Review

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Neurobiology of Cancer: A Review from Psychooncologic and Neuroscientific Perspective

Kanserin Nörobiyolojisi: Psikoonkolojik ve Nörobilimsel Perspektiften Bir Derleme

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ABSTRACT

This review emphasizes the need to understand not only the biological but also the psychological and neurobiological aspects of cancer. Factors such as psychosocial stress, depression and social isolation have important effects on cancer initiation and progression through the neuroendocrine system and the immune system. In this context, the effects of interactions between the nervous system and the immune system on the tumor microenvironment, neuroinflammation and neurotransmitter levels are detailed. In addition, the neurobiological effects of cancer treatments (chemotherapy, radiotherapy, hormone therapy, immunotherapy) on cognitive and emotional functions were discussed; "chemobrain", neuropathic pain and treatment-related neurocognitive impairments were explained. Recent research has shown that these effects can be mitigated by psychooncological approaches such as Cognitive Behavioral Therapy, Eye Movement Desensitization and Reprocessing Therapy and mindfulness. These interventions support neuroplasticity by regulating stress responses and their effects on brain regions are supported by neuroimaging studies. Finally, the critical role of neuropsychological assessments and cognitive rehabilitation programs in individualized intervention processes was emphasized and the importance of an interdisciplinary approach was revealed. This study aims to critically evaluate the existing literature and draw attention to the gaps in the research field by comprehensively examining the neurobiological and psychooncological effects of cancer.

Keywords: Cancer, neurobiology, cognitive impairment, psycho-oncology, neuropsychotherapy

ÖZ

Bu derleme çalışması, kanserin yalnızca biyolojik değil, aynı zamanda psikolojik ve nörobiyolojik yönleriyle de anlaşılması gerektiğini vurgulamaktadır. Psikososyal stres, depresyon ve sosyal izolasyon gibi etkenlerin nöroendokrin sistem ve bağışıklık sistemi aracılığıyla kanserin başlangıcı ve ilerleyişi üzerinde önemli etkileri bulunmaktadır. Bu bağlamda, sinir sistemi ile bağışıklık sistemi arasındaki etkileşimlerin tümör mikroçevresi, nöroinflamasyon ve nörotransmitter düzeyleri üzerindeki etkileri detaylandırılmıştır. Ayrıca, kanser tedavilerinin (kemoterapi, radyoterapi, hormon tedavisi, immünoterapi) bilişsel ve duygusal işlevler üzerindeki nörobiyolojik etkileri ele alınmış; "kemobeyin", nöropatik ağrı ve tedaviye bağlı nörokognitif bozulmalar açıklanmıştır. Son yıllarda yapılan araştırmalar, Kognitif Davranışçı Terapi, Göz Hareketleriyle Duyarsızlaştırma ve Yeniden İşleme Terapisi ve mindfulness gibi psikoonkolojik yaklaşımlarla bu etkilerin azaltılabildiğini ortaya koymaktadır. Bu müdahalelerin stres yanıtlarını düzenleyerek nöroplastisiteyi desteklediği ve beyin bölgeleri üzerindeki etkilerinin nörogörüntüleme çalışmalarıyla desteklendiği belirtilmiştir. Son olarak, nöropsikolojik değerlendirmeler ve bilişsel rehabilitasyon programlarının bireyselleştirilmiş müdahale süreçlerinde oynadığı kritik rol vurgulanmış, disiplinlerarası yaklaşımın önemi ortaya konmuştur. Bu çalışma, kanserin nörobiyolojik ve psikoonkolojik etkilerini kapsamlı biçimde inceleyerek, mevcut literatürü eleştirel biçimde değerlendirmeyi ve araştırma alanındaki boşluklara dikkat çekmeyi amaçlamaktadır.

Anahtar sözcükler: Kanser, nörobiyoloji, bilişsel bozukluk, psikoonkoloji, nöropsikoterapi

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Introduction

For many years, cancer has been treated as a biological disease explained solely through cellular and genetic mechanisms. However, current multidisciplinary research shows that this approach is inadequate and that psychosocial factors, neurobiological processes, and the interaction between the immune system and the nervous system play important roles in the development and progression of cancer (Lutgendorf and Andersen 2015, Henneghan et al. 2020, Mravec 2021).

Factors such as psychosocial stress, depression and social isolation can suppress the immune system through the hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic nervous system, leading to increased inflammation in the tumor microenvironment, increased risk of metastasis and decreased response to treatment (Eng et al. 2014). Chronic stress has been shown to increase cortisol levels, which impairs plasticity in neurogenesis regions such as the hippocampus and leads to functional changes in structures such as the amygdala and prefrontal cortex (Davidson and McEwen 2012, Monje and Dietrich 2012).

