

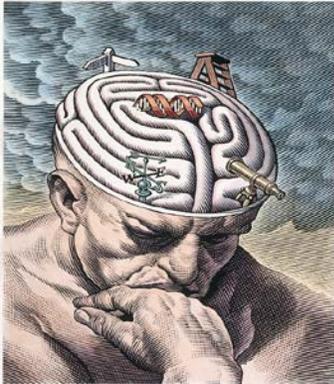
Type Three Diabetes: Are You at Risk?

A Systematic Review

Mary Ellen Yep
University of New England

Background

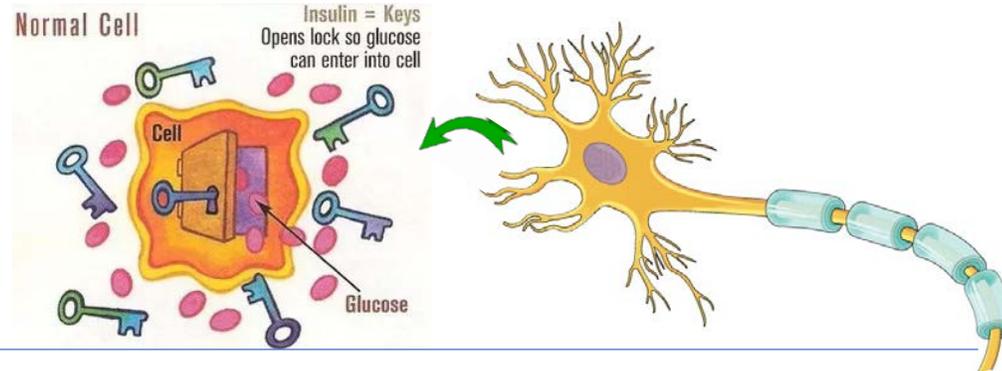
Type three diabetes is a term recently coined to unveil the link between type 2 diabetes mellitus (T2DM) and dementia, specifically Alzheimer's Disease (AD). In 2015,¹ type 2 diabetes was the sixth leading cause of disability in the United States. It is characterized by unusually high levels of glucose in the blood.² The etiology of T2DM is largely due to insulin resistance combined with disturbance in the key role of insulin producing beta cells.²⁻⁵ Alzheimer's disease is the most common form of dementia and becomes worse over time.^{6,7} Brain glucose metabolism is reduced in AD and glucose metabolism is also impaired in cells as an epidemiological characteristic of T2DM.⁸ There is a growing interest to study the link between these two diseases.



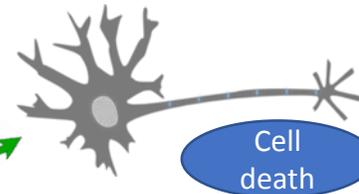
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Study Design

A systematic review was conducted by searching electronic databases of current literature, published from January 2010 to January 2019, using the PRISMA Protocol. Articles that met the criteria (subjects >18 years old) were selected by one reviewer. Electronic databases (PubMed, Cochrane, Proquest, Scopus, PsycInfo, and SocInfo) were used to find articles with key search words: "Dementia + Type 2 Diabetes Mellitus" OR "Alzheimer's Disease + Type 2 Diabetes Mellitus." Nine studies were used in this systematic review.



Insulin resistance → inability to uptake glucose in brain



Results

In this systematic review, the results show a positive association between type 2 diabetes mellitus in mid-life and later dementia, such as Alzheimer's Disease.⁸⁻¹³ At the cellular level insulin unlocks the cells' ability to metabolize glucose. In type two diabetes mellitus, insulin is resisted by the cell which leaves glucose roaming the blood with no where to go.¹⁻⁵ Likewise, the metabolism of glucose in the human brain is completely dependent on insulin.¹⁴ In the event where no insulin is present, glucose, which is an energy source for the neurons, can not be used and the neurons begin to degenerate.^{6,7,10} This degeneration leads to cell death of the neuron; as a result, cognitive and memory functions are impaired and lead to Alzheimer's Disease.⁸⁻¹⁶

