# Evidence of brain-derived **neurotrophic factor (BDNF) in ameliorating can**cer-related cognitive impairment: A systematic review of human studies

# Good evening, dear colleagues. My name is Lina. I`m a newcomer in the English medical translation realm but I`ll do my best to fascinate you by the subject arisen. Today I`d like to garner your attention to the neurotrophic factor efficient at alleviating cognitive impairment caused by cancer-related diseases.

# Cancer-related [cognitive impairment](https://www.sciencedirect.com/topics/medicine-and-dentistry/cognitive-defect) (CRCI), often referred to as “chemobrain”, is prevalent in up to 75 % of all cancer survivors. CRCI encompasses such symptoms as memory loss, inability to concentrate, poor response speed, and executive functioning. Brain-derived neurotrophic factor (BDNF) secreted by neurons is a significant component of synaptic plasticity. In humans, it is also present in blood platelets where it is accumulated following its biosynthesis in megakaryocytes. There is growing evidence that BDNF levels are thus readily detectable in the human serum and it has been abundantly speculated that they may somehow serve as an indicator of brain function. Expressed by the BDNF gene, BDNF belongs to the [neurotrophin](https://www.sciencedirect.com/topics/medicine-and-dentistry/neurotrophin%22%20%5Co%20%22Learn%20more%20about%20neurotrophin%20from%20ScienceDirect%27s%20AI-generated%20Topic%20Pages) superfamily and plays an essential role in the [neurogenesis](https://www.sciencedirect.com/topics/medicine-and-dentistry/neurogenesis) and neuroplasticity of the brain. BDNF signaling, via [tropomyosin receptor kinase B](https://www.sciencedirect.com/topics/medicine-and-dentistry/tropomyosin-receptor-kinase-b) (TrkB) receptors, supports the survival of existing neurons and facilitates the proliferation and differentiation of new neurons and synaptic plasticity in both the central and peripheral nervous systems. BDNF is extensively distributed within the central nervous system (CNS), highly expressed in the [hippocampus](https://www.sciencedirect.com/topics/medicine-and-dentistry/hippocampus), cortex, and [basal forebrain](https://www.sciencedirect.com/topics/medicine-and-dentistry/basal-forebrain). In particular, BDNF’s involvement in [neurotransmitter release](https://www.sciencedirect.com/topics/medicine-and-dentistry/neurotransmitter-release) and long-term potentiation is important to learning and memory consolidation.

# BDNF downregulation

# Numerous studies have unfolded that BDNF downregulation results in such cognitive disorders as Huntington’s disease, Alzheimer’s disease (AD), depression, schizophrenia, bipolar, and anxiety disorders. BDNF protein is also detectable outside of the nervous system in several non-neuronal tissues, such as in endothelial cells, cardiomyocytes, vascular smooth muscle cells, leukocytes, platelets, and megakaryocytes. Therefore, it may also be involved in cancer, angiogenesis, reduction of glucose production from the liver, and in the uptake of glucose in peripheral tissues. In addition, BDNF promotes the development of neuromuscular synapses and is required for fiber-type specification, suggesting a potential role as a therapeutic target in muscle diseases. In this review, we touch on the newly emerging role of BDNF in the pathogenesis of brain gliomas.