Chemotherapy, radiotherapy, hormone suppressive therapies and immunotherapies can affect cognitive balance, attention processes and mood-regulating mechanisms along with physical systems. Conditions such as chemobrain syndrome, neuropathic pain, attention and memory disorders are among the important outcomes that reduce the quality of life of cancer patients (Wefel and Schagen 2012, Ahles and Root 2018).

In this context, cancer is not only a biological disease but also needs to be addressed with its neurobiological and psychosocial aspects. The integration of the fields of psychooncology and neuroscience allows for both a better understanding of disease processes and the development of more effective and individualized intervention strategies. Neuroimaging and neuropsychological assessment studies reveal that psychotherapeutic approaches - particularly Cognitive Behavioral Therapy (CBT), Eye Movement Desensitization and Reprocessing Therapy (EMDR) and mindfulness-based methods - promote neuroplasticity and have therapeutic effects on the brain (Shapiro 2001, Zeidan et al. 2016, Beck 2020).

The main aim of this review is to examine the neurobiology of cancer in interaction with psychosocial factors and to evaluate psychotherapeutic approaches that may be effective in these processes in the light of scientific literature. In this direction, the contribution of the interactions between the nervous system and the immune system to tumor development, the cognitive and emotional effects of oncological treatments, and the effects of psychotherapies on neurobiological foundations are discussed from a holistic perspective. It also emphasizes the importance of multidisciplinary approaches in treatment processes. This review aims to help us understand the potential of psychotherapeutic approaches in the fight against cancer.

Neurobiology of Cancer and Psychooncology Effects

Cancer is not only the result of genetic mutations and immunological mechanisms; it is also closely related to psychological and neurobiological processes (Mravec 2021). The biological mechanisms of cancer have been investigated for many years, but recent studies have increasingly revealed the influence of psychosocial factors on cancer development and progression. Psychosocial factors such as stress, depression and social isolation are known to contribute to the progression of cancer and have a significant impact on an individual's overall health (Henneghan et al. 2020). Therefore, cancer should not only be treated as a biological disease but should be addressed from a holistic perspective.

Understanding the neurobiology of cancer is critical to more effectively manage the occurrence, progression and treatment of the disease. In particular, the effects of psychosocial stress on the neuroendocrine system may promote tumor growth by directly affecting the regulation of immune responses (Monje and Dietrich 2012). In this context, research on the neurobiology of cancer helps us better understand the interaction between the brain and the immune system, making treatments more precise.

The combination of psychooncological and neuroscientific perspectives offers a holistic approach to

explaining the complex nature of cancer. The neuroscientific perspective allows us to understand how cancer interacts with the nervous system, how stress alters biological processes and how neuroinflammation contributes to the disease course. On the other hand, the psychooncological perspective explores how patients' psychological well-being plays a role in the fight against cancer and how cognitive-behavioral therapies can support treatment processes. The intersections of these two disciplines emphasize why multidisciplinary approaches to cancer treatment are important.

A diagnosis of cancer can cause intense psychological burden in individuals, which can lead to various functional changes in regions of the brain responsible for emotion regulation, memory processing and coping with stress (e.g. amygdala, hippocampus and prefrontal cortex) (Carletto and Pagani 2016). At the same time, there is increasing research on how psychooncological approaches can modulate these processes. Neuroscientific research suggests that brain changes associated with trauma and stress are reversible through psychotherapeutic interventions.

Nervous System and Cancer

A diagnosis of cancer can cause high levels of psychological stress in individuals. This stress leads to over-activation of the HPA axis, increasing cortisol release. As a result, neuroplasticity is impaired in the hippocampus region, leading to loss of cognitive function and impairments in mood regulation. The sustained activation of the HPA axis by chronic stress may trigger inflammation in the tumor microenvironment by suppressing the immune system and contribute to cancer progression (Mravec 2021). Furthermore, stress has been shown to directly signal tumor cells through sympathetic nervous system activation and accelerate the metastasis process. Neuroimaging studies in PTSD and cancer patients reveal hyperactivity of the amygdala and decreased function of the prefrontal cortex, supporting the neurobiological basis of trauma-related symptoms.

The interaction between the nervous system and the immune system is central to understanding the neurobiology of cancer. These interactions not only shape the tumor microenvironment but also influence the disease process through neural processes such as neuroinflammation, neurotransmitter levels and neuroplasticity. The suppression of the immune system by psychosocial stress through the HPA axis and the sympathetic nervous system can lead to various physiopathological changes at the neurobiological level, accelerating tumor progression (Davidson and McEwen 2012, Mravec 2021). In this chapter, these neurobiological mechanisms are discussed in more detail and the biochemical and cellular processes underlying the interaction of cancer with the nervous system are explained.

