JOURNAL OF PHARMACOLOGICAL CHEMISTRY AND BIOLOGICAL SCIENCES

Vol.: 3(1). pp. 48-55, Jan-Jun
DOI: 10.36619/jpcbs.2021.3.52.59
ISSN: 2674-886X

Brain Skills ® promotes neuronal migration and development in cultivated human brain tissue

Fausto Pierdoná Guzen[1,2,3]*

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

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

[3]Medical School - State University of Rio Grande do Norte (UERN), Mossoró, Brazil.

Keywords:

Brain Skills ®
Culture
Plasticity
Neuron Development

Abstract

The evolution of large human brain size has had important implications for the nutritional biology of our species. The question of whether brain function is entirely genetically determined or may be influenced by the environment or by nutrition has been debated for decades. Large brains are energetically expensive, and humans expend a larger proportion of their energy budget on brain metabolism than other primates. Military interest in the effects of nutritional factors on brain function has stimulated considerable research on a variety of food constituents. In this perspective, Brain Skills®, which consists of an association of amino acids, vitamins, minerals, precursors of neurotransmitters and antioxidants, was tested in human neuron cultures. Brain Skills® promoted greater migratory and neuroplastic effects after 72 hours of treatment.

Introduction

Food supplies energy in the form of calories and the building block nutrients that create and maintain cells (Austin, 2016). Nutrition can affect the brain with profound implications for mental health and degenerative diseases throughout the life cycle. Since it is bonded with food, it is better to advocate in terms of food rather than nutrients. The role of nutrition in neuroscience is complex with all aspects of nutrition. The concern is not with the impact of a single nutrient rather with the multiple nutrients and their interactions. The overall nutrient content in the food directly affects the structure and function of the brain as they are dependent on the nutritional input. But it is difficult to access the specificity of the nutrient with regard to their brain function (Dauncey, 2009).

These include protein, zinc, selenium, iodine, folate, vitamins, choline, and long-chain polyunsaturated fatty acids (Georgieff and Rao, 2001; Dobbing, 1990; Rao and Georgieff, 2000). The effect of nutrient deficiency or supplementation on the developing brain is a function of the brain's requirement for a nutrient in specific metabolic pathways and structural components. The effects are regionally distributed within the brain on the basis of which areas are rapidly developing at any given time (Kretchmer, Beard and Carlson, 1996).

Methods

The biological samples were obtained from the brain tissue of patients traumatized with TBI, attended at the Regional Hospital Tarcísio de Vasconcelos Maia (HRTM), in Mossoró-RN, who required emergency neurosurgery, in some very specific situations.

Legal Requirements

The collection of the material was only carried out with the authorization of the legal representative of the patient through the signing of the Term of Free and Clarified Assent (TALE). The collection was carried out in accordance with the specific legislation (Resolution 441/2011 and ordinance of the Ministry of Health 2201/11). This research project was approved by the local Research Ethics Committee (CAAE 65640517.0.0000.5294).

Criteria for Inclusion

Age between 18 and 70 years; signature of TALE by the legal guardian; patients who require emergency neurosurgery due to TBI in very specific situations:

in cases of patients with cranial dandruff with laceration of the dura-mater and cerebral cortex, with spontaneous (caused by trauma) brain tissue, which obviously need neurosurgery ; and in patients with traumatic intracranial hematomas with subcortical component

and expansive effect, requiring surgical removal through a small opening in the cerebral cortex, known as corticectomy, for drainage of the clot.

Pre-Operative Preparation

After the indication of the need for surgical intervention, the patients were referred to the operating room of the surgical center in the usual manner, being routinely received by the nursing and anesthesiology team for anesthesia and subsequent surgery, as is the protocol for all patients who are operated. There was no change in the routine of the pre-surgery visits. Meanwhile, in another room, a member of the research team presented TALE with the legal guardian for the patient to read and authorize or not to collect the material.

Surgical Procedure

Surgical interventions followed the internationally agreed steps for the treatment required for the patients in question, according to the following sequence: surgical table positioning, asepsis and antisepsis, placement of sterile surgical fields, surgical incision in the skin and subcutaneous tissue, rotation of the cutaneous or myocutaneous flap, craniotomy (opening of the skull) and opening of the dura mater. In this stage of the surgical procedure, after drainage of acute subdural hematoma, a small area of cortical laceration of the right temporal lobe was visualized in patient 1, and the biological sample of brain tissue was collected and the surgery followed its normal steps with the hemostasis, closure of the wraps (dura mater, skull, muscle, subcutaneous tissue, skin) and dressing. I reiterate that the neurosurgical technique was in no way modified (except at the time of material collection), in order to guarantee the best available treatment for the patient and to minimize the risks involved.

