Effects of Dietary Omega-3 on Vascular Permeability, and the Implications for Cerebral Cavernous Malformations

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ABSTRACT

Cerebral cavernous malformations (CCMs) are deformations in endothelial cell thickness in the brain that decrease vascular permeability of cellular junctions and lead to strokes and brain hemorrhaging. Although there are treatments available for the symptoms of CCM, there is no therapy that increases cell thickness for CCM patients. We hypothesized that an increase in Omega-3 in the diet would lead to an increase in cell thickness, therefore reducing the vascular permeability. By using bovine red blood cells from cows as a model for endothelial cells, we can observe cell changes that can happen with the inclusion of Omega-3 in the diet using a microscope. One cow was fed Omega-3 fatty acids and one cow was fed a regular diet. We put both the control and Omega-3 blood in hypotonic and isotonic solutions made of varying concentrations, and then tracked cell thickness by taking pictures under a microscope every 15 seconds. Supporting our hypothesis, we found that the Omega-3 rich blood had increased cell thickness compared to the control blood. We present these data as a model of diet modified cell thickness, and as a potentially promising treatment for decreased cell thickness as seen with CCMs.

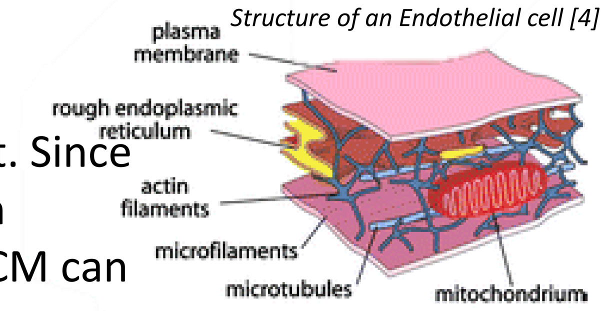
Hypothesis: An increase in Omega-3 in the cell will result in an increased cell thickness and decreased vascular permeability.

INTRODUCTION

Individuals who have cerebral cavernous malformations (CCMs) are predisposed to conditions such as strokes, seizures, and intracranial hemorrhaging [1]. In this condition, endothelial cells in the brain lose proteins in the membrane, leading to decreased cell thickness and increased permeability [2]. At the time, there are no current treatments for relieving CCMs other than surgery. The existing treatments also have no concrete evidence observed to definitively relieve the condition [1].

We aim to explore possible solutions for CCM by approaching a different angle. By observing the endothelial cells' thinning membrane, we searched for ways to thicken it. Since cell membranes mainly consist of lipids and proteins, we postulated that an increase in Omega-3, a fat already existent in the cell, would be the best solution. Patients with CCM can use Omega-3 supplements as a treatment – as a non-invasive and inexpensive solution opposed to surgery. This is important as not everyone can afford surgery or have the conditions to go through it. We wanted everyone with this condition to receive fair treatment, and to raise awareness to explore other possible solutions for this neglected condition in the future.

Structure of an Endothelial cell [4]

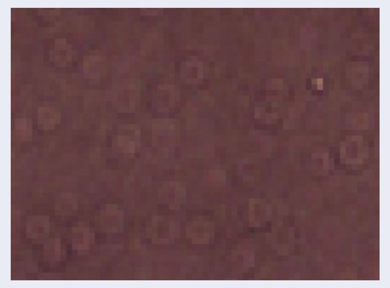
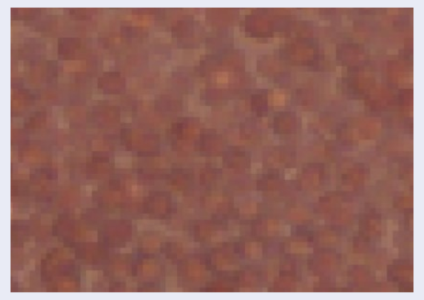
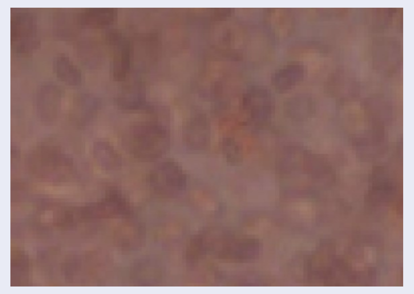
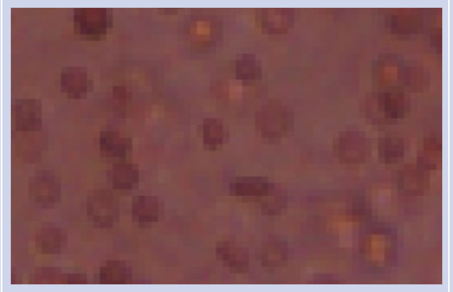
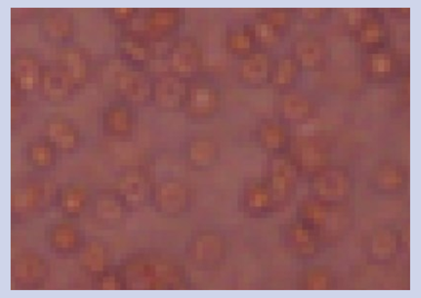


