

## Brain Repair – Application Guide

### Clinical Context

Fatigue and brain fog are among the most common patient concerns in functional medicine practice. And they're not just current concerns. They're potential markers of brain dysfunction that could increase the risk of problems like brain cell loss, CNS autoimmunity, and dementia. So, we want to be alert to symptoms of brain dysfunction, understand the parts of the puzzle, and know what to do to address the patient's brain properly.

### What the Brain Needs

#### Growth Factors

Growth factors like brain derived neurotrophic factor (BDNF) and nerve growth factor (NGF) are an essential component of CNS repair. Lion's Mane mushroom is a promoter of NGF. It's been used with excellent results in restoration of CNS integrity.

**Brain Reset** (Pure Encapsulation) – 2 BID or TID. Brain Reset contains Lion's Mane mushroom and other essential ingredients discussed next.

#### Circulatory Integrity

The brain needs oxygen and glucose to function. Without circulatory integrity, oxygen and glucose won't be delivered in adequate abundance.

**Brain Reset** (Pure Encapsulation) – 2 BID or TID. Brain Reset contains a special ginkgo-phosphatidylserine phytosome that provides bioavailable ginkgo and also phosphatidylserine. It also contains Butcher's Broom and Feverfew that add to ginkgo's circulation-enhancing properties. Brain Reset also contains Bacopa, which enhances neurotransmitter activation.

#### Histamine Clearance

Mast cells in the CNS are adjacent to microglial cells, the specialized macrophages that live in the brain and maintain the brain immunological environment. All mast cells have receptors for histamine. If the histamine level in the CNS gets high enough, mast cell histamine receptor stimulation will cause CNS mast cell degranulation. This shifts microglial cells to an inflammatory morphology, yielding CNS inflammation. So, it's essential to keep body and CNS histamine levels down to normal.

Keeping histamine levels low involves three steps:

1. Inhibition of mast cell degranulation.
2. Breakdown of mast cell mitochondrial DNA fragments (mtDNA's) released from mast cells in the intestine when the intestinal epithelial lining is inflamed. These mtDNA's re-inflate the intestinal epithelia, creating a loop of intestinal mast cell activation.
3. Support for aldehyde dehydrogenase (ALDH), a key enzyme required for histamine breakdown. The cofactors for ALDH are B2, B3, molybdenum, and iron.

**Hist Reset** (Pure) – 2 BID or TID. Hist Reset contains quercetin, luteolin, and rutin to inhibit mast cell degranulation, B2, B3, and molybdenum (cofactors for Aldehyde dehydrogenase), and bromelain to break down mast cell mitochondrial DNA fragments (mtDNA's). Iron is left out, so that it can be managed independently. Iron should only be given to patients with a verified need.

**Brain Reset and Hist Reset are often used in combination as a first step in restoring CNS integrity.** You'll find that they will sometimes be enough to get the job done. At other times, their use paves the way for whatever you use next to work better, since you will have installed supports without which other approaches may not work. In particular, it's essential that circulatory integrity be established, so that other substances you introduce can have a CNS impact.

### Autophagy

Autophagy is the process by which any cell repairs itself. In autophagy, a lipid sphere (autophagosome) is built around a broken organelle, then merged with a lysosome (lipid sphere containing enzymes), resulting in degradation and clearance of the broken organelle. Since neurons are post-mitotic tissue, you don't get a lot of new neurons. There is some adult neurogenesis, but not enough to rely upon to make a difference in clinical outcomes. So, the patient has to rely upon the nerve cells they've got. This makes repair of neurons through autophagy essential.

To support and promote autophagy, consider the following:

**Renual** (Pure) – 2 BID, to support mitophagy. Renual is urolithin A, a substance shown to promote mitophagy, the version of autophagy by which damaged mitochondria are eliminated. This is especially important if mitochondria dysfunction is contributing to the brain impairment picture.

