Neuroplasticity:

The role of BDNF in learning

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Introduction

Neuroplasticity refers to the brain's remarkable capacity to change, adapt and modify itself, functionally and structurally, as a result of interactions of the organism with its environment. Neural plasticity was first discovered in the hippocampus (Fig.1). This phenomenon evolved as **long-term potentiation (LTP)** and its counterpart, **long-term depression (LTD)**.

Brain-derived neurotrophic factor (BDNF) is one of the most widely studied neurotrophins in the mammalian brain. It plays numerous vital roles in neuronal and glial development, neuroprotection, modulation of short- and long-synaptic connections, and plasticity.

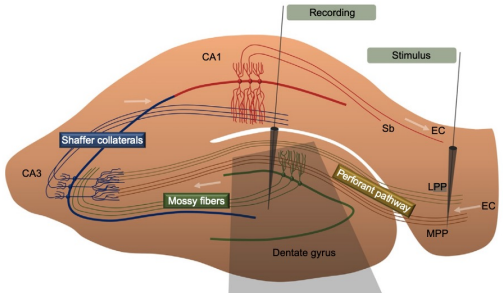

Figure 1. Brief stimulation of the perforant pathway increases the amplitude of the post-synaptic action potentials of the granular neurons of the dentate gyrus (Leal et al., 2016).

Materials and methods

The methodology of this project is based on literature research on online databases (NCBI PubMed and Google Scholar). The primary purpose of this project is to understand and analyse the role of BDNF in neuroplasticity related to memory, learning, and cognition.

Results

Human BDNF is expressed from a single gene locus controlled by neural activity. It can be found in **pro-BDNF** and **mature-BDNF** isoforms, which provide final opposed effects.

m-BDNF-TrkB interaction provides neural reorganization – spine and dendritic arborization – and enhances LTP induction. These physiological changes and re-modulation require the Ras-MAPK, PI3K, and PLCγ1 pathways, which trigger neuronal rewiring and survival (Fig.2). On the other hand, it has been demonstrated that **pro-BDNF-p75NTR signalling** promotes neuronal apoptosis.

Furthermore, the increase of BDNF in the CA3-CA1 activation of both pre- and postsynaptic sites is critical for memory performances (Wang et al., 2022).

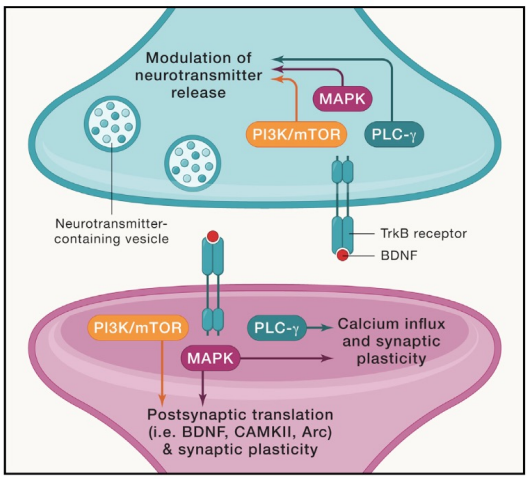

Figure 2. The binding of BDNF to its high-affinity TrkB receptor triggers the activation of different signalling pathways. The TrkB receptor has several phosphorylation sites, which can induce several cellular pathways at both the pre- and post- synaptic sides (Wang et al., 2022).

BDNF-TrkB pathways:

1 Ras-MAPK

Activation of **cytoskeleton protein synthesis** and **early neuronal genes**
Activation of **dendritic growth**

2 PI3K

Enhancement of **dendritic growth**
Anti-**apoptotic** activity
Modulation of **NMDA trafficking**

3 PLCγ1

Enhancement of **synaptic plasticity**
Increase of **DAG** and Ca^{2+} ions
Activation of **CAM kinase** and **PKC**

Moreover, a single-nucleotide polymorphism called **Val66Met** impairs BDNF release from neurons. This alteration may determine changes in different neural codification levels after memory, attention, and perception. It has been shown that individuals carrying this polymorphism have lower brain electrical activity.

There is enough evidence that corroborates the fundamental role of BDNF in hippocampal synaptic plasticity since seminal studies demonstrated a decreased LTP in BDNF knockout mouse lines. In addition, m-BDNF-TrkB signalling is required to sustain LTP consolidation at DG synapses. It requires the activation of postsynaptic Ca^{2+} channels and NMDAR to consolidate these synapses. BDNF signalling also increases the **trafficking** and **delivery** of **AMPAR** and **NMDAR** in hippocampal neurons. Thus, treatment with ketamine causes extracellular glutamate influx in the prefrontal cortex promoting AMPA receptor activation, which triggers BDNF signalling and release.

Discussion and perspectives

- **BDNF** is critical **to enhancing long-term potentiation** (LTP) in the hippocampus.
- **m-BDNF-TrkB signalling** is also required to sustain and **consolidate LTP** in the hippocampus. Although most studies have only analysed LTP in the hippocampus, BDNF plays a critical role in inducing neuroplasticity in other brain regions.
- **m-BDNF-TrkB signalling** triggers **neural rewiring** and **survival**, whereas **pro-BDNF-p75NTR signalling** induces **growth inhibition** and **apoptosis**.

References

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