Signing the Sample for Culture

After collection, this material was immediately stored in Leibovitz-15 preservative medium (L-15: GIBCO Invitrogen Corporation) and shipped for treatment and plating on the addition of D-10 culture medium, being maintained in CO2 greenhouse. The technique of human nerve cell culture was adapted from the work of Lucena *et al.* (Lucena *et al*., 2014) – performed with rodents -with some modifications and described in detail in item 2.7 below.

Culture Technique

Inside the laminar flow, the brain tissue was processed and submitted to the technique of cleaning and obtaining tissue ex-plants for posterior plating. New 15 ml Falcon conical tubes with 4 ml of Dulbecco`s modified Eagle medium medium supplemented with 10% fetal bovine serum and ceftriaxone, a medium designated D-10, all obtained from Cultilab®, were prepared and received the nerve tissue to perform the preparation. 35 mm culture plates (P35) for

plating were prepared with 1 ml of fetal bovine serum, which was removed and discarded after 30 minutes, and then 3.0 ml of D-10 was added to the P35, where, The plating of the explants was performed, and the plates were kept in a humid oven at 37°C with 5% CO2 and 95% air. In contrast light microscopy with phase contrast was used for the observation of the explants and the cell migration at the bottom of the plates. When the explant cells reached 70-90% confluence at the bottom of the plate, the basic medium was removed and 2 ml of trypsin / EDTA (0.25% trypsin containing 1 mM EDTA--Cutilab/Brazil®).

The cell suspension was then placed in Falcon-type conical tube with the same volume of D-10 medium for 10 minutes, in order to inactivate trypsin.

The suspension was centrifuged at 1500 rpm for ten minutes; after this procedure, the supernatant was discarded and the cells resuspended in 1 ml of medium. The cells were deposited in P60 and observed in 72 hours' time periods and, in this way, it was possible to evaluate the adherence, proliferation and trophism of brain tissue cells at different times. For cellular observation, a CKX41 (Olympus®) phase contrast inverted microscope with a Moticam 3.0 digital camera (Motic®) coupled was used, and photomicrographs of the groups were made at 72 hours, taking the morphological development of the cells.

Results

Brain skills® promoted cell migration and growth after 72 hours of treatment. In A we observe untreated neurological cells and in B neurological cells treated with Brain Skills®. Greater cell migration and development was observed in the group treated with Brain Skills®.

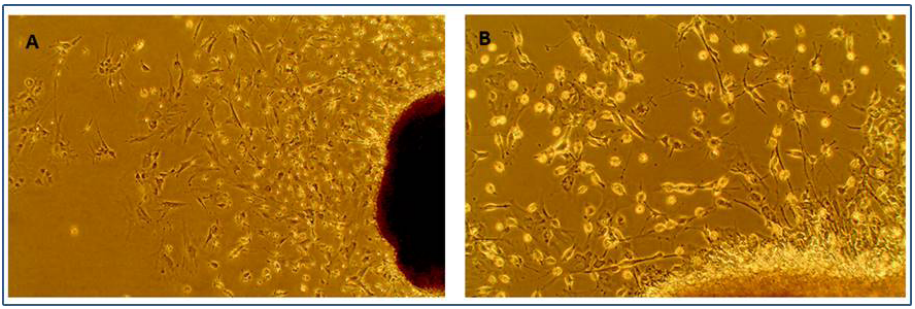

Figure: Demonstrates the migration and development induced by Brain Skills ®. In A we observe untreated neurological cells and in B neurological cells treated with Brain Skills ®.

Discussion

The notion that constituents of the normal diet can influence brain function is not novel. Perhaps the best-known example is caf- feine (and related methylxanthines), which is contained in coffee, tea, chocolate, and soft drinks. Caffeine is a mild stimulant that may improve mental alertness and performance (Battig and Welzl, 1993). In the past few decades, it has become clear that many other constituents of the diet, from macronutrients to vitamins, influence brain function. For some, the effects so far noted are biochemical, whereas for others, functional and behavioral effects have been observed (and the underlying biochemical mechanisms are obscure). Because the field of diet and brain function is very young, it should not be surprising that large gaps exist at the biochemical, physiologic and behavioral levels in our knowledge of the effects of nutrients on brain function.

In contrast, the influence of amino acids on the synthesis and release of the brain neurotransmitters into which they are converted has been quite well documented, whereas the consequences of this relation for brain function.

Interest in the amino acids tyrosine and tryptophan centers on their role as precursors to neurotransmitters, molecules that allow neurons to transfer electrical impulses to other neurons as well as other cells. Tryptophan is the precursor to the neurotransmitter serotonin. Numerous studies showed that the availability of this amino acid to brain neurons that synthesize serotonin directly influences the rate at which it is converted to a neurotransmitter (Fernstrom, 1983).

