Brain-derived Neurotrophic Factor

Authored by

mohammad looti

June 13, 2026

Brain-derived neurotrophic factor, also known as BDNF, is a protein that, in humans, is encoded by the BDNF gene. BDNF is a member of the "neurotrophin" family of growth factors, which are related to the canonical "Nerve Growth Factor", NGF. Neurotrophic factors are found in the brain and the periphery.

Function

BDNF acts on certain neurons of the central nervous system and the peripheral nervous system, helping to support the survival of existing neurons, and encourage the growth and differentiation of new neurons and synapses. In the brain, it is active in the hippocampus, cortex, and basal forebrain--areas vital to learning, memory, and higher thinking. BDNF itself is important for long-term memory. BDNF was the second neurotrophic factor to be characterized after nerve growth factor (NGF).

Although the vast majority of neurons in the mammalian brain are formed prenatally, parts of the adult brain retain the ability to grow new neurons from neural stem cells in a process known as neurogenesis. Neurotrophins are chemicals that help to stimulate and control neurogenesis, BDNF being one of the most active. Mice born without the ability to make BDNF suffer developmental defects in the brain and sensory nervous system, and usually die soon after birth, suggesting that BDNF plays an important role in normal neural development.

Tissue distribution

Despite its name, BDNF is actually found in a range of tissue and cell types, not just in the brain. It is also expressed in the retina, the central nervous system, motor neurons, the kidneys, and the prostate. BDNF is present in high concentration in hippocampus and cerebral cortex. BDNF is also found in human saliva.

Mechanism of action

BDNF binds at least two receptors on the surface of cells that are capable of responding to this growth factor, TrkB (pronounced "Track B") and the LNGFR (for low-affinity nerve growth factor receptor, also known as p75). It may also modulate the activity of various neurotransmitter receptors, including the Alpha-7 nicotinic receptor.

TrkB is a receptor tyrosine kinase (meaning it mediates its actions by causing the addition of phosphate molecules on certain tyrosines in the cell, activating cellular signaling). There are other related Trk receptors, TrkA and TrkC. Also, there are other neurotrophic factors structurally related to BDNF: NGF (for Nerve Growth Factor), NT-3 (for Neurotrophin-3) and NT-4 (for Neurotrophin-4). While TrkB mediates the effects of BDNF and NT-4, TrkA binds and is activated by NGF, and TrkC

binds and is activated by NT-3. NT-3 binds to TrkA and TrkB as well, but with less affinity.

The other BDNF receptor, the p75, plays a somewhat less clear role. Some researchers have shown that the p75NTR binds and serves as a "sink" for neurotrophins. Cells that express both the p75NTR and the Trk receptors might, therefore, have a greater activity, since they have a higher "microconcentration" of the neurotrophin. It has also been shown, however, that the p75NTR may signal a cell to die via apoptosis; so, therefore, cells expressing the p75NTR in the absence of Trk receptors may die rather than live in the presence of a neurotrophin.

Secretion

BDNF is made in the endoplasmic reticulum and secreted from dense-core vesicles. It binds carboxypeptidase E (CPE), and the disruption of this binding has been proposed to cause the loss of sorting of BDNF into dense-core vesicles. The phenotype for BDNF knockout mice can be severe, including postnatal lethality. Other traits include sensory neuron losses that affect coordination, balance, hearing, taste, and breathing. Knockout mice also exhibit cerebellar abnormalities and an increase in the number of sympathetic neurons.

Exercise has been shown to increase the secretion of BDNF at the mRNA and protein levels in the rodent hippocampus, suggesting the potential increase of this neurotrophin after exercise in humans.

Genetics

The BDNF protein is coded by the gene that is also called BDNF. In humans this gene is located on chromosome 11. Val66Met (rs6265) is a single nucleotide polymorphism in the gene where adenine and guanine alleles vary, resulting in a variation between valine and methionine at codon 66.

As of 2008, Val66Met is probably the most investigated SNP of the BDNF gene, but, besides this variant, other SNPs in the gene are C270T, rs7103411, rs2030324, rs2203877, rs2049045 and rs7124442.

The polymorphism Thr2Ile may be linked to congenital central hypoventilation syndrome.

In 2009, variants close to the BDNF gene were found to be associated with obesity in two very large genome wide-association studies of body mass index (BMI).

Disease linkage

Various studies have shown possible links between BDNF and conditions, such as depression,

schizophrenia, obsessive-compulsive disorder, Alzheimer's disease, Huntington's disease, Rett syndrome, and dementia, as well as anorexia nervosa and bulimia nervosa.

Increased levels of BDNF can induce a change to an opiate-dependent-like reward state when expressed in the ventral tegmental area in rats.

Depression

Exposure to stress and the stress hormone corticosterone has been shown to decrease the expression of BDNF in rats, and, if exposure is persistent, this leads to an eventual atrophy of the hippocampus. Atrophy of the hippocampus and other limbic structures has been shown to take place in humans suffering from chronic depression. In addition, rats bred to be heterozygous for BDNF, therefore reducing its expression, have been observed to exhibit similar hippocampal atrophy. This suggests that an etiological link between the development of depression and BDNF exists. Supporting this, the excitatory neurotransmitter glutamate, voluntary exercise, caloric restriction, intellectual stimulation, curcumin and various treatments for depression (such as antidepressants and electroconvulsive therapy and sleep deprivation) increase expression of BDNF in the brain. In the case of some treatments such as drugs and electroconvulsive therapy this has been shown to protect or reverse this atrophy.

Eczema

High levels of BDNF and Substance P have been found associated with increased itching in eczema.

Epilepsy

Epilepsy has also been linked with polymorphisms in BDNF. Given BDNF's vital role in the development of the landscape of the brain, there is quite a lot of room for influence on the development of neuropathologies from BDNF.

Levels of both BDNF mRNA and BDNF protein are known to be up-regulated in epilepsy. BDNF modulates excitatory and inhibitory synaptic transmission by inhibiting GABAA-receptor-mediated post-synaptic currents. This provides a potential mechanism for the observed up-regulation.

Alzheimer's disease

Post mortem analysis has shown lowered levels of BDNF in the brain tissues of people with Alzheimer's disease, although the nature of the connection remains unclear. Studies suggest that neurotrophic factors have a protective role against amyloid beta toxicity.

Interactions

Brain-derived neurotrophic factor has been shown to interact with TrkB. BDNF has also been shown to interact with the reelin signaling chain. The expression of reelin by Cajal-Retzius cells goes down during development under the influence of BDNF. The latter also decreases reelin expression in neuronal culture.