



Insight into the Link between Alzheimer's and Type 2 Diabetes

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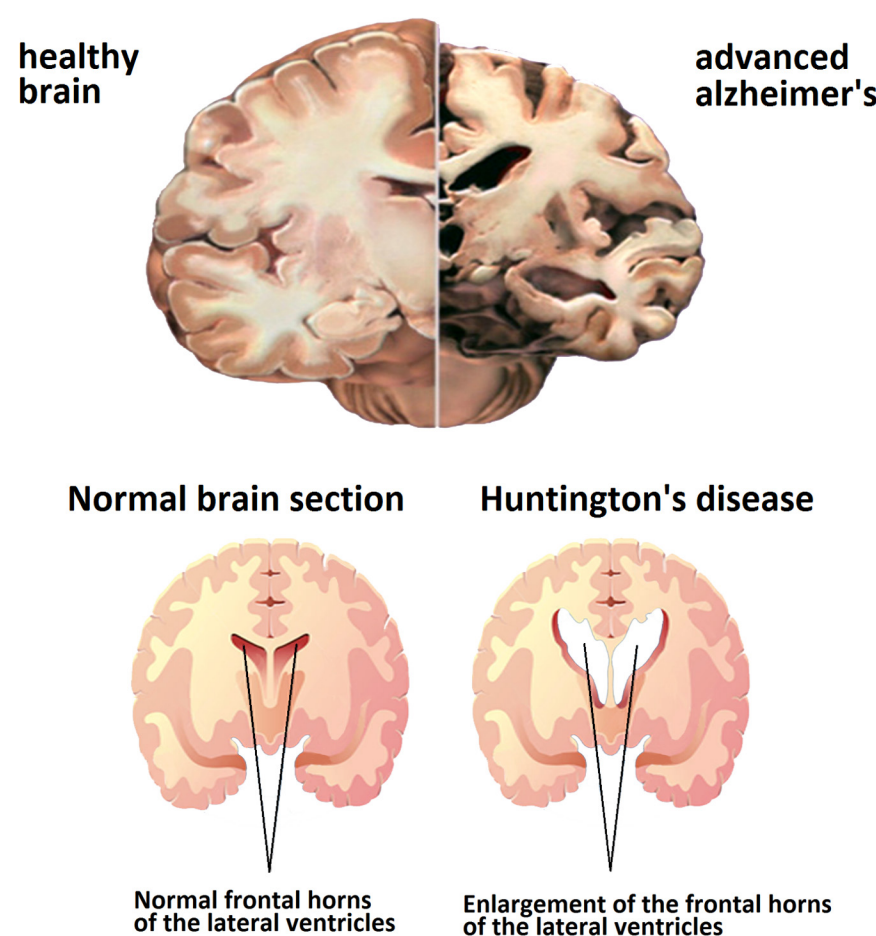
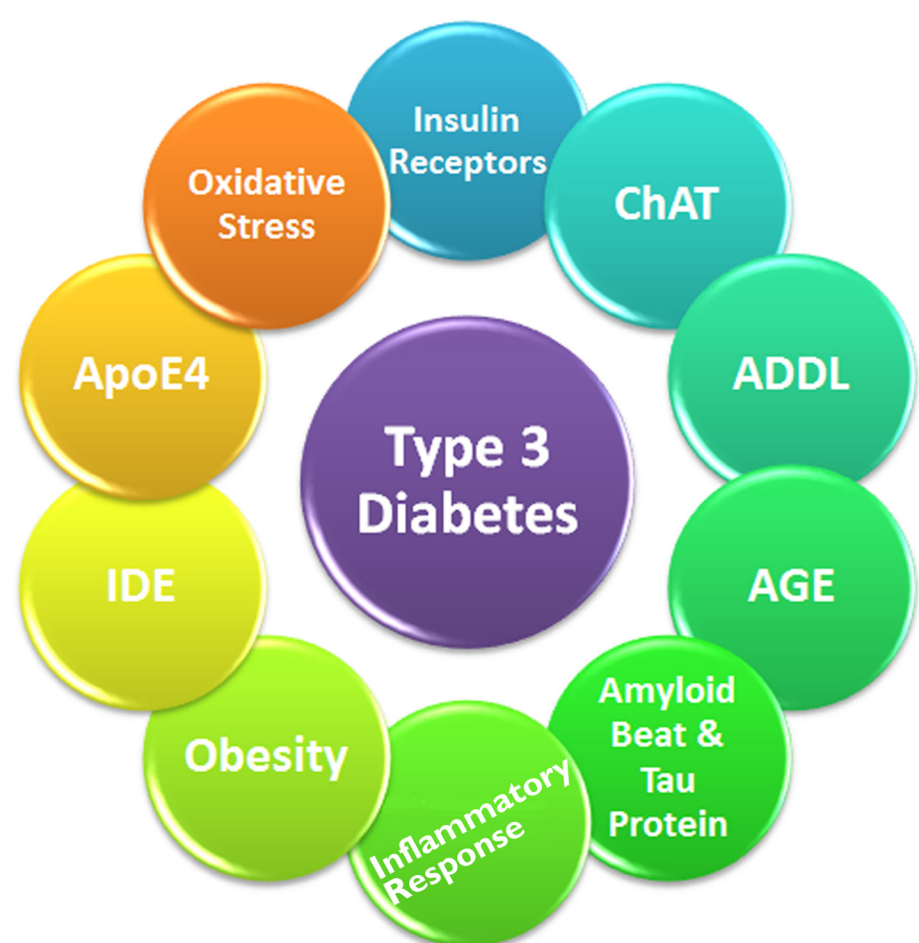
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Introduction

