negative words were not significantly different from each other, indicating that they both caused more physiological reactions than neutral words. It was also stated that those suffering from migraine pain remembered more negative words compared to the control participants (Tomé-Pires & Miro 2014). In another study conducted with 28 women

who suffered from chronic myofascial pain syndrome and 28 female control participants, the experiments were administered under two different conditions (Busch *et al*. 2006). In the first condition, the neutral condition, the participants were given a neutral word list and a memory game. In the second condition, all words and images given to the participants were related to pain. It was found that patients with chronic myofascial pain remembered more pain-related words than neutral words. Some studies suggest that this effect occurs due to depression, that is, since these patients tend to emotionally engage with negative words, they are more likely to remember those words later (Zhou *et al*. 2020). However, Edwards and colleagues' (1992) stated that this effect could not be due to the levels of depression only in patients suffering from CP. They conducted a study with 19 healthy participants with CP complaints but no depression, 16 with both CP and depression, and 18 with depression but no CP. The participants were given both recall and recognition tests consisting of two types of pain-related adjectives, sensory and affective, and neutral adjectives. Their findings showed that the nondepressed participants with CP were more likely to recall sensory adjectives, while those with depression and CP tended to remember adjectives related to both affective and sensory pain. Given all these studies, patients with CP exhibit an information-processing bias so that they process pain-related stimuli more easily and selectively (Edwards *et al*. 1992).

Studies have shown that comorbidities such as depression and anxiety disorder caused by psychological factors negatively affect memory performance (Kroenke *et al*. 1994; Muñoz & Esteve 2005; Tomé-Pires & Miro 2014). However, in terms of the mood-congruity effect, it is seen that the rate of remembering negative or pain-related words that might have an emotional connection in CP patients increased.

Social Factors Affecting Memory in CP Patients

The social component of the biopsychosocial model is defined as the influence of social connections on health (Gatchel *et al*. 2007). These social and environmental factors might positively or negatively affect patients' lives (Clare *et al*. 2012). Studies have shown that CP patients who have complained about impaired memory also might experience some problems in their social lives and CP patients had memory and concentration problems due to insufficient family support, emotional distress, and pain that hinders daily activities (Inoue *et al*. 2017; Jamison *et al*. 1989). For example, a study shows that domestic physical violence is associated with pain severity, depression, and anxiety symptoms (Özer *et al*. 2015). Mazza, Frot and Rey (2018) suggest that memory complaints might be a source of stress for CP patients by directly affecting the social lives of individuals. For example, in a long-term study by Peavy and her colleagues (2009), 41 participants with mild cognitive impairment and 61 cognitively healthy older adults were followed up for three years and were given repeated cognitive and stress assessments. These evaluations included episodic memory measurement such as the Wechsler Memory Scale, and the CVLT. In addition to these measurements, the participants' cortisol levels were measured. According to the results of the Life Events and Difficulties Schedule, the participants who experienced high chronic stress and had mild cognitive impairment exhibited extremely poor performance on the memory scales. It might be inferred that one of the reasons for memory deficits in CP patients is their stress levels (Hart *et al*. 2003).

Studies show that CP patients often complain of mood disorders due to sleep disturbance and chronic fatigue in addition to pain (Fitzcharles *et al*. 2018). Many researchers show a relationship between poor memory and sleep quality, fatigue, and negative mood (Mazza *et al*. 2018). In a study examining sleep and cognitive performance in fibromyalgia patients, the participants experienced more drowsiness, more fatigue, more intense pain, a more negative

mood such as depression, and lower performance accuracy compared to the healthy control participants (C-oté & Moldofsky 1997). Sayar and his colleagues (2002) compared 40 CP patients with 40 healthy control participants in terms of depression, anxiety, and sleep quality. Their results revealed that the CP patients were more anxious and depressive and experienced more sleep problems, and that the participants' depression levels were between 30% and 87% and these participants had more sleep problems (Sayar *et al*. 2002). The researchers emphasized that depression could cause a decrease in pain tolerance and an increase in pain sensitivity. Sleep problems could occur depending on both the cause and result of CP and depression. Furthermore, some studies claim that poor sleep affects memory and might cause problems in individuals' social lives. Thus, individuals with CP might experience difficulties in social functioning (Theadom *et al*. 2007)

In addition to the physical and psychological pain suffered by CP patients, Gatchel (2004) suggests that their social lives are significantly affected by a decrease in productivity, increased healthcare costs, and reduced earnings. Moreover, insufficient sleep might be considered a major factor that affects CP patients' mood and memory.