Neurobiological Mechanisms

Neurobiological mechanisms which are involved in cancer progression comprise multilayered processes involving the interplay between the nervous system and the immune system. These mechanisms include the effects of neurotransmitters, immune cells and stress response systems on the tumor microenvironment. Stress hormones such as norepinephrine and epinephrine can increase the proliferation and angiogenesis capacity of tumor cells through β-adrenergic receptors. Signaling of these neurotransmitters to tumor cells may lead to remodeling of the extracellular matrix and facilitate metastasis (Eng et al. 2014, Cole et al. 2015). Evidence that pharmacological blockade of these receptors reduces the rate of progression of some types of cancer suggests that neurobiological interactions offer therapeutic targets. However, the suppressive effects of chronic psychological stress on the immune system are also an important mechanism. Reduced activity of cytotoxic T cells and natural killer (NK) cells leads to weakened immune surveillance against cancer cells (Sanada et al. 2017). This immunosuppression facilitates tumors to escape the immune system and proliferate more rapidly.

Another important neurobiological problem that arises during the cancer process is neuropathic pain. Direct pressure of the tumor on nerve tissues, damage to nerve fibers or environmental inflammation are among the main causes of this type of pain. Neuropathic pain is not only a physical symptom; it is also a factor that severely affects the patient's emotional resilience and quality of life (Eng et al. 2014). Recent

research suggests that neuromodulation and interventions at the central nervous system level may be effective in the management of this pain.

One of the most investigated neurobiological effects of oncologic treatment is chemotherapy-induced cognitive impairment. This syndrome, known as chemobrain, is characterized by marked impairments in attention, memory, executive functions and information processing speed. Chemotherapy-induced neuroinflammation can cause neural damage, especially in brain regions vulnerable to neurogenesis, such as the hippocampus, preventing the formation of new neurons (Monje and Dietrich 2012). Increased oxidative stress, DNA damage and impaired synaptic plasticity also play an important role in this process (Ahles and Root 2018). These biological impairments may cause not only temporary but also permanent neurocognitive effects in some patients.

In addition to all these mechanisms, cancer diagnosis and treatment increase the risk of developing depression and anxiety disorders in individuals, which further complicates neurobiological responses. Depression and anxiety can create suppressive effects on the immune system by disrupting the balance of both the HPA axis and neurotransmitter systems (Davidson and McEwen 2012, Cole et al. 2015, Lutgendorf and Andersen 2015, Ahles and Root 2018). Therefore, understanding the neurobiological correlates of psychological processes is critical for both planning psychooncological interventions and developing more holistic treatment strategies.

Psychological Effects of Treatment

Understanding neurobiological mechanisms provides an important basis for explaining not only the processes of cancer development and progression, but also the cognitive and emotional side effects of treatment. Common oncological interventions such as chemotherapy, radiotherapy, hormone therapy, and immunotherapy can leave permanent scars on the central nervous system, leading to neuropsychological disorders such as chemobrain, neuropathic pain, depression, and attention-memory problems (Monje and Dietrich 2012, Ahles and Root 2018). These effects can profoundly affect patients' quality of life not only on a biological level but also on a psychological and functional level. Therefore, evaluating the psychological and cognitive consequences of cancer treatments from a multidimensional perspective forms the basis of psychooncologic care. Most of the existing studies are based on short-term follow-up data; follow-up of long-term effects is still limited. Moreover, it is controversial in the literature whether cognitive impairment after chemotherapy is directly related to the treatment or to other comorbid psychosocial factors.

Psychological and Cognitive Effects of Chemotherapy

Although chemotherapy is one of the most widely used methods in cancer treatment, it is not limited to physical side effects; it can also cause significant impairment in cognitive and emotional functions. These effects have important psychooncologic consequences that directly affect patients' quality of life and compliance with treatment. Among the most common cognitive side effects is the syndrome commonly known as chemobrain. Chemobrain is characterized by impairments in attention, memory, information processing speed and executive functions. These symptoms may start during the treatment process or may persist for a long time after the end of treatment in some individuals (Wefel and Schagen 2012).

Neuroscientific research is increasingly revealing the mechanisms behind these cognitive deficits. Chemotherapy-induced neuroinflammation in the brain leads to neural damage, especially in regions of neurogenesis such as the hippocampus, which prevents the formation of new neurons (Monje and Dietrich 2012). Furthermore, increased oxidative stress, DNA damage and impairments in synaptic plasticity further impair the cognitive functions of the brain (Ahles and Root 2018). These biological effects are not only limited to cognitive functions but can also cause significant changes in emotional state. Fatigue, loss of motivation and depressive symptoms due to chemotherapy are commonly observed in some patients (Ahles and Root 2018). These effects become more pronounced, especially in prolonged treatment processes, and may negatively affect the functionality in the social and professional life of the individual.