Conclusions:

This systematic review explains the relationship between type 2 diabetes mellitus and the formation of Alzheimer's disease. This review also indicates how those with type 2 diabetes mellitus are at an increased risk of Alzheimer's disease because of the metabolic problems of insufficient insulin for cells; this prevents the uptake of glucose in cells, as seen in the neurons of the brain. Further study into oxidative stress will be necessary to clarify the etiology of type 2 diabetes mellitus along with Alzheimer's disease.

References:

- Chatterjee S, Khunti K, Davies MJ. Type 2 diabetes. *The Lancet*. 2017;389(10085):2239-2251.
- Alonso-Magdalena P, Quesada I, Nadal A. Endocrine disruptors in the etiology of type 2 diabetes mellitus. *Nature Reviews*. 2011;7(6):346-353.
- Javeed N, Matyenko AV. Circadian etiology of type 2 diabetes mellitus. *Psychology*. 2018; 33(2):138-150.
- McGarry JD. Dysregulation of fatty acid metabolism in the etiology of type 2 diabetes. *Diabetes*. 2002;51(1):7-18.
- Sjoholm A, Nystrom T. Inflammation and the etiology of type 2 diabetes. *Diabetes/Metabolism Research and Reviews*. 2005;22(1).
- Peric A, Annaert W. Early etiology of Alzheimer's disease: tipping the balance toward autophagy or endosomal dysfunction? *Acta Neuropathologica*. 2015;129(3):363-381.
- Shcherbatykh I, Carpenter DO. The role of metals in the etiology of Alzheimer's disease. *Journal of Alzheimer's Disease*. 2007; 11(2):191-205.
- Pedditi E, Peters R, Beckett N. The risk of overweight/obesity in mid-life and late life for the development of dementia: a systematic review and meta-analysis of longitudinal studies. *Age and Ageing*. 2016; 45(1):14-21.
- Walker JM, Harrison FE. Shared neuropathological characteristics of obesity, type 2 diabetes and Alzheimer's disease: impacts on cognitive decline. 2015; 7(9):7332-7357.
- Arnoldussen IAC, Kiliaan AJ, Gustafson DR. Obesity and dementia: adipokines interact with the brain. *European Neuropsychopharmacology*. 2014; 24(12):1982-1999.
- Baglietto-Vargas D, Shi J, Yaeger DM, Ager R, LaFerla FM. Diabetes and Alzheimer's disease crosstalk. *Neuroscience & Biobehavioral Reviews*. 2016;64: 272-287.
- Reddy VP, Zhu X, Perry G, Smith MA. Oxidative stress in diabetes and Alzheimer's disease. *Journal of Alzheimer's Disease*. 2009;16(4):763-774.
- Moran C, Phan TG, Chen J, Blizzard L, Beare R, et al. Brain atrophy in type 2 diabetes: regional distribution and influence on cognition. *Diabetes Care*. 2013;36(12).
- Bingham EM, Hopkins D, Smith D, Pernet A, et al. The role of insulin in human brain glucose metabolism: an (18)fluoro-deoxyglucose positron emission tomography study. *Diabetes*. 2002; 51(12):3384-90.
- Shalev D, Arbuckle M. Metabolism and memory: obesity, diabetes, and dementia. *Biological Psychiatry*. 2017;82(11):e81-e83.
- Qiu WQ, Au R, Zhu H, Wallack M, Liebson E. Positive association between plasma amylin and cognition in a homebound elderly population. *Journal of Alzheimer's Disease*. 2014;42(2):555-563.

Objectives

The object of this systematic review is to investigate the following research question: How are patients with type 2 diabetes mellitus at an increased risk for dementia, such as Alzheimer's Disease, compared to patients without diabetes? This review examined the link between these two disease.