MRI of a Cerebral Cavernous Malformation in the brain [5]

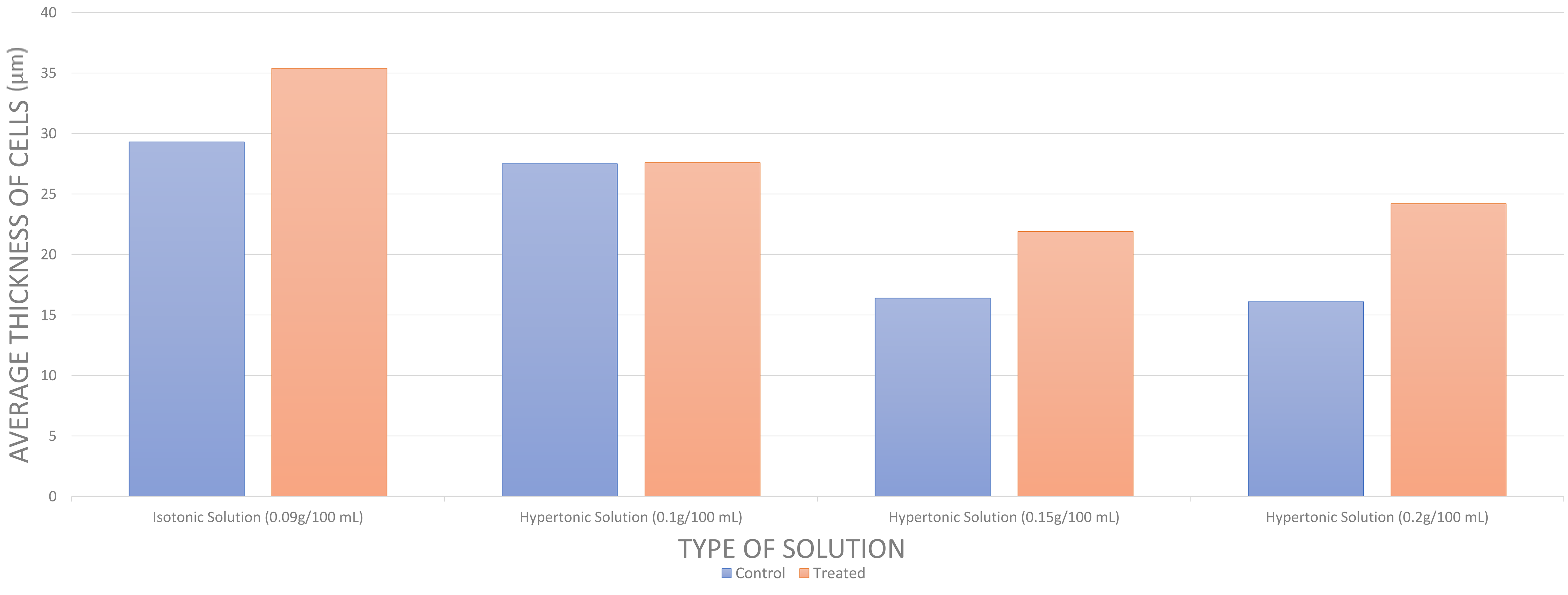
METHODS

- We used bovine red blood cells as a model for the endothelial cells. The pictures shown in the table below are the RBCs under the microscope.
- We put both the control and Omega-3 treated RBCs in concentration gradients (0.09%, 0.1%, 0.15%, 0.2%) of both hypertonic (salt and water) and isotonic solutions. We did this to emulate CCMs, because hypertonic solutions causes cells to shrink [3] similarly to CCMs.
- After a minute, we took pictures of the cells using a microscope.

DIFFERENCES OF BOVINE RED BLOOD CELLS IN ISOTONIC AND HYPERTONIC SOLUTIONS

Solution Type Concentration/ Solution	Isotonic Solution 0.09g/100 mL	Hypertonic Solution 0.1g/100 mL	Hypertonic Solution 0.15g/100 mL	Hypertonic Solution 0.2g/100 mL
Control				
Treated with Omega-3				
Notes	This is the control solution. As shown, there is no visible change because we need the hypertonic solution to shrink the cells first.	This is our lowest concentration. There is a slight change in size in the cells.	This is our second to highest concentration. Surprisingly, there is not a noticeable change in size, but the treated cells mostly kept their shape.	Our highest concentration shows the biggest difference. The control cells are shrunken and deformed, while the treated cells are thicker and circular.

Average Thickness of Bovine RBCs



RESULTS

We found that the Omega-3 treated red blood cells were bigger on average than the control cells. They also kept their circular shape while more of the control cells were split in half or deformed. By measuring 50 cells in each solution using Image J and averaging them to get a measurement of roughly how thick the cells are in each solution, we created the graph to the left to help visualize the differences in thickness between the control cells and the treated cells. This is in support of our hypothesis because it shows that Omega-3 will help RBCs keep their shape and increase thickness, opening new frontiers for possible CCM treatments in the future.