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英 語（応用薬学分野）

全文を和訳せよ

Alzheimer's disease (AD) is a progressive neurodegenerative brain disease and the most common type of dementia, which causes significant damage to learning and memory. The main characteristic of AD is the accumulation of intracellular neurofibrillary tangles^(注1) (NFTs), caused by hyperphosphorylation of tau protein and accumulation of extracellular amyloid- β (A β) plaques which are produced by enzymatic digestion of amyloid precursor protein (APP) by the sequential enzymatic activity of beta-secretase 1 (BACE1) and γ -secretase. Most AD cases (~ 98 %), are aging subjects and also suffer from various other comorbidities^(注2) (e.g. stress, obesity, diabetes, cancer, stroke, congestive heart failure, seizures, coronary artery disease, chronic kidney disease, osteoporosis, and renal disease). Among the comorbidities, obesity and diabetes are the most dominant metabolic disorders affecting the human population. According to the Alzheimer's Association Report, there is some 37 percent comorbidity between diabetes and AD. Several studies demonstrate that diabetes confers about a 1.6-fold increased risk of developing dementia. Besides, high body mass index (BMI) and central obesity during middle age, has consistently been associated with a higher risk of dementia later in life (3.5 times increased risk). As a result, glycemic control together with weight control at childhood and midlife become an immediate priority to prevent or moderate cognitive decline in aging.

Because of the strong linkage between these three disorders and increased financial costs for the treatment of the afflicted patients, using a triple therapeutic agent to modulate the onset and progression of the three disorders can lead to significant cost savings.

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注1: 神経原線維変化 注2: 併存症

採 点	
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