Psychological and Cognitive Effects of Radiotherapy

Radiotherapy can significantly affect cognitive and psychological functions, especially when applied close to the central nervous system. The severity and persistence of these effects may vary significantly depending on the type and stage of cancer. In primary brain tumors or cancers close to the head and neck region, neurocognitive effects such as short-term memory problems, distraction and impairment in executive functions are common due to the direct effect of radiation on brain tissue. These effects are associated with radiotherapy-induced inflammation, edema and decreased white matter integrity may increase the risk of cognitive decline in the long term (Monje and Dietrich 2012, Wefel and Schagen 2012). Furthermore, radiotherapy techniques affecting the hippocampal region have been shown to leave lasting effects on neurogenesis. In contrast, in non-brain tumors, such as breast or prostate, cognitive side effects often occur through more indirect pathways, for example through neuroinflammation, systemic fatigue or insomnia. These effects are often transient and may diminish over time in some patients (Ahles and Root 2018, Kesler et al. 2023). The stage of cancer is also a determining factor in psychological effects. In early-stage patients, factors such as uncertainty about the radiotherapy process, diagnostic shock and future anxiety are at the forefront, while in advanced cancers, symptoms such as fatigue, loss of physical function and pain may trigger mood disorders such as depression, hopelessness and death anxiety (Joly et al. 2020, Khan et al. 2021, Sharpe et al. 2022, Farina et al. 2023, Yin et al. 2023). Especially in patients receiving prolonged or high-dose radiotherapy, cancer-related fatigue and major depressive symptoms are frequently observed. These effects are not limited to physical side effects; they have a profound impact on patients' adherence to treatment, daily life functioning and overall quality of life. Therefore, it is of great importance to assess the potential psychological and cognitive consequences of radiotherapy in advance and to implement individualized support programs.

Psychological and Cognitive Effects of Hormone Therapy

Hormone therapy is a common treatment for hormone-sensitive cancers, especially breast and prostate cancer. However, this treatment not only suppresses the growth of tumor cells but can also have various effects on brain function and mood regulation. Artificially lowering hormone levels can lead to significant changes on both cognitive and psychological levels. Decreased levels of estrogen or testosterone can cause neurochemical changes in brain regions responsible for mood and cognitive processing, particularly in the hippocampus and prefrontal cortex. These changes can lead to impairments in memory, attention, verbal fluency and executive functions. Some studies have shown that symptoms such as decreased verbal memory performance, mental fatigue, and slowing of cognitive speed in breast cancer patients receiving estrogen suppressive therapy emerged from the first months of treatment (Ahles and Root 2018). Similarly, androgen deprivation therapy (ADT) used in the treatment of prostate cancer may have negative effects on cognitive functions. Declines in working memory, visuospatial skills and attention have been reported in men undergoing ADT. It is stated that these effects are more pronounced especially in older patients and cognitive impairments may become permanent with long-term treatment (Wefel and Schagen 2012, Kesler et al. 2023).

On a psychological level, symptoms such as depression, anxiety and emotional sensitivity are common with decreasing hormone levels. This is due to the regulatory role of hormones, which are not only physical but also directly affect mood through neurotransmitter systems (Davidson and McEwen 2012). A decrease in the supportive effect of estrogen on the serotonergic system may cause mood fluctuations, especially in female patients. Similarly, low testosterone has been associated with loss of motivation, increased anxiety and emotional withdrawal in men. These effects can severely affect patients' quality of life, especially in long-term hormone suppressive therapies. Therefore, both the cognitive and emotional status of patients undergoing hormone therapy should be monitored regularly, and psycho-oncological support and cognitive rehabilitation should be integrated into the process if necessary.

Psychological and Cognitive Effects of Immunotherapy

In recent years, immunotherapies, which have become increasingly common in cancer treatment, offer an

effective and targeted therapeutic approach by activating the immune system against tumor cells. However, these treatments can have significant effects not only on physical health but also on psychological functions and neurocognitive processes. A fundamental role in understanding these effects is played by the bidirectional communication between the immune system and the brain. Immunotherapies can trigger inflammatory processes in the brain by increasing cytokine release. Increases in proinflammatory cytokines such as interleukin-6 and TNF-α are associated with neuroinflammation, neural network dysfunction, and cognitive impairment (Ahles and Root 2018). This process can lead to symptoms in some patients defined as immune-related brain fog, such as attention deficits, slowed thinking, memory difficulties, and cognitive fatigue (Sharpe et al. 2022). These effects may vary depending on the type of cancer. For example, in metastases close to the central nervous system or in brain-related tumors, the effects of immunotherapy may be felt more directly, whereas in immunotherapy-responsive cancers such as breast, lung, or skin cancer, inflammatory responses may be more systemic but widespread. Additionally, the stage of cancer is also a determining factor: in advanced or metastatic cancers, immunotherapies are often administered through long-term and intensive protocols, which can lead to more severe and persistent symptoms such as cognitive slowing, mental fatigue, and emotional instability (Joly et al. 2020, Yin et al. 2023).