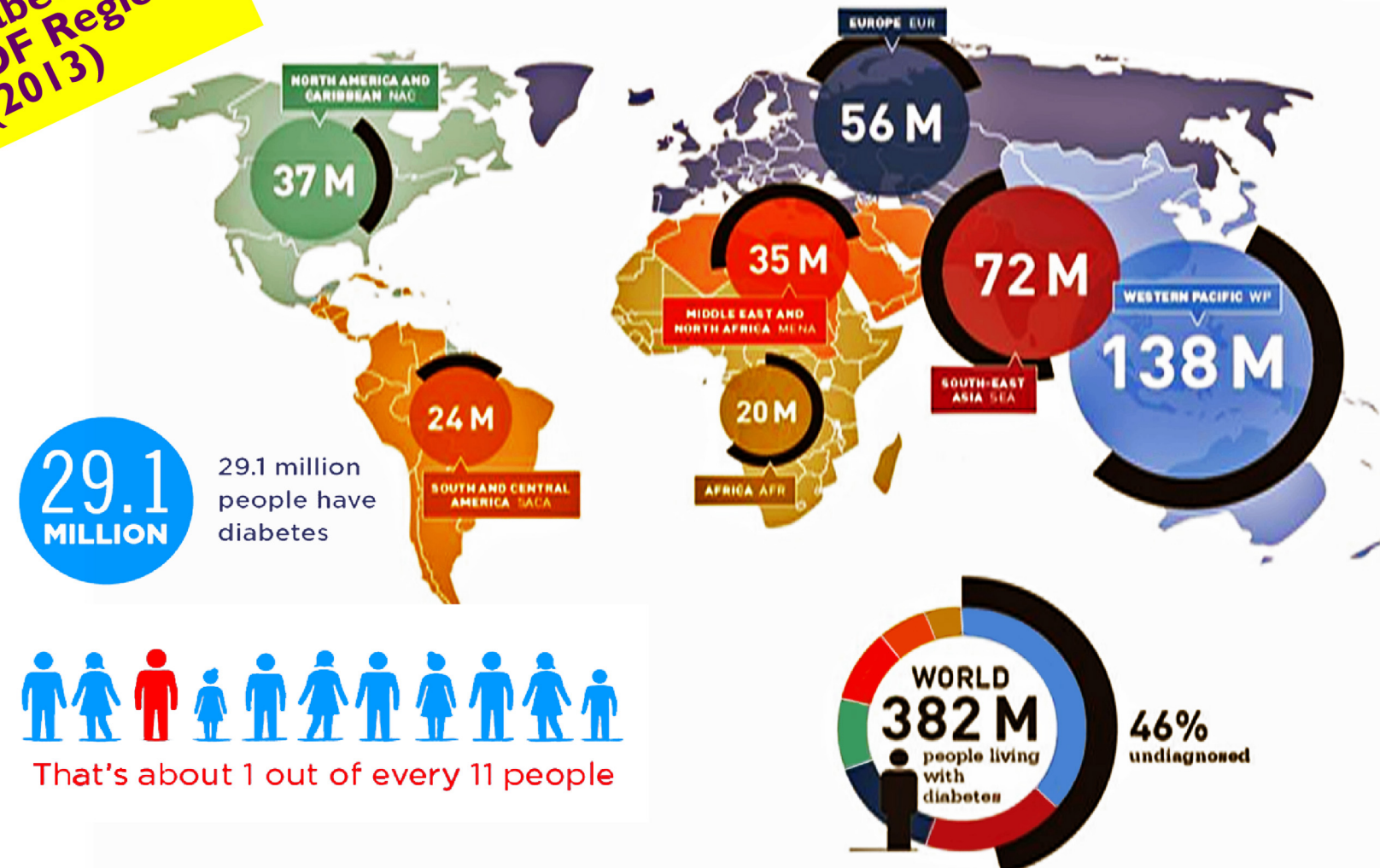
Studying about links between diabetes and Alzheimer disease is one of the most significant fields in which many researchers of life science or medicine have done examinations on them. According to statistics released by the World Health Organization «diabetes is the sixth and Alzheimer's is the seventh leading cause of worldwide death» and it makes us do more research on the subject. Among the relationship between the two diseases can be noted to beta-amyloid, oxidative stress, tau protein, insulin receptors, advanced glycation end products (AGE), which the better understanding of these diseases can be a way to better control them.