# BDNF and Brain Cancer

# Not a long time ago the study showed that exposing mice to an enriched environment is able to decrease the growth of intracranial glioma, decreasing proliferation and invasion, and improving overall survival. Such an effect is achieved by means of both indirect and direct mechanisms. The former acts via natural killer cells of the innate immune system, whereas the latter utilizes BDNF stimulation of its truncated receptor TrkB.T1 on glioma cancer cells. BDNF binding the TrkB.T1 receptor signals to the Rho protein dissociation inhibitor (RhoGDI), the latter detaches from TrkB.T1 and binds to the small G protein RhoA, leading to its inhibition. The authors found that an enriched environment causes the synthesis of IL-15 and BDNF. When mice bearing the glioma and not housed in enriched environments were infused with BDNF, they reduced tumor size and macrophage infiltration. Thus, showing that at least in part, BDNF accounts for the oncolytic effect elicited by the enriched environment. In a more recent study, the same group delved deeper into the mechanisms, finding that enriched environment changes glioma-associated myeloid cells. BDNF plays a central role by stimulating the production of IL-15 in microglia, which in turn stimulates the natural killer cells to produce IFN-γ. Natural killer cells were responsible for the switch to an oncolytic environment. Taken together, a scenario emerges where BDNF, acting on different cells is able to reorganize the brain microenvironment in such a way that it becomes resilient to neurodegeneration or oncolytic for tumors. In this regard, although supported by much more preliminary data, it seems that also other compounds might share these properties.

# Considering BDNF properties from different angles it is worth mentioning that low serum levels have been correlated with AD and [mild cognitive impairment](https://www.sciencedirect.com/topics/medicine-and-dentistry/mild-cognitive-impairment), and high serum BDNF levels have been associated with better cognition in healthy older adults. Many factors, including age, degree of exercise and [single nucleotide polymorphisms](https://www.sciencedirect.com/topics/medicine-and-dentistry/single-nucleotide-polymorphism) (SNPs) of the BDNF gene, may impact BDNF levels and subsequently cognitive performance, suggesting that BDNF is an important target for the study of cognitive health.

# Exposure to [neurotoxins](https://www.sciencedirect.com/topics/medicine-and-dentistry/neurotoxin)

# Exposure to [neurotoxins](https://www.sciencedirect.com/topics/medicine-and-dentistry/neurotoxin) has been linked to long-term cognitive disturbances because of long-lasting reductions of BDNF mRNA levels in the brain. Therefore, it is postulated that the neurotoxic effects of chemotherapy on BDNF expression can occur after the completion of chemotherapy and in cancer survivors, resulting in CRCI. However, it is currently unknown whether BDNF as a biomarker is associated with cognitive changes in cancer patients receiving chemotherapy and whether BDNF alone is an effective biomarker to evaluate the success of interventions for improving cognitive health in cancer patients. To evaluate whether BDNF is a potential monitoring or therapeutic target for CRCI, a systematic review was conducted to assess the association between BDNF biomarkers and cancer-related neurocognitive outcomes in the current literature.

# BDNF levels and Cognitive Performances in Observational Studies

A total of 10 observational studies assessed the association between BDNF levels and cognitive performances. Of these studies, five (50 %) demonstrated a positive association. Four of these studies revealed a positive association between BDNF levels and objective cognitive tests, including patients diagnosed with [multiple myeloma](https://www.sciencedirect.com/topics/medicine-and-dentistry/multiple-myeloma), [metastatic cancer](https://www.sciencedirect.com/topics/medicine-and-dentistry/metastatic-carcinoma), B-cell non-Hodgkin lymphoma (B-cell NHL), and hepatocellular carcinoma (HCC). One study evaluated intra-tumoral levels of BDNF in diffuse [glioma](https://www.sciencedirect.com/topics/medicine-and-dentistry/ganglioglioma) patients and reported a negative association with memory.

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| brain-derived neurotrophic factor (BDNF) | нейротрофический фактор головного мозга |
| cancer-related cognitive impairment (CRCI) | нарушения когнитивных функций на фоне раковых заболеваний |
| “chemobrain” | «химический мозг» |
| basal forebrain | базальный передний мозг |
| Huntington’s disease | болезнь Гентингтона |
| truncated receptor | усеченный, укороченный рецептор |
| microglia | микроглии |
| IFN-γ | интерферон гамма |
| oncolytic | онколитический |
| B-cell non-Hodgkin lymphoma (B-cell NHL) | В-клеточная неходжкинская лимфома (НХЛ) |
|  [tropomyosin receptor kinase B](https://www.sciencedirect.com/topics/medicine-and-dentistry/tropomyosin-receptor-kinase-b) (TrkB) | киназа рецептора тропомиозина B |