Table 1. Cognitive and psychological effects by type of treatment

Treatment Type	Cognitive Effects	Psychological Effects	Variation by Cancer Type/Stage	Need for Intervention
Chemotherapy	Impairments in attention, memory, executive functions; "chemo brain"; neuroinflammation; reduced neurogenesis	Depression, fatigue, anxiety	Cognitive effects may be observed across all cancer types; effects tend to be more persistent in advanced stages and prolonged treatments	Cognitive rehabilitation, psychotherapy (especially CBT, mindfulness) recommended
Radiotherapy	White matter damage, slowed information processing, cortical thinning (especially when applied near the brain)	Anxiety, uncertainty related to treatment, depressive symptoms	Effects are more direct and severe in brain-adjacent tumors; fatigue and depression are more common in advanced stages	Psychoeducation, anxiety management, cognitive interventions supporting attention and memory are recommended
Hormone Therapy	Slowing in verbal memory, attention, and executive functions; changes in neurotransmitter systems	Mood fluctuations, depression, anxiety	Common in breast and prostate cancer; cognitive decline may become more pronounced with long-term use	Psychological support, training in cognitive strategies, mood monitoring
Immunotherapy	Brain fog, attention deficits, memory problems, cognitive slowing; increased inflammatory cytokines	Fatigue, irritability, depressed mood, sleep disturbances	Frequently seen in melanoma, lung, and renal cancers; effects more intense in advanced stages and prolonged treatments	Neuropsychological assessment, stress management, psychoeducation, pharmacological support if necessary

(Davidson and McEwen 2023, Zeidan et al. 2023)

On a psychological level, the activation of the immune system caused by immunotherapies can affect the HPA axis and neurotransmitter systems, leading to symptoms such as anxiety, irritability, depressed mood, and low motivation in patients. These symptoms become particularly pronounced during long-term treatment processes and can negatively impact the patient's overall quality of life, social functioning, and treatment adherence (Davidson and McEwen 2012, Zeidan et al. 2016). Therefore, it is important to regularly

monitor the psychological and cognitive functions of patients undergoing immunotherapy and, when necessary, integrate neuropsychological assessments, psychoeducation, mood-regulating interventions, and stress management techniques into the treatment process.

Neuropsychological Approaches

The cognitive and emotional difficulties arising from cancer treatments can significantly affect patients' quality of life; thus, neuropsychological approaches play a critical role in the evaluation and management of these effects. These approaches provide multifaceted information in both diagnostic and intervention planning processes.

Neuropsychological Assessment

Neuropsychological assessments allow for a detailed evaluation of cognitive functions in cancer patients. Assessing neurocognitive functions is especially crucial for identifying changes in attention, memory, and executive control. Since these impairments vary depending on the clinical presentation, it is important that test batteries are structured according to the targeted symptoms to ensure accurate measurement (Wefel and Schagen 2012, Ahles and Root 2018).

There are tests that evaluate different functions of neuropsychological assessments. The Wechsler Memory Scale measures verbal and visual memory capacity and is especially used for chemotherapy-related memory impairments and temporal lobe involvement (Monje and Dietrich, 2012). The Stroop Test assesses attention, cognitive control, and inhibition ability and is particularly effective for patients suspected of executive dysfunction following brain tumors or hormone therapy (Monje and Dietrich, 2012). The Trail Making Test A-B measures processing speed and cognitive flexibility/set-shifting skills and is frequently preferred for evaluating cognitive slowing or attention deficits after radiotherapy (Wefel and Schagen 2012). The Wisconsin Card Sorting Test evaluates cognitive flexibility, abstract thinking, and problem-solving abilities and provides significant results for patients with frontal cortex damage or executive function impairments (Sharpe et al. 2022). The Digit Span Test measures short-term memory and attention span and is used to assess severe attention deficits or early signs of chemo brain syndrome (Ahles and Root 2018). The choice of these tests should be shaped according to cancer type, stage, treatment method, and the patient's current complaints. However, before applying a comprehensive test battery, conducting a preliminary assessment with short and structured screening scales is highly valuable both for practicality and guidance (Wefel and Schagen 2012, Ahles and Root 2018).

