CONCUSSIONS, DIET, AND NEURODEGENERATIVE DISEASE PART 1

READERS SUMMARY:

1. How does energy depletion link neurodegenerative, concussions, and diet?
2. Why are diabetics more at risk for concussion and neurodegenerative diseases?
3. What is the NMDA receptor and why should I care?
4. How does the NMDA receptor work normally and in diseases like concussion to protect us?
5. How does glutamate, aspartate, and glycine tie into this story?

This series of blogs is going to focus in on neuronal injuries and how they all have a common tie to defective energy metabolism. The initial blog will be heavy on biochemistry but it will set the tone for you gaining a deeper appreciation of how damage to a receptor in our brains may cause different diseases, but have very common symptoms. I have focused in on energy depletion in some neurodegenerative diseases already, but we need to expand the net to explain how cerebral concussions and dietary choices are linked and can cause a less than optimal result for the person suffering from it. In this series I will also write a blog about chronic traumatic encephalopathy (CTE) since football season is now in session and this injury tends to make news in the fall sports sections. How this ties to diet may be new news for some of you.

In my recent Alzheimer's blog, we spoke of how neurons in AD become deficient in energy as they slowly die off. This is an example of **chronic energy depletion** enhancing a pathological

cellular process. An example of **acute energy depletion** is that of a concussed athlete. Once the head is impacted, it causes a dramatic alteration in the neurochemistry of the brain and leaves the person with a constellation of symptoms based upon the severity and duration of the impact. We have all seen pictures or heard stories of how concussions have caused athletes to miss games and have their career's threatened. The concept of energy deficiency is vitally important to remember when we talk about neuronal injury types. The injury can be from metabolic damage, trauma, or from dietary toxins. We also showed how devastating magnesium depletion is in the development of insulin resistance and diabetes in this blog. Nutrient depletions can play major co morbid roles when energy is also lacking in neurons. These factors alone are bad enough for neurons, but when they are combined, the summated results are even more problematic for the person to withstand.

I have a few patients in my practice whose professional careers were ended because their healthcare providers and employers did not understand these dynamics and how to optimally treat them. The loss of energy in a neuron is the initial critical event that can cause major pathologic problems to develop longer term. This is especially true if the correct information is not given to the person at this time. It is particularly bad if the person is already functioning sub-optimally and has compromised energy generation from leptin resistance, multiple traumas, or other diseases processes that limit us in some way. Even if one is in the best physical and mental shape of their life, it might have devastating consequences if other critical factors are present simultaneously as well.

In 1989, we learned that neurons deficient in energy became much more sensitive to the effects of excitatory neurotransmitters like glutamate and aspartate. I distinctly remember giving several talks about this finding during my residency in neurosurgery. These studies showed that if we

took cerebellar neurons in a glass jar and the surrounding terroir was designed to contain high levels of glucose (sugar) and magnesium, that even high levels of excitatory neurotransmitters could not cause neuron cell death. In impact studies we have also found that diabetics cannot withstand head impacts as well as those who were non diabetic. That stands to reason because the cells cannot use glucose normally and diabetics all tend to be magnesium deficient. The most interesting effect occurred when glucose was removed from the neurons surroundings and it was made energy depleted. Then even a small amounts of the excitatory glutamate or aspartate could kill the neurons. Many foods are loaded with these chemicals. The brain is usually protected from the dietary assault by its blood brain barrier, but this is not the case in trauma or in many neurologic conditions. This allows the brain to be further assaulted in these cases. For example, in traumatic injury, right after the impact their is a huge surge of these excitatory chemicals liberated from our damaged brain cells. This clinical situation is important given what we learned from the 1989 experiments cited here. When the researchers then decided to also remove the magnesium from the experimental surroundings of the nerve cells as well, even smaller doses of the glutamate were able to induce neuronal death. The depletion of magnesium and glucose are clearly critical to energy generation in neurons. Energy depletion sensitized the neurons to death or injury depending upon the level of insult. Even today in brain trauma or stroke care, physicians are taught not to start IVs containing glucose so as to protect brain cells from damage and to supplement with magnesium to protect the brain from further injury.