Conclusion

In the current review, the main purpose is to investigate and examine the relationship between CP and memory performance within the framework of the biopsychosocial model. Findings show that biological factors mostly affect CP patients' memory performance negatively. Many researchers indicated that attention to the manipulation of the process by pain messages also negatively affects memory processes. For this reason, CP patients may have demonstrated low performance on tasks used to measure memory in studies. However, there are conflicting views on attention and memory deficits in CP patients. For example, Dick and his colleagues (2002) found that CP patients demonstrated impairments in sustained attention, selective attention, and WM abilities, but they did not differ in attention compared to healthy controls. Moore et al. (2012) did not observe any decrease in selective attention or sustained attention performance, although pain reduced WM and attention span. In other words, they discovered that there was a decrease in memory performance even though no deterioration was seen in the attention processes. Therefore, the two processes are not affected by each other.

Research on this subject is not sufficient, but this question mark can be removed by conducting studies examining the attention and memory processes, and the interaction between these two processes in more detail. Secondly, it has been observed that comorbidities such as depression and anxiety disorder caused by psychological factors in CP patients negatively affect memory performance. Some studies argue that this condition might be bidirectional; memory performance might decrease both due to the increase in depression and anxiety levels because of the increase in CP and the increase in CP as a result of the increase in depression and anxiety levels (Kroenke *et al*. 1994; Mazza *et al*. 2018). However, in addition, the mood-congruity effect means that CP patients have increased memory performance in response to words related to pain (Drace 2013; Tomé-Pires & Miro 2014). Finally, the most prominent social component factor may be the decrease in CP patients' sleep quality, as its negative effect on memory, in this case the inability to perform daily tasks such as working, cooking, and personal care, might affect individuals' relationships (Fitzcharles *et al*. 2018; Sayar *et al*. 2002). In the light of the literature, it can be inferred that biological factors significantly impact memory performance in CP patients; however, biological consequences might also affect psychological factors. Moreover, psychological and social factors might be evaluated together because memory deficits in CP patients due to depression are mostly caused by low sleep quality, and there is

considerable evidence that quality of sleep decreases due to depression (Muñoz & Esteve 2005; Berryman *et al*. 2013).

Some limitations were encountered in the present review study. The relationship between CP and memory has been examined according to the biopsychosocial model, widely used in CP patients. Still, some of the weaknesses of this model should be mentioned. The first one is that the model is highly inclusive, which may require many things to be considered simultaneously, and therefore the intervention time can be prolonged, and the situation can become confusing for patients (Ghaemi 2011). Secondly, in CP studies, the effects of gender are rarely taken into consideration. However, some studies show that female CP patients experience pain more intensely; therefore, it might be predicted that female CP patients' memory performance will be affected more (Samulowitz *et al*. 2018). Another limitation is that most of the studies are not up to date. Treatment methods for CP are continually being developed and diversified; considering these, more recent studies can be carried out so that intervention techniques appropriate to the needs of patients can be developed, and memory complaints can be reduced (Koechlin *et al*. 2018). Grandhi *et al*. (2017) have claimed that there is a relationship between CP and psychopathology, and even that these psychopathologies emerge because of inadequate and inappropriate management of CP. For this reason, by reducing CP complaints through correct and appropriate intervention, the adverse cognitive, psychological, and social effects of CP might be reduced, and memory improvement can be achieved in these patients. The biopsychosocial model is a remarkably successful method used in CP interventions. Thanks to this model, a unique intervention method might be developed for each patient, enabling him or her to cope with the cognitive and behavioral difficulties caused by pain (Gatchel *et al*. 2007). These interventions may vary according to the needs of patients; mindfulness, relaxation techniques, and Cognitive Behavioral Therapy (CBT) seems to be the most effective techniques (Carpenter *et al*. 2012). CBT has been found to be effective in patients with arthritis, chronic LBP, fibromyalgia, and temporomandibular joint disorder to improve their function and mood (Keefe & Caldwell 1997; Thieme *et al.* 2006; Turner *et al.* 2006; Glombiewski *et al.* 2010). Moreover, exercise intervention as a biopsychosocial model intervention approach for chronic musculoskeletal pain patients has been found to promote confidence, assist them accelerate their daily activities, and improve their quality of life by minimizing the influence of pain (Booth *et al.* 2017). The caregiver and the patient make collaborative decisions about the intervention plans, considering the patient's symptoms, dysfunctions, and psychological issues. There are four stages to the procedure. The diagnosis is confirmed first, then the symptoms and psychosocial problems are prioritized; third, the management of specific problems is discussed (assurance, physical/psychological methods, medications, and other measures), and finally, periodic follow-up is maintained to achieve individual-focused goals; and the plan can be re-evaluated and revised if necessary (Masi *et al*. 2002). The literature indicates that CP patients' memory problems might be due to biological changes caused by pain; the negative impact of comorbid diseases, such as depression and anxiety disorder, on memory; and social factors such as a decrease in individuals' sleep quality. Therefore, it is clear that CP and memory deficits are affected by biological, psychological, and social components, and these components also interact with each other, thus affecting memory. As mentioned above, there are deteriorations in the cognitive skills of CP patients, and treatments with a multidisciplinary approach might provide more effective results. Studies that directly address memory difficulties and CP are needed; the current review study aims to draw attention to this gap in the literature.

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