Effectiveness of Pentavalent Vanadium Ion Water in Treating Alzheimer's-Type Cognitive Disease (1)

1 Introduction

（1） In this ever-aging society, the number of cognitive disease pateints, including those with mild cognitive impairments, is at 8 million and rising. At the center of this societal issue is Alzheimer's disease, which constitutes 70% of all patients with cognitive dysfunction. The histopathological characteristics of Alzheimer's disease are commonly recognized as senile plaque (amyloid β peptide accumulation) and neurofibril changes all over the world. Still, the fundamental cause of Alzheimer's disease outside of old age is not known. As a result, 30 years of effort in drug development and testing in countries all over the world has produced absolutely no results.

（2） 15 or 16 years ago, I began my research into vanadium ion water. Before long, there were reports from several vanadium water suppliers who experienced drastic improvements in elderly symptoms of senility such as wandering, etc. by drinking vanadium water. I was asked the reason for this repeatedly. I had been researching vanadium ion water for about 2 years at the time, before any "Aoki Hypothesis" (Activity inhibition of cell membrane Na^+-K^+ATPase by pentavalent vanadium ion, resulting in a cascade chain reaction of various ion channels that rapidly increases calcium ion concentration which is then finally taken up and stored by organelles including the mitochondria, endoplasmic reticulum, and nucleus. Refer to the attached "Wonders of Vanadium" for more on how this process can be hypothesized in light of the varied physiological function of pentavalent vanadium ion and without contradicting pre-existing theories.), there was not a single out-of-the-ordinary phenomenon that indicated vanadium ion water had some therapeutic effect on Alzheimer's disease. However, the core of the "Aoki Hypothesis" is that calcium ions unmistakably play some key role in the improvement of Alzheimer's disease symptoms.

（2） A report was published in the July 2009 issue of Nature by the Harvard Medical School neurological diseases research group related to the fundamental cause of senility in Alzheimer's disease and neurological degradation. In the report, the authors indicated a deep connection between fundamental pathological phenomena in Alzheimer's disease and neuron Ca^{2+} concentration. Upon encountering this report, I formulated a tentative "Aoki Hypothesis" that

concluded that the total physiological activity of pentavalent vanadium ion was due to elevation of intracellular Ca^{2+} concentration.

2 Key points of the Harvard group report

（1） In patients with onset familial Alzheimer's disease, it has been confirmed that the intracranial metabolic product presenilin causes genetic changes and becomes inactive. The current cause of Alzheimer's disease onset, it is therefore the loss of presenilin activity followed by β amyloid peptide accumulation. However, there is no understanding or clear synapse dysfunction location or quality.

（2） The authors used genetic methods to carry out experimentation from multiple angles, including the relationship between presenilin deactivation and synapse location, and presenilin deactivation and intraneuronal Ca^{2+} concentration. The examination showed presynaptic deactivation of presenilin led to decreased release efficiency of the neurotransmitter glutamate, and it was shown that this was largely related to intraneuronal Ca^{2+} concentration changes. In conclusion, depleted intraneuronal Ca^{2+} inflow of electric potential-preserving calcium channels are strongly related to presynaptic terminal presenilin deactivation and these processes are indicated as early causal phenomena of senility and neurological deterioration with Alzheimer's disease.

3 Action of Ca^{2+} on brain neurons

If the hypothesis that states "brain neuron Ca^{2+} depletion is the fundamental cause of AD" is correct, the answer to the question of what sort of action Ca^{2+} exhibits in brain neurons can be understood as follows.

（1） Promotion of mitochondrial activity

Mitochondria are the organelles that produce the energy（ATP）required to sustain life and act depending on the activity of a given organism. The brain consumes 25% of the entire energy requirements of the body, which makes it easy to see why only a few minutes without blood flow due to heart attack or stroke can cause oxygen deprivation and brain death.

Mitochondrial activity fluctuates with Ca^{2+} concentration with a large increase (10^2 to 10^4) of possibly several hundreds-fold, but activity likewise decreased with decreases Ca^{2+} concentration. This can lead to sluggishness of life activities. ATP production and other biophysical research in recent years have taken Ca^{2+}

concentration into account, leading to a detailed understanding of the relationship between mitochondria and Ca^{2+}.

(2) The role of Ca^{2+} in maintaining homeostasis of astroglia

Astroglial cells move substances between neurons and blood vessels, as well as participate in the uptake of neurotransmitters released from the synaptic end of neurons. With these combined actions, they regulate the development and maintenance of neurons through the production of many neurotrophic factors. In recent years, it has been shown that astroglia, which perform the important role of constantly maintaining neurons in this manner, release Ca^{2+}-containing D-serine to the thousands of surrounding synapses in order to maintain synaptic plasticity.

Ca^{2+} also plays a regulatory role via glutamate and other compounds.

(3) The role of Ca^{2+}in maintaining homeostasis of neurotransmitter release

With chemical synapses, an impulse occurs at a neuron terminal. Then electric potential-dependent calcium channels in the presynaptic membrane open to allow the inflow of Ca^{2+}, thereby inducing the rapid (<1 mmsec) release of neurotransmitters from inside the synapse once Ca^{2+} reaches a very high concentration. Release occurs from synaptic vesicles in particular locations undergoing exocytosis. Released neurotransmitters disperse throughout the synaptic cleft and bond with the receptors on the postsynaptic membrane to illicit a variety of postsynaptic responses.

(4) The role of Ca^{2+} in maintaining homeostasis of the hippocampus

The hippocampus's basic function is in short-term memory, and abnormalities in the hippocampus can inform us of the onset of early-stage AD symptoms.

Furthermore, NMDA (N-methyl-D-aspartic acid) receptor channels that block Mg^{2+} to maintain a membrane potential, through the depolarization of the cell membrane, can no longer block Mg^{2+}. Ca^{2+} subsequently flows into the cell via the channel, activating intracellular signaling pathways. This has been shown to result in the strengthening of long-term memory.

Ca^{2+} in the neurons constantly play this crucial role, which is why a non-depleted supply of Ca^{2+} is required for maintained neuronal function. Given this, it is natural that a hypothesis stating "Ca^{2+} depletion in brain neurons is a

fundamental cause of AD" should be correct.

4 Future developments

Pentavalent vanadium ion water increases total intracellular calcium concentration through inhibiting Na^+-K^+ATPase activity. The "Aoki Hypothesis" which does not conflict with previously accepted theories, as well as the above Harvard group study, together provides cases 14 or 15 years prior that make this clear.

Future pentavalent vanadium ion water clinical studies related to Alzheimer's disease in the setting of the medical institution will reinforce and further the Harvard group research results that apply the "Aoki Hypothesis". Ingestion of pentavalent vanadium ion water will be seen as the sole treatment method that can be employed without fear of side effects to improve intraneuronal Ca^{2+} depletion: a fundamental cause of the onset of Alzheimer's disease. The author also believes that such research will help develop effective drugs that suppress the progression of Alzheimer's-type cognitive diseases.

April 2, 2016
April 25, 2017 partial revision

Takaomi Aoki

References

1. Takaomi Aoki, "Wonders of Vanadium" 2010
2. Chen Zhang et al., "Presenilins are essential for regulating neurotransmitter release." Nature. 2009 Jul 30;460(7255):632-6.
3. Kazuhiko Kohno et al., "Encyclopedia for Comprehensive Understanting of Cognitive Disorder" 2016
4. Kazutoshi Mori, "Intracellular Molecular Biology" 2016
5. NHK Special "Cure Alzheimer Disease"
6. Biochemistry Encyclopedia, Third Eddition