In clinical practice, due to factors such as patient fatigue, time constraints, or treatment conditions, the use of brief and effective screening tools is important. These scales aim to quickly detect potential neurocognitive impairments and determine whether further testing is necessary (Wefel and Schagen 2012). There are several tools available for cognitive assessment in cancer patients. The Montreal Cognitive Assessment (MoCA) is a short test covering memory, attention, executive function, language, and visuospatial skills, and it is reported to be more sensitive than the MMSE in detecting mild cognitive impairment (Ahles and Root 2018). The FACT-Cog (Functional Assessment of Cancer Therapy – Cognitive Function) is a self-report scale developed specifically for cancer patients, evaluating perceived cognitive deficits, attention problems, and their impact on quality of life (Sharpe et al. 2022). The Cognitive Failures Questionnaire (CFQ) is another self-report tool that assesses how frequently patients experience cognitive failures in daily life, providing an effective initial screening when used alongside clinical interviews (Broadbent et al. 1982). Lastly, the Mini-Mental State Examination (MMSE) is a tool used to assess general cognitive status, but it may miss mild impairments in highly educated individuals.

In a structured clinical interview, clues about cognitive performance can be obtained. For this purpose, questions such as "Have you been experiencing forgetfulness recently?", "Do you find it difficult to concentrate?", "Are tasks that you used to do easily now becoming difficult for you?", and "Do you feel that your thoughts have slowed down or that your mind feels foggy?" may be asked. These types of questions are used to reveal changes in an individual's cognitive functions. If a person experiences symptoms such as forgetfulness, attention deficits, difficulty performing tasks, or mental fog, such interviews can help

determine whether there is a problem with cognitive performance. In this way, it is possible to assess the person's mental health and provide appropriate treatment or support if necessary. These preliminary assessments are guiding both for early detection of cognitive impairments and for identifying the need for rehabilitation. Based on the screening results, detailed neuropsychological testing can be planned, or the individual can proceed directly to an intervention program (Kesler et al. 2023).

In the post-diagnosis process, cognitive rehabilitation programs provide a fundamental approach to managing treatment-related cognitive impairments in cancer patients. These programs include structured interventions aimed at optimizing patients' cognitive functions and improving daily living skills. Commonly used techniques in cognitive rehabilitation include cognitive strategy training, attention management, memory strategies, and tasks aimed at enhancing executive functions. For example, computer-assisted cognitive training programs target specific cognitive domains such as memory and attention to achieve effective outcomes (Kesler et al. 2023). Additionally, psychotherapeutic interventions like mindfulness and attention-based approaches are used as effective tools to enhance both cognitive and emotional well-being (Sharpe et al. 2022).

The effective implementation of cognitive rehabilitation should be supported by a multidisciplinary approach. Collaboration among psychologists, neurologists, oncologists, and rehabilitation specialists enables the design of personalized interventions tailored to patients' needs. Moreover, individualized approaches allow patients to better cope with cognitive impairments and adapt more effectively to the treatment process. Recent research shows that such programs provide improvements not only in cognitive functions but also in patients' overall quality of life (Wefel and Schagen 2012). Neuropsychological approaches in psycho-oncology play a critical role in assessing and managing cognitive impairments caused by cancer treatments. The effective use of diagnostic tools and the integration of cognitive rehabilitation programs contribute to optimizing both treatment processes and patient quality of life.

Neuropsychotherapeutic Applications

Cancer diagnosis and treatment impose significant burdens not only at the physical level but also at the cognitive and emotional levels. Therefore, psycho-oncological interventions can serve not only supportive but also reparative functions at neurobiological and neuropsychological levels. Particularly in recent years, strong scientific evidence has accumulated showing that certain psychotherapeutic approaches have positive effects on brain structure and functioning (Davidson and McEwen 2012). Although the effects of CBT in the oncology context are generally reported with positive findings, it is noteworthy that the effect sizes reported in studies vary considerably. It is thought that cultural factors, individual coping styles, and the quality of the therapeutic alliance may play roles in these differences. Among the neuropsychotherapeutic methods commonly applied to cancer patients, CBT, EMDR, and Mindfulness-Based Interventions stand out. These approaches not only enhance psychological well-being but also support cognitive functions by regulating the neurobiological effects of stress.

Cognitive Behavioral Therapy (CBT)

CBT is a structured psychotherapy method aimed at transforming negative thought patterns by targeting cognitive distortions frequently seen in cancer patients. This approach seeks to alleviate emotional burdens by restructuring patients' beliefs about diagnosis, treatment, and life. Research has shown that CBT not only reduces symptoms of depression and anxiety but also strengthens cognitive control mechanisms by increasing prefrontal cortex activity (Beck 2020). These neurocognitive changes facilitate emotional regulation and improve patients' stress coping skills. Additionally, the regulatory effects of CBT on the HPA axis reduce systemic stress response by balancing cortisol release related to stress and contribute to strengthening the immune system (Monje and Dietrich 2012). These biological effects play a crucial role in mitigating the long-term impacts of chronic stress associated with cancer treatment.

