



# Type 1 Diabetes and Risk of Neurodegenerative Disease: Evidence from Human and Preclinical Studies

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## Abstract

Type 1 diabetes is an autoimmune condition affecting over 1.8 million Americans and is steadily growing. Individuals with Type 1 diabetes appear to have an increased risk of certain neurodegenerative diseases compared to non-diabetic populations. *BMJ Diabetic Research & Care* performed a clinical study of a large Finnish cohort comprising of diabetics and non-diabetics. They observed significantly elevated standardized incidence ratios (SIRs) for Alzheimer’s disease and vascular dementia, and a modest increase in Parkinson’s disease. The *International Journal of Molecular Sciences* examined short-term Type 1 diabetes in female rats. The researchers found increased neuroinflammatory markers and reduced synaptic proteins in the hippocampus, suggesting early synaptic dysfunction. These findings provide biological plausibility for the increased incidence of neurodegenerative disease observed in human populations. The results from both studies support an association between type 1 diabetes and neurodegenerative diseases.

## Background

Type 1 diabetes is an autoimmune condition affecting over 1.8 million Americans and is steadily growing. The immune system recognizes beta cells as a threat and mounts an attack against them. Hyperglycemia is known as high blood sugar, which can be dangerous over an extended period. Oxidative stress is an imbalance in the body where oxygen is used to produce harmful and reactive products, leading to decreased oxygen in the body. Insulin signaling refers to how cells respond to insulin once it binds to receptors. In the brain, disruptions in this signaling pathway may contribute to neuronal dysfunction and degeneration. Diabetic encephalopathy is a complication of diabetes mellitus that affects the central nervous system and often shows up as cognitive impairment and motor dysfunctions. Neurodegenerative diseases can cause mental deterioration, which can potentially affect gross and fine motor skills as well as memory.

An SIR greater than 1 indicates that the disease occurs more frequently in the Type 1 diabetes population than in the reference population, particularly between ages 60–79. Type 1 diabetes may promote neurodegenerative processes through chronic neuroinflammation and synaptic dysfunction, increasing risk for multiple neurodegenerative diseases.

## Do individuals with Type 1 diabetes have an increased risk of neurodegenerative diseases beyond Alzheimer’s disease and dementia?

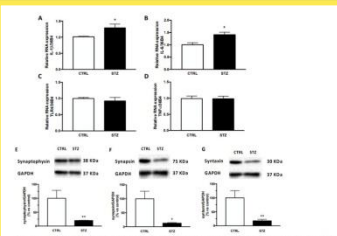
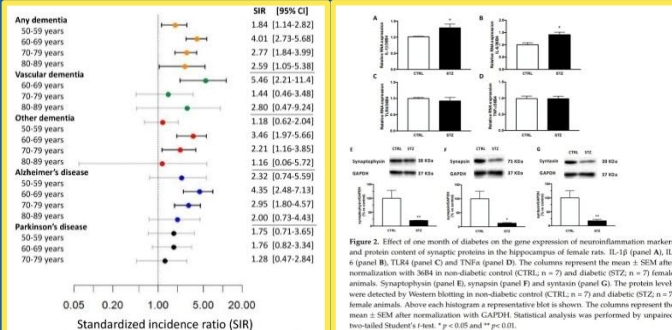


Figure 2. Effect of one month of diabetes on the gene expression of neuroinflammation markers and protein content of synaptic proteins in the hippocampus of female rats. IL-1β (panel A), IL-6 (panel B), TNF-α (panel C) and TNF-β (panel D). The columns represent the mean ± SEM after normalization with 58k in non-diabetic control (CTRL; n = 7) and diabetic (DIAB; n = 7) female animals. Synaptophysin (panel E), synapain (panel F) and synaptin (panel G). The protein levels were detected by Western blotting in non-diabetic control (CTRL; n = 7) and diabetic (DIAB; n = 7) female animals. Above each histogram a representative blot is shown. The columns represent the mean ± SEM after normalization with GAPDH. Statistical analysis was performed by unpaired two-tailed Student's t-test. \*p < 0.05 and \*\*p < 0.01.

## Discussion/Figures

The figure on the left describes the Standardized Incidence Ratio (SIR) of neurodegenerative diseases between type 1 diabetics and control groups. The SIRs are all greater than 1, meaning disease occurs more frequently in the study population compared to the reference population. *BMJ Diabetic Research & Care* performed a clinical study of a large Finnish cohort comprising of diabetics and non-diabetics. They observed significantly elevated SIRs for Alzheimer’s disease and vascular dementia, and a modest increase in Parkinson’s disease. The risk varied by age and disease type but was 2-3 times more prevalent in several categories.

The authors of the *BMJ Diabetic Research & Care* article said that “The excess mortality in people with type 1 diabetes might influence our results since NDs increase with aging.” Neurodegenerative diseases are closely associated with old age. Type 1 diabetics have a higher mortality rate than non-diabetics. Trying to establish a correlation between NDs and diabetes becomes more difficult with this information in mind.

The figure on the right shows the results of the effects of neuroinflammation in female rats with type 1 diabetes after a month. The researchers found increased neuroinflammatory markers and reduced synaptic proteins in the hippocampus, suggesting early synaptic dysfunction. In the *International Journal of Molecular Sciences*, they tested the short-term effects of type 1 diabetes on memory in adult female rats. This journal article helped narrow down what could potentially be a factor in type 1 diabetes contributing to a cognitive decline. After this article was published, other research groups could use these findings to design clinical studies.

The authors of the *International Journal of Molecular Sciences* article said that “one limitation of this study is the use of the NOR as a unique test to evaluate memory dysfunction.” The Novel Object Recognition (NOR) test is primarily used on rodents. This means that to further their research on human participants, they would have to perform different memory tests, potentiating different results.

## Conclusion

Individuals with Type 1 diabetes appear to have an increased risk of certain neurodegenerative diseases. These studies support the argument that type 1 diabetes may contribute to neurodegenerative processes through inflammatory and synaptic mechanisms. Preclinical data suggest that chronic hyperglycemia induces neuroinflammation and synaptic protein loss in the hippocampus, providing biological plausibility for the increased incidence observed in human populations. The results from both studies support an association between type 1 diabetes and neurodegenerative diseases; however, more research is needed to delve further into possible improvements for the mental deterioration it causes.

## References

- Satuli-Autere, Susanna, et al. “Increased Incidence of Neurodegenerative Diseases in Finnish Individuals With Type 1 Diabetes.” *BMJ Open Diabetic Research & Care*, vol. 12, no. 4, Sept. 2024, p. e004024. <https://doi.org/10.1136/bmjdr-2024-004024>.
- Falvo, Eva, et al. “Diabetic Encephalopathy in a Preclinical Experimental Model of Type 1 Diabetes Mellitus: Observations in Adult Female Rat.” *International Journal of Molecular Sciences*, vol. 24, no. 2, Jan. 2023, p. 1196. <https://doi.org/10.3390/ijms24021196>.

## Sex Differences in Diabetic Neurodegeneration: An Understudied Variable

The *International Journal of Molecular Sciences* stated that “...diabetic encephalopathy shows sex-dimorphic features” (Falvo et al., 2023), meaning that male and female brains are wired differently, creating room for different reactions to certain stimulants. In this case, the female rats produced different results compared to their male counterparts when given type 1 diabetes for one month.