Omega-3s for protecting the brain

Richard Béliveau

Translated from Le Journal de Montréal, June 05, 2017

A study has shown that one omega-3 fatty acid in the diet, docosahexaenoic acid (DHA), plays a predominant role in the sealing of the barrier of blood vessels which protects the brain.

The **brain** is separated from the rest of the body by a tightly sealed barrier which provides very precise control of the entry and exit of substances essential to the brain's activity. This blood-brain barrier (BBB) plays an essential role in maintaining cerebral homeostasis by controlling the highly selective processes which capture nutrients essential to the brain (glucose, amino acids and certain hormones, amongst others) while preventing the entry of most foreign substances and toxins. However, this barrier also prevents chemotherapy medications from reaching brain tumours.

Two principal characteristics of the BBB are responsible for this tight seal: 1) the cells of the blood vessels (endothelial cells) which form the barrier are joined together by tight junctions which prevent small molecules present in the circulating blood from crossing the barrier by slipping between the cells and 2) these endothelial cells also have a membrane which is abnormally selective, preventing nearly all the large molecules in the blood from adhering to the cell surface and reaching the brain by diffusing across the cells.

PROTECTIVE MEMBRANE

This very high selectivity of the cell membrane which composes the barrier is unique in several distinct ways. By definition, the function of a membrane is to separate two different compartments; in the case of cells, the presence of a cell membrane formed of fatty acids which are insoluble in water permits the formation of a protective layer which isolates the interior of the cell from the external world.

However, this protection is generally not complete because cell membranes also contain transport systems which enable the import of many substances that are essential to cells or the export of substances which are harmful to cells. The near-absence of these transport activities in the cell membranes of the BBB is thus quite mysterious.

A SEALANT BASED ON OMEGA-3

Recent results have shed some light on the factors responsible for this weak transport activity and could thus permit us to better understand the tight seal provided by the BBB.

A group of researchers at Harvard University have shown that the membrane of the endothelial cells which faces the circulating blood contained elevated quantities of docosahexaenoic acid (DHA), a long-chain omega-3 fatty acid[1]. They found that this particular composition is due to the activity of a protein called

Mfsd2a which captures DHA and inserts it into this membrane, and that this phenomenon made these cells incapable of forming the vesicles necessary to transport macromolecules from the blood.

In other words, it is the abundance of omega-3 in the membrane of the endothelial cells which is directly responsible for the integrity of the BBB, an essential function which adds to the numerous beneficial properties of these fats on the optimal functioning of the human body.

TRAVERSING THE BARRIER

While it is essential to the functioning of the brain, the BBB unfortunately prevents the majority of medications from reaching cerebral tissue and thus represents the major obstacle to treatment of tumours or cerebral metastases. It is thus possible that the discovery of ways of blocking the insertion of omega-3 into the membrane of the BBB, for example by specifically targeting the protein which captures this fatty acid (Mfsd2a), would thus diminish this tight seal and permit chemotherapeutic medications to reach cancerous cells in the brain.

Another approach, developed in our laboratory, consists of using certain peptides which possess the ability to traverse the barrier and which can consequently be used as "ferries" to transport a large variety of medications from the blood to the brain[2].

The rapid advancement of knowledge on the mechanisms responsible for the impermeability of the BBB allows us to believe that we will be able, in the near future, to overcome this obstacle and to considerably improve the survival of the numerous people affected by cerebral tumours.

(1) Andreone BJ et al. Blood-brain barrier permeability is regulated by lipid transport-dependent suppression of caveolae-mediated transcytosis. Neuron 2017;94:581-594.

(2) Demeule M et al. Identification and design of peptides as a new drug delivery system for the brain. J. Pharmacol. Exp. Ther. 2008;324:1064-1072.

You find the content of this column useful? Make a donation at www.richardbeliveau.org to speed up our research

You find the content of this column useful? Make a donation at www.richardbeliveau.org to speed up our research

You find the content of this column useful? Make a donation at www.richardbeliveau.org to speed up our research