Mechanisms that may link diabetes and dementia

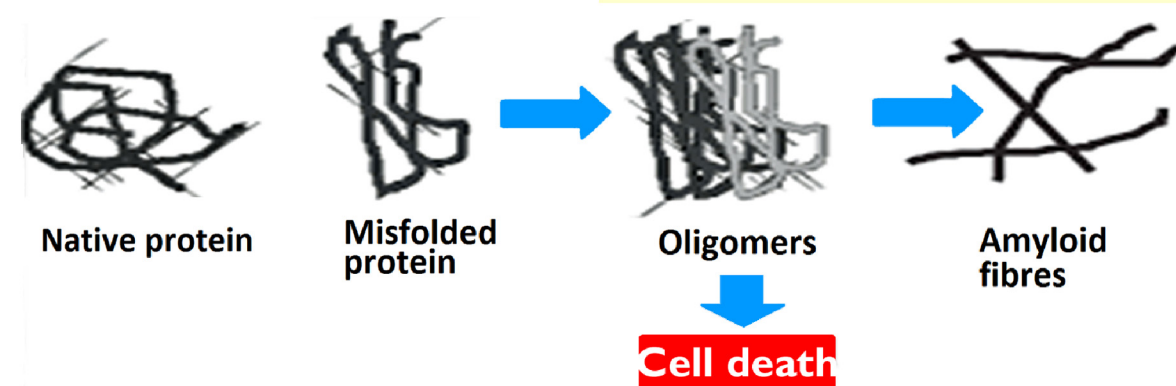


Alzheimer's Disease (AD) is the most common form of dementia culminating in the gradual accumulation of amyloid-beta protein into microscopic "plaques" and the twisting of tau proteins into strands of dead and dying neurons.

Population of diabetics by IDF Region (2013)