In the human brain glutamate is used as a neurotransmitter in over 50% of the synapses in the neocortex of the frontal and temporal lobes. These are the areas of the brain where many neurodegenerative disorders are also found. This is also happens to be the place where the brain is injured in most cerebral concussions as well. I believe this is not a

coincidence either. Glutamate's main action is to excite the brain and prepare it for action. When this part of the brain is damaged it causes memory loss, learning disability, inability to act and plan, and a loss of cognition. These symptoms are all commonly seen in neurodegenerative disorders, trauma, and metabolic conditions that patients can suffer. These symptoms tend to occur together when excessive glutamate or aspartate is allowed to remain around nerve cells no matter the cause.

The action of glutamate occurs at several receptors. We will focus on the most common receptor in this blog. The most common is the N-methyl-D-aspartate receptor. We refer to it as the NMDA receptor for short. Glutamate, aspartate and glycine (dietary amino acids) can all stimulate this receptor. The NMDA receptor is a non-specific cation channel which can allow Ca^{2+}, Na^{+}, and K^{+} to pass into the nerve cell under normal conditions to facilitate neurochemical messages between cells. The net influx creates and excitatory post synaptic potential (EPSP) to occur between neurons. This is how nerve cells communicate in learning and memory and to initiate behavior. Mg^{2+} not only blocks the NMDA channel in a voltage-dependent manner but also potentiates NMDA-induced responses at positive membrane potentials. This means that Magnesium glycinate and magnesium taurinate treatment can be used to produce rapid recovery from depression and in post concussive patients. We know it is very effective in diabetics because of their inherent metabolic depletion. The reason Mg works, is that it blocks the NMDA receptor from firing constantly to cause neurons damage because of the low magnesium levels in those nerve cells. These findings are also seen in concussed depressed patients, those with diabetes, and those with AD or PD too. Na^{+}, K^{+} and Ca^{2+} not only pass through the NMDA receptor channel in normal conditions but also modulate the activity of NMDA receptors. Zn^{2+} (zinc) and Cu^{2+} (copper) generally block NMDA current activity in a noncompetitive and a voltage-independent manner. However, zinc may potentiate or inhibit the current depending on the surrounding neural

activity. The levels of Zn and Cu in the body are directly tied to diet, stress response, and to the integrity of the gut's brush border. The NMDA receptor therefore functions in the human brain as a "molecular coincidence detector". Its ion channel only opens when the following two conditions are met simultaneously: glutamate is bound to the receptor, and the postsynaptic cell is depolarized (which removes the Mg2+ blocking the channel). This specific property of the NMDA receptor explains many aspects of long term potentiation (LTP) and synaptic plasticity and it confers to humans the ability to learn and adapt.
NMDA receptor function is also strongly regulated by chemical reduction and oxidation status, via the so-called "redox modulatory site." Through this site, reductants dramatically enhance NMDA channel activity, whereas oxidants either reverse the effects of reductants or depress native responses. It is generally believed that NMDA receptors are modulated by endogenous redox agents such as glutathione, alpha lipoid acid, and the essential nutrient pyrroloquinoline quinone (PQQ) which is a B vitamin. Glutathione is the bodies major antioxidant and it acts to protect neurons under assault. Alpha lipoid acid and PQQ have major beneficial effects on mitochondrial function in nerve cells and improve energy utilization. I often consider prescribing these to patients who are concussed or suffer from neurodegenerative diseases for this reason. (see my peripheral neuropathy post under the AGE tab)

In the next blog we will see how excitatory amino acids in foods and introduced to our GI tract could cause us some problems with normal functioning, cause plateaus, and interfere directly with weight loss. We will discuss how MSG and Splenda could wreck havoc with the human brain. This is especially true if that brain already has been concussed many times or is afflicted with some neurodegenerative disorder.

Cites:

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