

Medical Food to Stop the Progression of Parkinson's Disease

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Abstract

No progress has been made in the development of drugs to stop the progression of Parkinson's Disease. Here the author has presented a novel approach to stopping the disease using a dietary supplement primarily composed of Mannitol. *In vivo* animal studies have shown that Mannitol was able to break up alpha-synuclein clusters and restore functioning in transgenic drosophila and mice. The author, who has Parkinson's, used himself as a subject and was able to achieve similar results.

Keywords

Mannitol

1. Introduction

Parkinson's disease is a progressive neurological brain disorder characterized by tremors and difficulty with walking, movement and coordination. It is diagnosed by behavioral observation and reports. There is no blood or urine or tissue test for the disease. The disorder is most frequently diagnosed in someone in their middle 60's and is more common in men than in women. Evidence suggests that the neurons in the brain which produce dopamine play a crucial role in regulating movement and cognition. The degeneration and death of these dopaminergic cells produce the symptoms of Parkinson's disease. As the dopaminergic cells die, control over movement is diminished and Parkinson's disease symptoms are presented. One of the first observable symptoms of Parkinson's disease is trembling or shaking of a limb when the body is at rest. Other common symptoms include slow movement, a shuffling gait and a stooped posture. The disease can result in other secondary symptoms such as depression, anxiety, personality change, cognitive impairment, dementia, sleep disturbances, speech impairment and sexual problems. Sadly, there is no known "cure" for Parkinson's disease. The disease gets progressively worse as the neurons in the brain die. Current medication treatment is aimed at controlling the symp-

toms of the disease by attempting to increase the dopamine in the brain. The medications do not permanently increase dopamine and cannot restore the dopamine producing cells in the brain. As Parkinson's disease progresses, more dopamine cells die and the remaining cells cannot store sufficient dopamine to maintain the benefits of the medications. As the disease develops, the medications become less helpful and, usually after 6 months to 6 years, the full blown symptoms of Parkinson's disease return. There is an increase in both the frequency and severity of the symptoms over time. About 30% of cases end in dementia.

2. What Causes the Death of the Dopamine Producing Neurons?

The majority of the dopamine producing cells in the brain are lost by the end of the disease process. The root cause of this neurodegeneration is unknown. A major pathological event in Parkinson's disease is the formation of Lewy bodies which are deposits of proteins and lipids. How this relates to the extent of cell loss is not well known. Lewy bodies are also seen in Lewy Body dementia. In Parkinson's disease, there is substantial neuron loss in the substantianigra part of the brain [1].

Biochemical analyses have shown that alpha-synuclein is a major protein component of Lewy bodies and alpha-synuclein protein deposits in Lewy bodies are a marker of Parkinson's disease. Whether Lewy bodies are causal or consequential is unclear, however data supports a causal role for alpha-synuclein. A variety of evidence identifies defective alpha-synuclein as a potentially toxic protein to human neurons and toxicity is higher for dopamine producing neurons. Defective alpha-synuclein proteins have a tendency to aggregate and this aggregation may be a contributor to toxicity. There is no proof however that aggregation is relevant to the toxic effects of alpha-synuclein [2].

3. Recent Research

Researchers at the Albert Einstein College of Medicine of Yeshiva University have discovered recently how a mutation of a gene called leucine-rich repeat kinase-2 disrupts a garbage disposal process in cells that normally digest and recycle unwanted proteins, including alpha-synuclein. The disrupted disposal process is called chaperone-mediated autophagy. Autophagy means "self-eating". Normally old and damaged proteins are guided to enzyme-filled structures called lysosomes where the proteins are digested into amino acids and then recycled within the cell. When the mutated gene inhibits chaperone-mediated autophagy, alpha-synuclein doesn't get digested and instead accumulates to toxic levels in nerve cells [3].

(Excerpted from Science Daily, June 17, 2013) Profs. Ehud Gazit and Daniel Segal of Tel Aviv University's Department of Molecular Microbiology and Biotechnology and the Sagol School of Neuroscience, along with their colleague Dr. Ronit Shaltiel-Karyo and Ph.D. candidate Moran Frenkel-Pinter, have found that mannitol prevents clumps of the protein α -synuclein from forming in the brain—a process that is characteristic of Parkinson's disease [4].

These results were published in the *Journal of Biological Chemistry* and presented at the Drosophila Conference in Washington DC in April, 2013 [5]. After identifying the structural characteristics that facilitate the development of clumps of α -synuclein, the researchers began to hunt for a compound that could inhibit the proteins' ability to bind together. In the lab, they found that mannitol was among the most effective agents in preventing aggregation of the protein in test tubes. The benefit of this substance is that it is already approved for use in a variety of clinical interventions, Prof. Segal says.

