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Diabetes & its Complications

Hypoglycemia and Dementia: Is Alzheimer's Disease a Consequence of Sugar Deficiency?

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ABSTRACT

This next essay will bring proof of reductions in cerebral glucose metabolism found in AD patients, possibly indicating that AD stems from Glucose insufficiency. It would later counter this assumption by showing the extremely high prevalence of AD among diabetics, and then, solve the mystery by proving that what's causing the dementia among diabetics is actually avoiding sugar according to doctor's orders. It will prove it by showing an unbreakable link between hypoglycemic (hypo, not hyper) events in diabetics and the risk of developing Alzheimer's disease.

It's therefore will prove that AD in fact stems from lack of glucose consumption over the years and would suggest glucose as a possible treatment to AD patients.

Keywords
Hypoglycemia, Dementia, Alzheimer's disease.

Introduction

Part 1: Reductions in cerebral glucose metabolism are observed in Alzheimer's disease

"One of the main features of Alzheimer's disease is impairment of brain energy. ***Hypometabolism caused by decreased glucose uptake is observed in specific areas of the AD-affected brain.*** *Therefore, glucose hypometabolism and energy deficit are hallmarks of AD"* [1]

"One of the main features of Alzheimer's disease (AD) is the severe reduction of the cerebral metabolic rate for glucose (CMRglc). In vivo imaging using positron emission tomography with 2-[(18)F] fluoro-2-deoxy-D-glucose (FDG-PET) demonstrates consistent and progressive CMRglc reductions in AD patients, the extent and topography of which correlate with symptom severity. Increasing evidence suggests that CMRglc reductions occur at the preclinical stages of AD. CMRglc reductions were observed on FDG-PET before the onset of disease in several groups of at-risk individuals, including patients with mild cognitive impairment (MCI), often a prodrome to AD" [2]

"Another characteristic of AD is regional hypometabolism in the brain. This decline in cerebral glucose metabolism occurs before pathology and symptoms manifest, continues as symptoms progress, and is more severe than that of normal aging." [3]

And also here: *"Variants of the apolipoprotein E allele appear to account for most cases of late-onset Alzheimer's disease, and persons with two copies of the ε4 allele appear to have an especially high risk of dementia. Positron-emission tomography (PET) has identified specific regions of the brain in which the rate of glucose metabolism declines progressively in patients with probable Alzheimer's disease. We used PET to investigate whether these same regions of the brain are affected in subjects homozygous for the ε4 allele before the onset of cognitive impairment.*

Results

The ε4 homozygotes were cognitively normal. They had significantly reduced rates of glucose metabolism in the same posterior cingulate, parietal, temporal, and prefrontal regions as in previously studied patients with probable Alzheimer's disease.

They also had reduced rates of glucose metabolism in additional prefrontal regions, which may be preferentially affected during normal aging." [4]

We can also see the same findings here: "Reductions in regional cerebral glucose metabolic rate (CMRglu) as measured by fludeoxyglucose F 18–positron emission tomography (FDG-PET) is also associated with increased AD risk and can be observed years before dementia onset." [5]

"We show that lowering glucose level to 2mM leads to dramatic increases of neuron degeneration on day 3 and 5 of treatment and decreased cell viability on day 7" [6]

Part 2: Hypoglycemic events and correlation to higher Alzheimer's risk

According to this, one could assume that AD or Dementia are caused by glucose insufficiency but this is challenged by AD's extremely high prevalence among diabetics which even led several scholars to even call AD "Type 3 diabetes" [7]

How could we settle these conflicting reports? Simply, diabetics avoid sugar according to doctor's orders, that's why they develop dementia. And this has been proved by the unbreakable bond between hypoglycemia (Hypo, not hyper) episodes among diabetics and the risk of developing Alzheimer's. like seen here: *"Individuals in the severe hypoglycemia group were more likely to be diagnosed with dementia compared to individuals without severe hypoglycemia (23.3% vs 7.3%; P < .001) and the overall incidence of Alzheimer disease was higher than vascular dementia. Dementia risk rose with increasing number of severe hypoglycemic episodes (1 episode [hazard ratio (HR) = 1.54; 95% CI, 1.48-1.60], 2 or more episodes [HR = 1.80; 95% CI, 1.66-1.94])."* [8] and here: *"Those who experienced a hypoglycemic event had a 2-fold increased risk for developing dementia compared with those who did not have a hypoglycemic event (34.4% vs 17.6%, P < .001; multivariate-adjusted hazard ratio, 2.1; 95% CI, 1.0-4.4). Similarly, older adults with DM who developed dementia had a greater risk for having a subsequent hypoglycemic event compared with participants who did not develop dementia (14.2% vs 6.3%, P < .001; multivariate-adjusted hazard ratio, 3.1; 95% CI, 1.5-6.6)"* [9]

