JOURNAL OF PHARMACOLOGICAL CHEMISTRY AND BIOLOGICAL SCIENCES

Vol.: 3(1). pp. 16-23, Jan-Jun
DOI: 10.36619/jpcbs.2021.3.16.24
ISSN: 2674-886X

Neuroprotective Effect Promoted by Bitartrate

Mariana Mendes Pinto[1] and Fausto Pierdoná Guzen[2]

[1] Postgraduate Program in Biotechnology – Potiguar University (UnP), Natal, Brazil

[2] Postgraduate Program in Physiological Sciences, Department of Biomedical Sciences, Faculty of Health Sciences, State University of Rio Grande do Norte (UERN)

Keywords:

Hippocampus
Bitartrate
Neuroprotection

Abstract

The hippocampus is considered a central brain structure in memory formation mechanisms. With regard to Choline Bitartrate, it can be said that it is a substance capable of helping to improve an individual's memory. Chronic choline intake has been suggested to improve behavioral, oxidative, and neurochemical outcomes in the normal population, as a safe and effective supplement to improve neurological health in normal individuals, and that they may also be beneficial in preventing more phased cognitive and motor disorders late in life. In addition to observing behavioral changes after choline administration, the effect of chronic choline administration on changes in the redox state of the brain and on neurochemical changes in the brain and hippocampus was also determined.

1. Introduction

In more advanced multicellular animals, the receptor system captures information from the external environment, being located at a considerable distance from Organs effector organs, thus, there is a need to transmit information quickly and over long distances. In this requirement, there is a set of specialized and organized cells that act as communication channels between sensory receptors, on the one hand, and effectors, on the other.

This set of cells comprises the nervous system (BRANDÃO, 2004). For a long time it was believed that the central nervous system (CNS), after its development, became a rigid structure that could not be modified and that lesions would be permanent, as its cells could not be reconstituted or reorganized (KESSLER et al. , 2011). However, in view of the studies it was observed that the brain is a modifiable structure as it is stimulated. During the learning process, structural and functional changes occur in neurons, that is, this process promotes plastic changes (PASCUAL-PEONE, 2005).

Located in a region known as the insula or limbic lobe, the limbic system is mainly responsible for human emotional behavior and is related to olfaction, memory, neuroendocrine and autonomic homeostasis (OLIVEIRA, 2012). The hippocampus belongs to the limbic system, located in the temporal lobe, playing an important role in the processes of learning and memory formation.

It is considered a central brain structure in the mechanisms of memory formation: the acquisition, consolidation and recall, of both short-term and long-term memories. The hippocampus has connections, through the entorhinal cortex, with several brain structures, such as neocortical areas, hypothalamus, amygdala and nucleus accumbens (SANTOS, 2018).

With regard to Choline Bitartrate (BC), it can be said that it is a substance capable of helping to improve the memory of an individual, especially when he is affected by diseases such as Alzheimer's, liver damage or cholesterol. It is noteworthy that it is indicated for the treatment of these diseases, but it can also be used by healthy young people, aiming to improve their memory with regard to quick thinking issues, for example (LIPPELT, 2020).

2. Development

2.1 Neuroprotection in the hippocampus

According to Castro, Gil and Brocardo (2017), so that it is possible To understand how hippocampal neuroprotection works, it is necessary to define which structures make up the hippocampus and how they act within it, making it perform all its actions in the brain (CASTRO & BROCARDO, 2017).

The hippocampus is responsible for coding the Long-term memories, moreover, also serve to aid in navigation. space. It makes up the brain and is phylogenetically the oldest part of the even

(MELO, 2017). According to França (2019), the emotions suffered by a subject and their personal experiences are events that are associated with the hippocampus, as it has the function of consolidating all these actions (FRANÇA, 2019).

The hippocampus is a deep structure located bilaterally in the third turn of the temporal lobe, participates in some modalities of the learning and memory process. It constitutes an important region of the system. limbic, which in turn forms a circuit where the main functions are emotion and motivation (TAVARES, 2020).

The brain has a unique symmetry, so within it, the hippocampus can be found in all hemispheres. When the individual causes some type of trauma that ends up affecting the hippocampus, it results in the difficulty or inability to build new long-term memories, however, the individual is able to learn routine activities or procedures during their daily lives, that is, situations to short term (BARRETO, 2016). The limbic system is formed by a group of regions that includes: the anterior thalamic nuclei; amygdala; the hippocampus; the limbic cortex and hypothalamic regions. The learning process depends on hippocampal synaptic plasticity (BARRETO, 2010).