Next, to test the capabilities of mannitol in the living brain, the researchers turned to transgenic fruit flies engineered to carry the human gene for α -synuclein. To study fly movement, they used a test called the "climbing assay," in which the ability of flies to climb the walls of a test tube indicates their locomotive capability. In the initial experimental period, 72 percent of normal flies were able to climb up the test tube, compared to only 38 percent of the genetically-altered flies.

The researchers then added mannitol to the food of the genetically-altered flies for a period of 27 days and repeated the experiment. This time, 70 percent of the mutated flies could climb up the test tube. In addition, the researchers observed a 70 percent reduction in aggregates of α -synuclein in mutated flies that had been fed mannitol, compared to those that had not.

These findings were confirmed by a second study which measured the impact of mannitol on mice engineered to produce human α -synuclein, developed by Dr. Eliezer Masliah of the University of San Diego. After four months, the researchers found that the mice injected with mannitol also showed a dramatic reduction of α -syn-

uclein in the brain.

The mechanism for disruption of alpha-synuclein clusters is explained in the paper presented in *The Journal of Biological Chemistry*, 288, 17579-17588.

4. Starting with N = 1

It is known that defective alpha-synuclein aggregates in Lewy bodies in the brain of Parkinson's disease patients. It is thought that these clusters have a toxic effect on dopamine producing cells in the brain. It is also known that mannitol breaks up alpha-synuclein clusters in the test tube and that mannitol crosses the blood brain barrier. Animal studies have shown that mannitol breaks up alpha-synuclein clusters in the brains of fruit flies that ingested mannitol and also in mice that were injected with mannitol. It is known that when alpha-synuclein clusters in the brains of fruit flies and mice were broken up that a majority of the mice and fruit flies dramatically improved their functioning.

Mannitol is FDA approved as a food for human consumption without a prescription and is on the FDA GRAS inventory (Generally Recognized As Safe). It is not known if mannitol would have the same effect on alpha-synuclein clusters in humans. Mannitol is used as an adjunct in certain therapies where the mannitol helps the active chemicals cross the blood brain barrier.

It was hypothesized that if mannitol and other chemicals were ingested in the right dosage by human subjects that they could pass the blood brain barrier and break up alpha-synuclein clusters, potentially stopping the progression of Parkinson's disease.

I am 66 years old and had all the symptoms of Parkinson's disease *i.e.* tremors, drooling, tiredness, falling down, loss of balance, trouble urinating, handwriting problems, shuffling, not sleeping etc. I used myself as a research subject. I started taking mannitol orally in small doses until I found a therapeutic dose that began to restore my functioning. There were some negative side effects including diarrhea, gas and urinary retention so I reduced the dose and added alpha-galactosidase to offset the side effects. I added vitamin D3 and vitamin K2 to feed the mitochondria that power the lysosomes that consume the defective alpha-synuclein. After 30 days I could stand and walk regularly. I had a great deal more energy, had much better balance, slept 8 to 10 hours a night, no longer had problems urinating, could walk up and down stairs without holding the rails and no longer drooled as often. I still had tremors but they were diminished. I have given the compound to others with Parkinson's who have had similar results. I have two patents pending on the compound. The supplement is prepared as a powder and the recommended dosage is one tablespoon daily dissolved in a cup of hot caffeinated coffee or tea.

5. Conclusions

I have been taking the supplement for over seven months as of January, 2014. I have had no new Parkinson's symptoms during that period of time. During a one week period I stopped taking it because my left eye swelled and I was fearful it was a side effect. I saw my primary care doctor and was diagnosed with an eye infection which was treated with a topical antibiotic. However, after 7 days off the supplement, I started having an increase in Parkinson's symptoms again. The symptoms diminished after 4 days back on the supplement.

Based on animal studies, it is believed that the supplement broke up alpha-synuclein clusters in my brain which resulted in stopping the progression of Parkinson's disease and restoring much of my functioning. It is also believed that the supplement rejuvenated the mitochondria in the lysosomes that consume the defective alpha-synuclein. The only definitive way to verify that is by autopsy. My neurologist is Dr Robert Hauser at the University of South Florida in Tampa, Florida.

Is this a cure for Parkinson's disease? No, however the daily dosage of the supplement has dramatically restored my functioning and I hope the major symptoms of the disease will stay in remission as long as I take a therapeutic daily dose. I believe the supplement I developed has stopped the progress of the disease and I know that it has greatly improved the quality of my life.

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