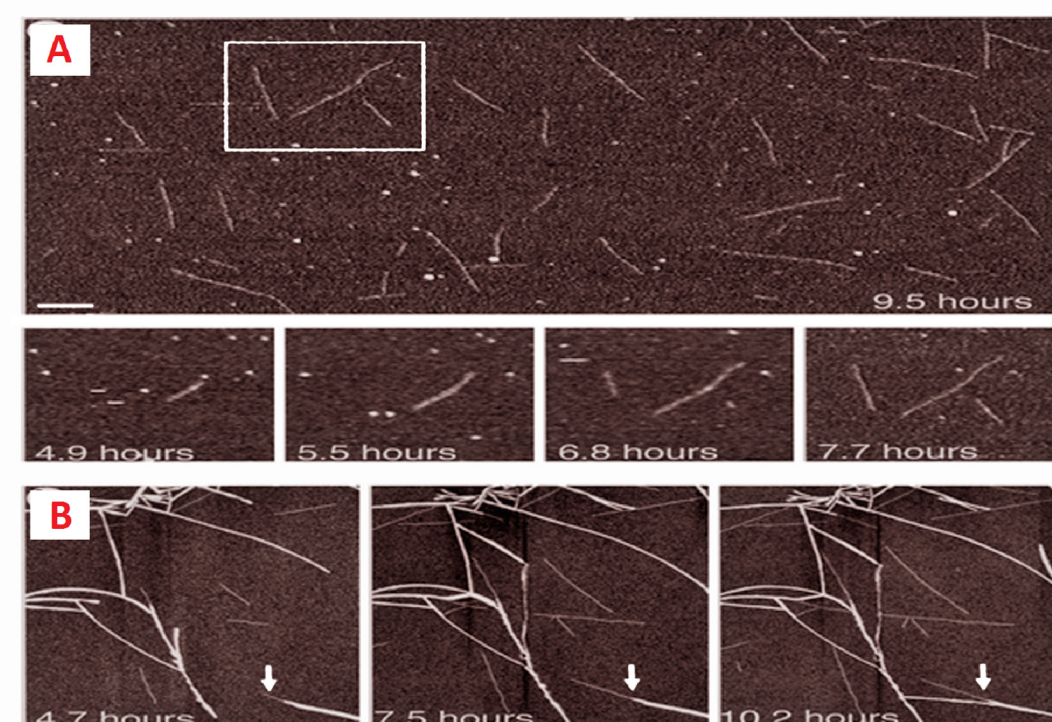
The Pathway of amyloid fibrillation



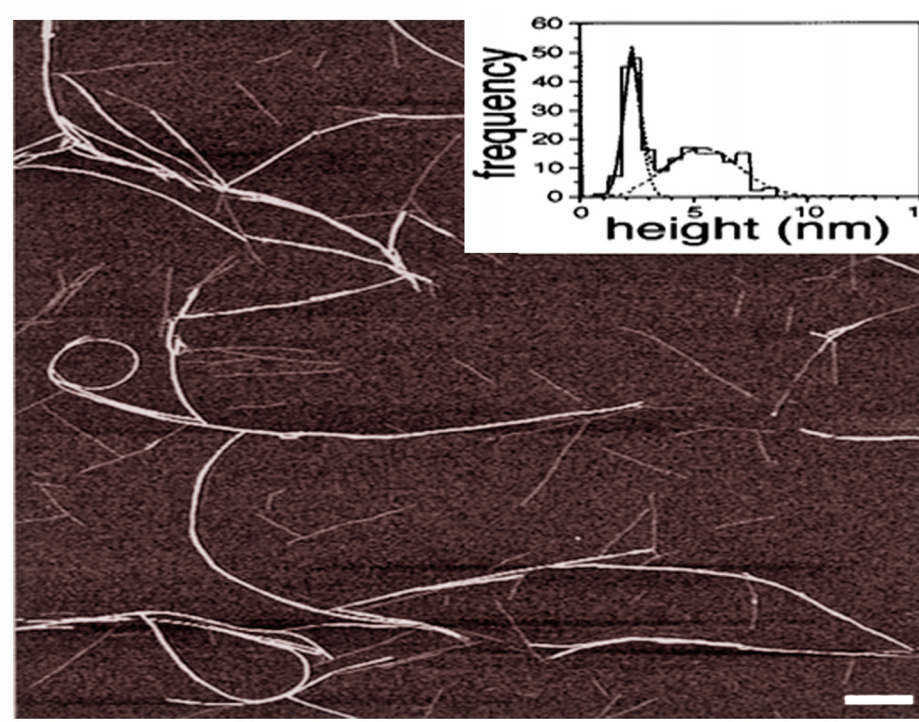
Methods

We investigated several physical properties by means of techniques such as isoelectric focusing (IEF), fluorescence, Mass Spectrometry, Atomic Force Microscopy (AFM), and Nuclear magnetic resonance spectroscopy (NMR).