According to Castro, Gil and Brocardo (2017), synaptic plasticity is defined as alterations in postsynaptic neurons caused by structural and biochemical changes in synapses, thus, if a synapse is active simultaneously with a postsynaptic neuron, it will be strengthened. Electrical stimulation in hippocampal formation can lead to Long-term structural and biochemical changes in neurons facilitating thus learning, the hippocampal formation is divided into three parts: subicular complex; hippocampus and dentate gyrus. The main references and cortical afferents originate in the entorhinal cortex, where information is transmitted from this structure to the dentate gyrus through the perforating pathway (CASTRO & BROCARDO, 2017; TAVARES, 2020).

The dentate gyrus is a region in the hippocampal formation with which it receives information from the entorhinal cortex through the perforating pathway and sends it through the pathways to the nerve fibers, which are the axons emitted by the granulosa cells of the dentate gyrus to the CA3 region (MOREIRA, 2017). The layers of CA3 are regions of the hippocampus that receive information from the dentate gyrus and sends to the CA1 layer through Schaffer's collateral, these neurons also project through the fornix to basal forebrain structures that include a septum and the mammillary bodies (TORRES, 2010).

The CA1 layers of the hippocampus are also called "horn of ammon" in ancient literatures. The pyramidal cells of the CA1 layer send primary efferents from the hippocampus, thus, these cells project out of the hippocampal formation through axons projected in the subicular region towards the entorhinal cortex (GAMBOA, 2019).

From the entorhinal cortex, the perforating pathway communicates with the dentate gyrus, by in turn, another communication occurs, this time through the rough fiber pathways with the CA1 layer. From the CA1 layer, Schaffer's collateral communicates with the CA3 layer, and thus, it sends eference to the subicular region and entorhinal cortex. There is a process of synaptic plasticity, developing mutually with synaptic potentiation and this potentiation is considered long-lasting and known by the acronym LTP (HOFNER, 2018).

LTP stands for "Long Term Empowerment". On the face of it, she is characterized as the persistent and lasting increase between hours and days of amplitude of postsynaptic potentials after repetitive pre-stimulation synaptic. LTP is linked to the mechanisms involved with synaptic plasticity and consequently with learning (FRANÇA, 2019).

For the production of LTP it is necessary to use a strong stimulus that simultaneously activates several afferent fibers. One of the stimulus points is located in Shaffer's collateral, an afferent pathway that communicates the CA3 layer with the CA1 of the hippocampus.21 Repetitive stimuli of 100 hz passed for 20 seconds with modulation of 1 second are sufficient to generate LTP, according to the data collected by the recording electrode located in the pyramidal neurons of CA1. This measure was evaluated using postsynaptic excitatory potentials, which are graduated variations of a cell's membrane potential, in this case, it makes the interior of the neuron increasingly positive, which facilitates neural communication (BARRETO, 2016).

Shaffer's collateral stimulation records the CA1 layer of the hippocampus, thereafter, increases the velocity of postsynaptic potentials excitatory. With this, it increases the release of neurotransmitters and the decreased neurotransmitter release failures. Long-term enhancement is the persistent, long-lasting increase in amplitude of postsynaptic potentials after continuous stimulation of the pre-synaptic element, where the element has a glutamate neurotransmitter. This is the main excitatory neurotransmitter of the central nervous system, which acts on inotropic receptors; NMDA receptor, and also acts on metabotropic receptors (MACHADO, KUNICKI & SAMESHIMA, 2012).

In a low-frequency synaptic transmission, glutamate is released from the pre-synaptic neuron and acts on both NMDA and non-NMDA receptors, however, the conformational change and consequently the sodium ion influx will only occur in non-NMDA receptors, considering that NMDA receptors are blocked by magnesium ions. The consequence of this event is the depolarization of the postsynaptic neuron (BARRETO, 2010).

Through the input of positive electrical charges, the opening of inotropic channels with independent voltage occurred, allowing a greater influx of sodium into the postsynaptic neuron, making it even more positive. The increase in positive electrical charges releases magnesium from the NMDA receptor, which is already stimulated by glutamate, making the NMDA receptor active, allowing the influx of calcium and sodium ions into the postsynaptic neuron (SANTOS, 2020).