**Th1 Support** (Pure) – 2 breakfast 2 lunch. The first step of autophagy is formation of the autophagosome, which is the lipid sphere encasing the broken organelle. This step depends on interferon gamma (IFN $\gamma$ ) which is a Th1 cytokine, and is inhibited by interleukin 4 (IL-4), a Th2 cytokine.

**Perilla Extract** (Pure) – 2 or 3 BID, to downregulate IL-4, to allow autophagosome formation.

**Balanced Immune** (Pure) – 2 BID, to downregulate NFkB, an inhibitor of autophagy.

**Glutathione or alpha lipoic acid** – 400 BID, to downregulate ROS, an inhibitor of autophagy.

**Lithium Orotate** – 10 to 20mg QD, to prevent inhibition of autophagy. Lithium blocks formation of inositol triphosphate, a blocker of autophagy.

A **fasting mimicking diet** (FMD) also promotes autophagy. This is often a great way to help patients turn the tide when they're in need of a strong push to shift them in a better direction. FMD also helps to reorganize metabolic integrity, so it helps with mitochondrial integrity and insulin resistance.

### Fatty Acid Support

The DHA component of fish oil is transformed into the D series resolvins and neuroprotectins that are essential for reducing inflammation in the CNS.

**DHA** – 1 gram BID

### Mitochondrial Repair

Over-fueled mitochondria make less ATP and generate abundant superoxide, a reactive oxygen species (ROS). ROS inhibit autophagy and upregulate NFκB, another inhibitor of autophagy. So, mitochondrial dysfunction can be a significant inhibitor of autophagy. Keeping in mind that brain repair depends upon autophagy, this is consistent with the view that dementia should be thought of as Type 3 diabetes. Things to consider in support of mitochondrial integrity:

**Renual** (Pure) – 2 BID, to support mitophagy. Renual is urolithin A, a substance shown to promote mitophagy, the version of autophagy by which damaged mitochondria are eliminated. This is especially important if mitochondria dysfunction is contributing to the brain impairment picture.

**Berberine** – 500mg BID. Berberine unloads over-fueled mitochondria by diverting some fuel into heat production. Patients who are cold all the time but have normal thyroid labs may have inadequate uncoupling proteins (UCPs) that divert fuel into heat production. Berberine increases UCP's. If you're giving **Th1 Support** in service of promoting autophagy, the Berberine in Th1 Support will serve this function well.

**Glucofunction** (Pure) – 1 per meal. This is a particularly good combination of substances that support glycemic control, in support of avoiding over-fueling mitochondria.

**Coenzyme Q10 and carnitine** are often important to consider for mitochondrial support.

**Glutathione or alpha lipoic acid** – 400 BID. One of these may be important to give, to downregulate the ROS being generated by mitochondrial dysfunction. If the blood glutathione level is low, you can give glutathione. If the patient has dysautonomia, you would favor giving alpha lipoic acid.

A **fasting mimicking diet** (FMD) also promotes autophagy. This is often a great way to help patients turn the tide when they're in need of a strong push to shift them in a better direction. FMD also helps to reorganize metabolic integrity, so it helps with mitochondrial integrity and insulin resistance.

### Identification and Downregulation of Body Inflammation

Body inflammation is a known promoter of brain inflammation. Inventory the factors contributing to the patient's body inflammation and address them.

**Balanced Immune** (Pure) – 2 BID, to downregulate body and CNS inflammation.

### Infection Detection and Eradication

Especially in older adults, an occult infection in places like lung or bladder can create a smoldering infection that significantly increases body and therefore CNS inflammation.

### Sleep

Deep sleep reduces inflammation and supports adequate Th1 response. This is why people sleep so much when they are fighting the flu or other serious infections.

**Melatonin** – 1 to 15mg at bedtime. Melatonin supports sleep initiation and Th1 response.

### Exercise

Exercise is very important, to stimulate circulation and oxygenation, improve aerobic integrity, and create neurosensory stimulation upon which the brain depends for activation.