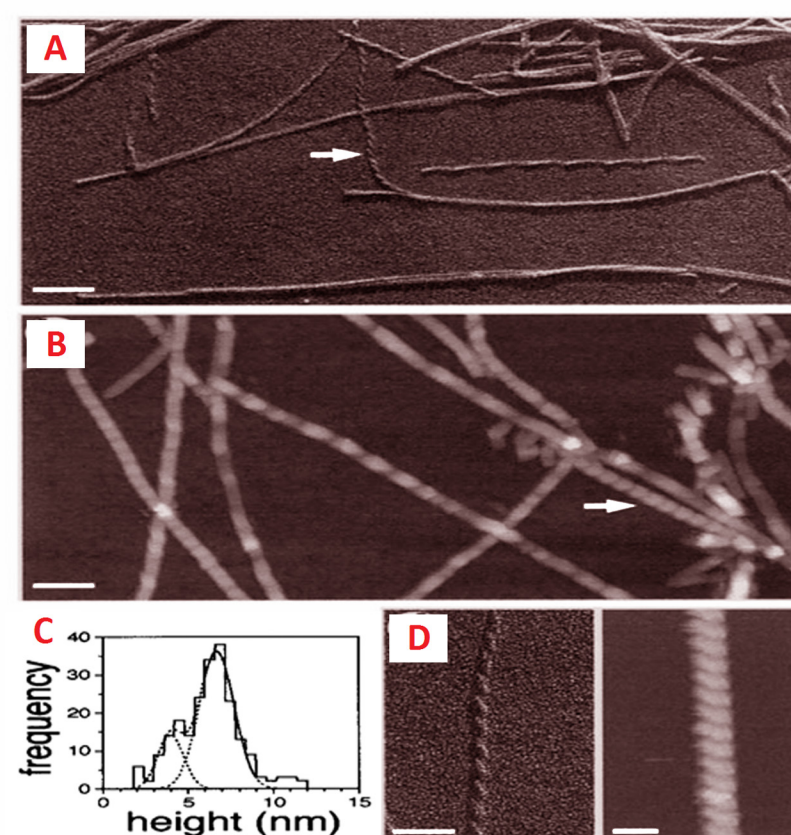
Watching amyloid fibrils' growth by time-laps atomic force microscopy



Amylin fibrils' growth in the AFM. (a) 2.4-nm protofibrils. The gallery displays previous scans of the boxed area in the larger overview picture at the times indicated. Bidirectional fibril growth is evident. (b) 2.4-nm protofibrils and higher-order fibrils growing over time. Arrows point to a protofibril growing from the end of a higher-order fibril. The scale bar represents 200 nm.