"In the fully adjusted model that controlled for all confounders, the occurrence of at least one hypoglycemia episode was associated with 27% higher odds of subsequent dementia (hazard ratio = 1.27; 95% confidence interval = 1.06–1.51). The risk increased with the number of hypoglycemia episodes: one episode (hazard ratio = 1.26; 95% confidence interval = 1.03–1.54); two or more episodes (hazard ratio = 1.50; 95% confidence interval = 1.09–2.08)." [10]

"Patients with underlying hypoglycemic events had an increased risk for all-cause dementia, Alzheimer's dementia (AD), and vascular dementia (VaD) compared with those who had not experienced a hypoglycemic event (hazard ratio [HR], 1.254; 95% confidence interval [CI], 1.166 to 1.349; P<0.001 for all-cause dementia; HR, 1.264; 95% CI, 1.162 to 1.375; P<0.001 for AD; HR, 1.286; 95% CI, 1.110 to 1.490; P<0.001 for VaD). According to number of hypoglycemic episodes, the HRs of dementia were 1.170, 1.201, and 1.358 in patients with one hypoglycemic episode, two or three episodes, and more than three episodes, respectively. In the subgroup analysis, hypoglycemia was associated with an increased risk for dementia in both sexes with or without T2DM microvascular or macrovascular complications" [11].

Materials and Methods

In total, 45 patients with type 1 diabetes, age 74.9±6.7 years, and HbA1c levels of 7.9±0.9% were studied. Severe hypoglycemia occurred in 33% of patients, and the number of severe hypoglycemia episodes was 0.6±1.2 in the past 5 years before the time of the cognitive function tests. We analyzed clinical data and dementia scores on the Revised Hasegawa's Dementia Scale (HDS-R), Mini-Mental State Examination (MMSE), and Dementia Assessment Sheet for Community-based Integrated Care System, and 21 items (DASC-21).

Results

There was a significant correlation between HbA1c and HDS-R, MMSE, respectively. There was a significant correlation between the number of severe hypoglycemic episodes and HDS-R, MMSE, and DASC-21, respectively. When the group with experience of severe hypoglycemia was compared to the control group, HDS-R, MMSE, and DASC-21 were meaningfully different after adjusting for age modeling analysis of covariance." [12]

"Ten studies with a total of 1,407,643 patients were included. Pooled analysis of all ten studies indicated that hypoglycemic episodes were associated with a statistically significant increase in the risk of dementia in DM patients as compared to those not experiencing hypoglycemic episodes (HR: 1.44 95% CI: 1.26, 1.65 I2 = 89% p<0.00001). The results did not change on the exclusion of any study. Sub-group analysis based on the study population, type of study, adjustment for glycated hemoglobin, gender, and the number of hypoglycemic episodes also presented similar results." [13]

According to this study: "Diabetes mellitus was managed more intensively in older veterans with dementia and cognitive impairment, and dementia and cognitive impairment were independently associated with greater risk of hypoglycemia." [14] and here the researchers studied not hypoglycemic events, but a state they call RH – Recurrent moderate hypoglycemia: *"we report that insulin-controlled hyperglycemia slightly aggravated AD-type pathologies and cognitive impairment; however, RH (Recurrent moderate hypoglycemia) significantly increased neuronal hyperactivity and accelerated the progression of cognitive deficits in streptozotocin-induced (STZ-induced) diabetic APP/PS1 mice. Glucose transporter 3-mediated (GLUT3-mediated) neuronal glucose uptake was not significantly altered under hyperglycemia but was markedly reduced by RH, which induced excessive mitochondrial fission in the hippocampus."* [15]

We know that Glucose has an important part in bodily processes, we know that for example glucose is secreted by Cortisol to handle stressful situations so it's not surprising to find out that "Blood collected during the PET scans showed, for the normal group, a rise in plasma glucose levels, starting approximately 25 min after hydrocortisone administration. The AD group did not show this effect" [16].

Discussion and Conclusions

It seems essential to re-think science and medicine stance against glucose and to thoroughly examine glucose deficiency in dementia. This could have revolutionary effect but this change must happen sooner rather than later. In a world where so many people and organizations are preaching against eating sugar it's not even surprising that AD rates are higher than ever, this further understanding of the disease could have enormous consequence. Doctors should begin advocating eating at least some sugar a day to avoid developing dementia.

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