At the same time, glutamate also stimulates channels calcium metabotropics, generating a cascade of biochemical events that results in the conversion of ATP to cyclic AMP by phospholipase C and the release of calcium from the sarcoplasmic reticulum. The resulting increase in calcium activates the calcium-dependent kinase (BARRETO, 2016).

These proteins produce and release a retrograde messenger which is a gas called nitric oxide, this is a highly soluble gas, so it diffuses easily between the synaptic elements and acts on the pre-element. synaptic. In the presynaptic element, the retrograde messenger intensifies the release of glutamate which increases the induction of LTP (ENGELHARDT, 2016).

There is a release of glutamate in the presynaptic neuron and this causes a stimulation of the receptors thus facilitating the entry of calcium and sodium, forming cyclic AMP through ATP and releasing calcium from the reticulum sarcoplasmic. Thus, it forms the tyrosine kinase and causes the formation of the nitric oxide, this gas that goes to the presynaptic neuron where it intensifies the release of glutamate, facilitating the induction of LTP (MELO, 2017).

Given the above, it is clear that all these processes are necessary to ensure that the hippocampus works properly and that it performs its neuroprotection with the help of all receptors and channels involved in different phases of operation.

2.2 Choline Bitartrate

In 1998, choline was officially recognized by the Institute of Medicine (IOM) as an essential nutrient, which plays an important role in various biological processes in mammals. it becomes necessary to production of the neurotransmitter acetylcholine and to form phosphatidylcholine, essential in the construction of cell membranes. Long--term choline deficiency can lead to an increased risk of neurological diseases such as Alzheimer's Disease (MODINGER, 2019).

Lippelt; Kint; Herk and Naber (2016) emphasize that Choline Bitartrate is a substance capable of assisting in the better development of the human brain, as well as being able to help individuals who present some pathology that may affect their psychic condition. In a study carried out by Zakka (ZAKKA, 2020), it was possible to identify that subjects who did not use the substance, when subjected to certain tasks, could not develop as those who used it, which allowed the tested subjects stay with lower concentration levels than those who used the substance.

Naber; Hommel and Colzato (2015) reported in their study that the use of choline Bitartrate in healthy individuals caused them to have an improvement in their visual-motor performance, however, the same authors argue that in the same proportion there was a minimization of pupils in these subjects. It is understood that the use of this substance is important because it is a supplement to foods eaten by subjects with or without specific diseases.

In the study by Borges (2011), after administering some doses of Choline Bitartrate in rats submitted to global brain ischemia transitory, it became evident that, over the months, they began to have a considerable improvement frequency. According to the author, in the first applications they left in the field of survival for the neural survival, soon after became more stable and with a 2-month survival, that is, greater than the previous survival. In the same study, the author presents which composition he used to reach the presented result, namely: C5H14NO.C4H5O6; PM=253.3. It was also highlighted, in the same study, that for the effectiveness to be proven, it was necessary that the composition was properly prepared before ingestion (BORGES, 2011). Below, you can see some foods that contain Choline bitartrate in its composition and are consumed by all ranges ages, from childhood to adulthood.

Conclusion

Hippocampus, the main seat of memory, needs stimuli for its growth to take place, making possible the emergence of mechanisms that allow a better processing of a subject's declarative memories. Chronic choline intake has been suggested to improve behavioral, oxidative, and neurochemical outcomes in the normal population, as a safe and effective supplement to improve neurological health in normal individuals, and that they may also be beneficial in preventing more phased cognitive and motor disorders. late in life. In addition to observing behavioral changes after choline administration, the effect of chronic choline administration on changes in the redox state of the brain and on neurochemical changes in the brain and hippocampus was also determined.

References

BARRETO, Davi. A área hipocampal CA1 é essencial para a memória similar à episódica. Universidade Federal da Paraíba. PPGNEC. João Pessoa, 2016.

BARRETO, João; SILVA, Luciane. Sistema límbico e as emoções: uma revisão anatômica. Rev Neurocienc. v. 18, n. 3. 2010.

BORGES, Andreia Aurélio. Avalição do efeito terapêutico da colina após a recirculação em ratos submetidos a isquemia encefálica global transitória. São Paulo, 2011. Disponível em: http://repositorio.unifesp.br/bitstream/handle/11600/9082/Publico-12648a.pdf?sequence=1&isAllowed=y. Acesso em 17 dez. 2020.