The use of CBT programs designed for managing psychosocial stress in cancer patients is becoming increasingly widespread. For example, a study on the Women Do Cognitive Behavioral Therapy Program demonstrated that this method reduces levels of depression and anxiety while increasing levels of hope

(Savaş 2024). Similarly, online CBT-based stress management programs have been found to strengthen coping with stress, especially in breast cancer patients undergoing chemotherapy, and to positively affect psychosocial adjustment and anxiety management (Savaş 2024). These findings indicate that CBT is an effective therapy method at both psychological and neurobiological levels and provides a holistic contribution to the adaptation processes in cancer patients.

Eye Movement Desensitization and Reprocessing Therapy (EMDR)

EMDR is an effective psychotherapy method that alleviates trauma, anxiety, and stress responses developing after a cancer diagnosis by facilitating the reprocessing of traumatic memories. A cancer diagnosis can cause a profound shock not only physically but also emotionally and cognitively for most individuals. EMDR enables the adaptive reprocessing of these traumatic experiences, providing both psychological relief and neurobiological recovery. Systematic review studies also support the effectiveness of EMDR as a psychotherapy method in cancer patients (Portigliatti et al. 2021).

The bilateral stimulation used in EMDR supports information transfer between the right and left hemispheres of the brain. This process facilitates the extraction of traumatic content from episodic memory and its transfer to semantic memory. Neuroimaging studies reveal that EMDR decreases limbic system activity, regulates neural communication between the prefrontal cortex and amygdala, improves emotional regulation, and supports neuroplasticity in the hippocampus region (Shapiro 2001, van der Kolk 2014, Carletto and Pagani 2016).

In cancer patients, the process of synaptic remodeling alleviates symptoms such as anxiety, insomnia, and loss of control. EMDR reduces cortisol responses to stress and enhances learning and adaptation. The EMDR Flash Technique, derived from the classical EMDR protocol, is a gentle and rapid intervention that enables working without direct exposure to traumatic memories. It is based on the principle that the client briefly activates the distressing memory mentally while simultaneously being directed to a positive focus of attention. The therapist manages attention shifts during this process with intermittently delivered "flash" commands.

Research shows that the Flash Technique rapidly reduces PTSD symptoms, decreases emotional intensity, and can be applied with less distress compared to classical EMDR (Wong 2023). It is also suggested that the Flash Technique effectively engages working memory capacity and makes reprocessing traumatic material more accessible (Wong 2023). For this reason, it is a preferred approach particularly for cancer patients who have dissociative tendencies or exhibit intense emotional reactions. EMDR and the Flash Technique provide holistic support to the psychological processes of cancer patients. These methods not only help alleviate symptoms but also produce positive outcomes in areas such as neurobiological stress regulation, increased emotional resilience, and the development of cognitive balance and adaptation skills. The integration of EMDR techniques into clinical protocols is especially important to reduce the impacts of traumatic experiences during the cancer treatment process (diagnosis, treatment, losses, uncertainty).

Mindfulness-Based Approaches

Mindfulness-based approaches aim to direct an individual's attention consciously and non-judgmentally to the present moment. They offer an effective intervention area for coping with stress, anxiety, depression, cognitive fog, and adjustment difficulties commonly seen in cancer patients. These approaches are structured and implemented primarily through Mindfulness-Based Stress Reduction and Mindfulness-Based Cognitive Therapy protocols. These therapeutic programs help patients develop a more conscious, accepting, and flexible attitude toward stressful thoughts, thereby strengthening emotional resilience, self-compassion, and psychological flexibility (Zeidan et al. 2016).

Recent research shows that mindfulness practices have direct effects on brain structure and function. These practices lead to increases in gray matter volume in brain regions such as the hippocampus and prefrontal cortex (Tang et al. 2015) and promote neuroplasticity in areas associated with attention and emotional regulation (Shao et al. 2021). Additionally, mindfulness reduces cortisol levels, thereby regulating

stress responses and strengthening the immune system. Mindfulness-based interventions have been found effective in managing uncertainty, loss of control, and physical fatigue during the post-diagnosis period and treatment process. Clinical studies have demonstrated that mindfulness reduces symptoms of stress, anxiety, and depression (Labelle et al. 2010), improves sleep quality, and alleviates fatigue and pain perception (Zainal et al. 2013). In the long term, mindfulness positively influences patients' treatment adherence and motivation for survival (Lengacher et al. 2016). Therefore, mindfulness is used as a therapeutic tool supporting recovery both psychologically and neurobiologically.