Administering either the amino acid itself (Ashcroft, Eccleston and Crawford, 1965) or meals that raise tryptophan access to serotonin neurons (Fernstrom and Wurtman, 1971; Fernstrom and Fernstrom, 1995) rapidly stimulates serotonin production; tryptophan administration is also known to enhance serotonin release in neurons that are actively firing (Sharp and Bramwell, 1992). These treatments can produce changes in brain function; for example, in humans, administration of oral tryptophan can modify sleep and mood via its actions to stimulate neuronal serotonin production and release (Borbély and Youmbi-Balderer, 1987; Young and Gauthier, 1981). Such functional effects are also reputed to accompany the ingestion of carbohydrates (Sayegh *et al*., 1995) and, in rats, are said to involve a known action of carbohydrate ingestion to stimulate brain tryptophan uptake and serotonin synthesis (Fernstrom and Fernstrom, 1995).

Certain dietary components have effects on cognitive abilities. Dietary factors can affect multiple processes of the brain by regulating neurotransmitter pathways, membrane fluidity, signal transduction pathways, and synaptic transmission. Proper nutritional status is required for proper brain development and maintenance of its normal functioning. Through biological functions, certain micronutrients affect the function of the brain.

Conclusion

Brain Skills® promoted greater migratory and neuroplastic effects after 72 hours of treatment.

References

Ashcroft GW, Eccleston D, Crawford TBB. 5-Hydroxyindole metabolism in rat brain: a study of intermediate metabolism using the technique of tryptophan loading-I. J Neurochem 1965;12:483–92.

Austin, D. (2016). Food for Thought: The Neuroscience of Nutrition to Fuel Cognitive Performance. Or L Rev 95:425.

Bättig K, Welzl H. Psychopharmacological profile of caffeine. In: Garattini S, ed. Caffeine, coffee and health. New York: Raven Press, 1993:213–53.

Borbély A, Youmbi-Balderer G. Effects of tryptophan on human sleep. Interdisciplinary Top Gerontol 1987;22:111–27.

Dauncey, M. J. (2009). New insights into nutrition and cognitive neuroscience: Symposium on 'Early nutrition and later disease: current concepts, research and implications'. Proceedings of the Nutrition Society 68(4):408-415.

Dobbing J. Vulnerable periods in the developing brain. In: Dobbing J ed. Brain, behavior and iron in the infant diet. London, United Kingdom: Springer, 1990: 1–25.

Fernstrom JD, Wurtman RJ. Brain serotonin content: increase following ingestion of carbohydrate diet. Science 1971;174:1023–5.

Fernstrom JD. Role of precursor availability in control of monoamine biosynthesis in brain. Physiol Rev 1983;63:484–546.

Fernstrom MH, Fernstrom JD. Brain tryptophan concentrations and serotonin synthesis remain responsive to food consumption after the ingestion of sequential meals. Am J Clin Nutr 1995;61:312–9.

Georgieff MK, Rao R. The role of nutrition in cognitive development. In: Nelson CA, Luciana M eds. Handbook in developmental cognitive neuroscience. Cambridge, MA: MIT Press, 2001: 491–504.

Kretchmer N, Beard JL, Carlson S. The role of nutrition in the development of normal cognition. Am J Clin Nutr. 1996; 63 (suppl): 997S–1001S.

Lucena, E. E. de S. *et al*. Plasticity of mesenchymal stem cells from mouse bone marrow in the presence of conditioned medium of the facial nerve and fibroblast growth factor-2. The Scientific World Journal, v. 2014, p. 457380, 2014.

Rao R, Georgieff MK. Early nutrition and brain development. In: Nelson CA ed. The effects of early adversity on neurobehavioral development. Minnesota Symposium on Child Psychology. Vol 31. Hillsdale, NJ: Erlbaum Associates, 2000: 1–30.

Sayegh R, Schiff I, Wurtman J, *et al*. The effect of a carbohydrate rich beverage on mood, appetite, and cognitive function in women with premenstrual syndrome. Obstet Gynecol 1995;86:520–8.

Sharp T, Bramwell SR, Grahame-Smith DG. Effect of acute admin istration of L-tryptophan on the release of 5-HT in rat hippocampus in relation to serotoninergic neuronal activity: an in vivo microdialysis study. Life Sci 1992;50:1215–23.

Young SN, Gauthier S. Tryptophan availability and the control of 5-ydroxytryptamine and tryptamine synthesis in human CNS. Adv Exp Med Biol 1981;133:221–30.