BRANDÃO, Marcus Lira - As bases biológicas do comportamento: introdução à neurociência. São Paulo, Editora Pedagógica e Universitária, 2004. 223p. ilus. ISBN 85-12-40630-5 Disponível em: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0036-46652005000300013

CASTRO, Cristine de Paula Nascimento; GIL, Joana; BROCARDO, Patricia S. Exercício físico e neuroplasticidade hipocampal: Revisão de literatura. VITTALLE--Revista de Ciências da Saúde, v. 29, n. 2, p. 57-78, 2017.

DOS SANTOS, B. G.. A suplementação pré-natal com narigina altera a homeostase redox e função mitocondrial cerebral da prole de ratas Wistar. 123f. Dissertação (Mestrado) – Universidade Federal do Rio Grande do Sul, Instituto de Ciências Básicas da Saúde,Programa de Pós-graduação em Ciências Biológicas: Bioquímica, Porto Alegre, BR-RS, 2018.

ENGELHARDT, Eliasz. O descobrimento do hipocampo: primeiros passos. Dementia & Neuropsychologia, v. 10, n. 1, p. 58-62, 2016.

FRANÇA, Thiago. Plasticidade, topografia e alocação de memórias: Uma investigação teórica sobre o código neural no hipocampo. Universidade Federal do Rio Grande. FURG. Rio Grande. 2019.

GAMBOA, Patrícia. Avaliação do Volume do Hipocampo no Idoso em Imagens de Ressonância Magnética: Comparação de Diferentes Métodos de Segmentação. Instituto Politécnico de Lisboa. Lisboa. 2019.

HOFNER, Matheus. Estudo de plasticidade paralela baseado em FEPSP no Hipocampo CA1. Universidade Federal de Minas Gerais. Belo Horizonte. 2018.

KESSLER, N et al. Balance Rehabilitation Unit (BRUTM) posturography in relapsing-remitting multiple sclerosis. Arq Neuropsiquiatr. v. 69, n. 3, p.90-485, 2011.

LIPPELT, D. P; KINT, S. VANDER; HERK, K. VAN; NABER, M. Sem efeitos agudos de suplementos alimentares de bitartarato de colina na memória em adultos jovens e saudáveis. PLOS ONE, 2016. Disponível em: DOI: 10.1371. Acesso em 10 dez. 2020.

MELO, Tiago Lira. Neuroplasticidade. Revista de trabalhos acadêmicos-universo Recife, v. 4, n. 2, 2017.

MOREIRA, Édisom. O sistema límbico: seu estudo morfo-funcional, histórico. A formação hipocampal, o complexo amigdalino e seu envolvimento com a formação reticular. As memórias, o aprendizado e as emoções. A biologia molecular,base estrutural da vida. Unifoa. v. 24. 2017.

OLIVEIRA, Maria Cristina Souza Pereira. Efeitos da exposição crônica ao etanol da adolescência à fase adulta em ratos sobre o processo mnemônico e na densidade celular no hipocampo. 2012. 68 f. Dissertação (Mestrado) - Universidade Federal do Pará, Instituto de Ciências da Saúde, Belém, 2012. Programa de Pós-Graduação em Ciências Farmacêuticas. Disponível em: http://repositorio.ufpa.br/jspui/handle/2011/6174

PASCUAL-LEONE, A.; AMEDI, A.; FREGNI, F.; MERABET, L.B. The Plastic Human Brain Córtex. Annual Review of Neuroscience. Vol. 28, p. 377-401, 2005.

SANTOS, Beatriz. Guanosina e Neuroplasticidade: Estudo de Proteínas Envolvidas na Sinaptogênese e na Transmissão Glutamatérgica e Purinérgica. Universidade Federal de Santa Catarina. Florianópolis. 2020.

TORRES, Laila. Estudo Morfológico do Hipocampo de uma espécie de primada da Amazônia: Cebus apella, (Linnaeus, 1758). Universidade Federal de São Paulo. 2010.

ZAKKA, T. R. M. Cognição e desempenho visomotor & suplementação de colina. Eurofarma News. Material exclusivo para a classe médica, 5º edição, 2019. Disponível em: https://cdn.eurofarma.com.br//wp-content/uploads/2019/12/537676.pdf. Acesso em 12 dez. 2020.