Mindfulness programs, including techniques such as meditation, yoga, breath awareness, and body scanning, can be applied in both individual and group formats. Their use is increasingly common, especially in breast cancer, hematologic malignancies, and advanced-stage cancer patients. Within a neuropsychotherapeutic framework, mindfulness-based interventions provide holistic recovery at both psychological and physiological levels. Their effects on cortisol regulation, neuroplasticity, and immune response have made these approaches not only supportive but also evidence-based and transformative therapies. In addition to improving quality of life in cancer patients, mindfulness balances stress responses, thereby creating a healthier psychological foundation for treatment.

However, the effectiveness of mindfulness-based interventions has shown inconsistent findings in the literature (Goyal et al. 2014, Davidson and Kaszniak 2015). Some meta-analyses report significant effects (Gotink et al. 2016), while other studies have not found a direct relationship between neuroimaging findings and clinical improvement (Fox et al. 2014, Tang et al. 2015).

Neuroplasticity and Treatment Effects

Neuroplasticity refers to the brain's ability to make structural and functional adaptations in response to experiences, learning, and environmental changes. This capacity underlies one of the fundamental mechanisms driving the effectiveness of psychotherapeutic interventions. Particularly, CBT, EMDR, and mindfulness-based approaches activate neuroplasticity processes, supporting the brain's remodeling and facilitating improvements in stress coping, emotional regulation, and cognitive functions (Davidson and McEwen 2012).

CBT increases prefrontal cortex activity through interventions aimed at modifying dysfunctional thought patterns, regulates amygdala responses, and thereby enhances emotional regulation. During this process, cognitive control circuits are strengthened, forming a neural structure protective against mood disorders (Beck 2020). EMDR, especially effective in processing traumatic memories, facilitates the reorganization of neural connections among structures such as the hippocampus, anterior cingulate cortex, and amygdala. It supports neuroplasticity by reducing trauma-related hyperactivation and balancing processing systems (Pagani et al. 2012, van der Kolk 2014). Mindfulness-based practices induce neuroanatomical changes by increasing gray matter volume in brain regions related to attention and emotional regulation—such as the anterior insula, prefrontal cortex, and hippocampus (Tang et al. 2015).

These approaches not only reduce current symptoms but also enhance patients' capacity to cope with future challenges, thereby strengthening long-term psychological resilience. Therapies that support neuroplasticity provide multifaceted benefits such as increased emotional flexibility, cognitive adaptation, and improved quality of life (Davidson and McEwen 2012, Shao et al. 2021).

The literature on the cognitive effects of immunotherapy and hormone treatments remains limited and heterogeneous (Wefel and Schagen 2012, Ahles and Root 2018, Joly et al. 2020, Kesler et al. 2023). Another factor limiting the widespread use of cognitive rehabilitation programs in clinical practice is the lack of standardization (Wefel and Schagen 2012, Kesler et al. 2023).

Conclusion

This review reveals that cancer is closely related not only to biological processes but also to psychological and neurobiological mechanisms. Recent randomized controlled trials have demonstrated that psychotherapeutic interventions produce significant effects on neuroplasticity and regulate physiological

systems that may indirectly contribute to tumor progression (Lutgendorf and Andersen 2015). Psychosocial stress plays a critical role in tumor development and progression through the neuroendocrine and immune systems. The cognitive and emotional effects of cancer treatments are explained by mechanisms such as chemobrain, neuropathic pain, and neuroinflammation; these effects can be better understood through neuroscientific and psycho-oncological approaches. Psychotherapeutic interventions, particularly CBT, EMDR, and mindfulness-based techniques, not only enhance psychological well-being but also support neuroplasticity, playing an important role in preserving cognitive functions. Neuropsychological assessments and cognitive rehabilitation programs enable the development of individualized intervention plans tailored to patients' specific needs and contribute valuable support to the treatment process through a multidisciplinary approach.

The standardization of neuropsychological assessment procedures in cancer patients undergoing treatment is emphasized as crucial. Early Identification and management of cognitive impairments become possible through such standardization. Integrating psycho-oncological and neuropsychotherapeutic interventions into oncological treatment processes holds potential for improving patients' quality of life. It is recommended that approaches that enhance neuroplasticity—such as mindfulness, EMDR, and CBT—be incorporated more systematically into clinical protocols. Multidisciplinary teamwork, involving psychologists, neurologists, oncologists, and rehabilitation specialists, will facilitate the creation of individualized intervention plans in collaboration. Increased research in this field will deepen our understanding of the impact of psychosocial factors on the neurobiological mechanisms of cancer, thereby enabling the development of holistic, biopsychosocial-based approaches to cancer treatment.

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