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PII: S2214-6474(16)30039-3
DOI: doi: 10.1016/j.bbacli.2016.09.003
Reference: BBACLI 125

To appear in: *BBA Clinical*

Received date: 17 August 2016
Revised date: 28 September 2016
Accepted date: 29 September 2016

Please cite this article as: Moon K. Song, David S. Bischoff, Albert M. Song, Koichi Uyemura, Dean T. Yamaguchi, Metabolic Relationship Between Diabetes and Alzheimer's Disease Affected by Cyclo(His-Pro) Plus Zinc Treatment, *BBA Clinical* (2016), doi: 10.1016/j.bbacli.2016.09.003

Metabolic Relationship Between Diabetes and Alzheimer's Disease Affected by Cyclo(His-Pro) Plus Zinc Treatment

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ABSTRACT

Background: Association of Alzheimer's disease (AD) with Type 2 Diabetes (T2D) has been well established. Cyclo(His-Pro) plus zinc (Cyclo-Z) treatment ameliorated diabetes in rats and similar improvements have been seen in human patients. Treatment of amyloid precursor protein (APP) transgenic mice with Cyclo-Z exhibited memory improvements and significantly reduced Aβ-40 and Aβ-42 protein levels in the brain tissues of the mice.
Scope of review: Metabolic relationship between AD and T2D will be described with particular attention to insulin sensitivity and Aβ degradation in brain and plasma tissues. Mechanistic effect of insulin degrading enzyme (IDE) in decreasing blood glucose and brain Aβ levels will be elucidated. Cyclo-Z effects on these biochemical parameters will be discussed.
Major conclusion: Stimulation of IDE synthesis is effective for the clinical treatment of metabolic diseases including AD and T2D.
General Significance: Cyclo-Z might be the effective treatment of AD and T2D by stimulating IDE synthesis.

1.0 INTRODUCTION

Alzheimer's disease (AD) is the most common form of dementia culminating in the gradual accumulation of amyloid-beta (Aβ) protein into microscopic "plaques" and the twisting of tau proteins into strands of dead and dying neurons. It is also characterized in the early stages with defects in inflammation and oxidative stress [1]. Inflammation is especially important as it occurs in pathologically vulnerable regions of AD and can influence AD development. Individuals suffering from AD exhibit several behavioral symptoms including: confusion, disorganized thinking, memory loss, impaired judgment, and disorientation. In the final stages, they lose the ability to communicate, fail to recognize loved ones, and become bed-bound, which is ultimately fatal. About 5 million Americans were afflicted with AD in 2013 [2] and this number is projected to be 14 million in the USA alone by the year 2050. Worldwide, nearly 44 million individuals are currently afflicted with this disease [3]. The cost of caring for AD patients in the US was estimated to be $226 billion in 2015 with the global cost for caring estimated to be $605 billion [4].

Diabetes, both Type 1 and 2, are also major health concerns. The pathology of Type 1 diabetes (T1D) is insulin deficiency with no β-cell response to glucose. Type 2 diabetes (T2D) starts with hyperinsulinemia, but this condition deteriorates during the progression of diabetes until the patients can