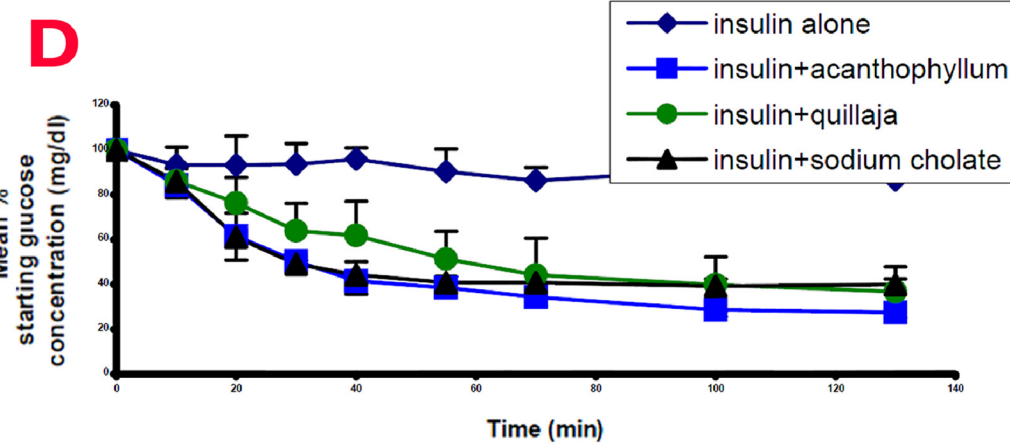
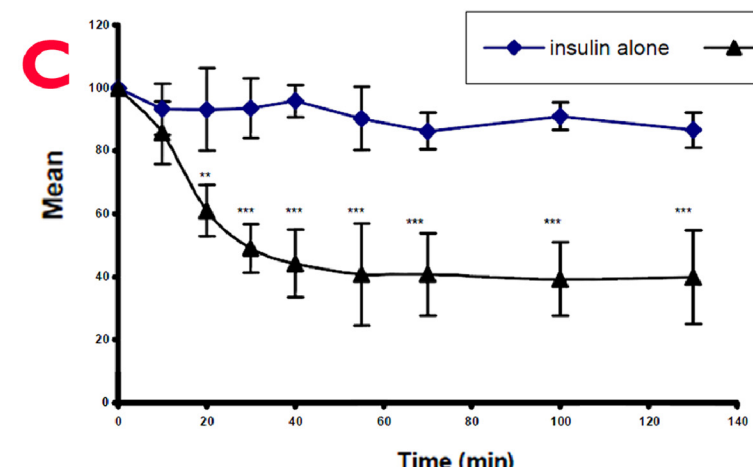
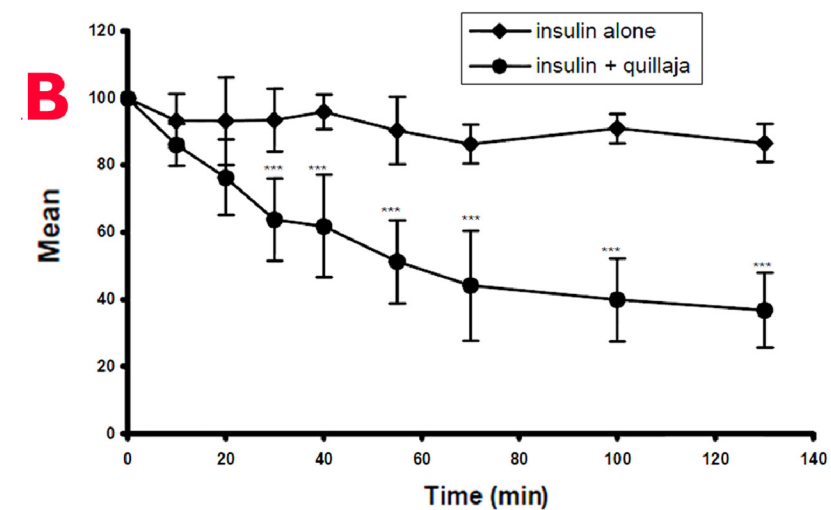
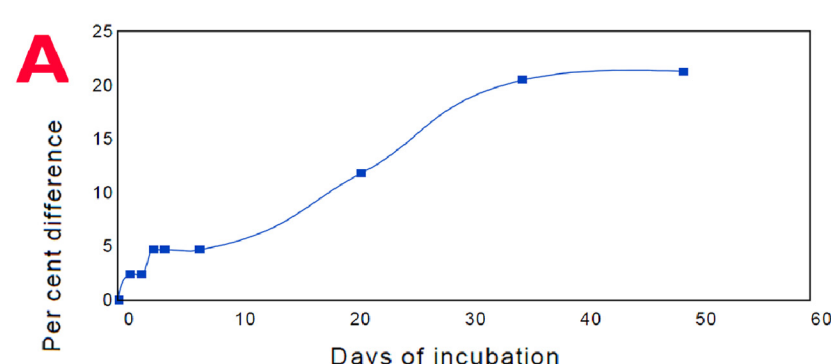
Amylin fibrils assembled on a mica surface. AFM of sample under buffer showing both the prominent fibril type with a height of 2.4 nm, and higher order fibrils. The scale bar represents 200 nm. The inset shows the fibril height distribution which has been fitted with Gaussian curves.



Formation of amylin fibrils in the test tube (a) Freeze-dried tungsten-shadowed amylin fibrils visualised by EM. (b) AFM in buffer reveals polymorphic fibrils including the fibril type with a regular 25-nm cross-over periodicity (arrow). (c) AFM fibril height distribution fitted with Gaussian curves. (d) Comparison of the fibril type with a distinct 25-nm left handed cross-over periodicity imaged by EM after freeze drying/tungsten shadowing (left), and by AFM in buffer (right). The scale bars represent 100 nm (a), (b)); and 50 nm (d).

Results & discussion

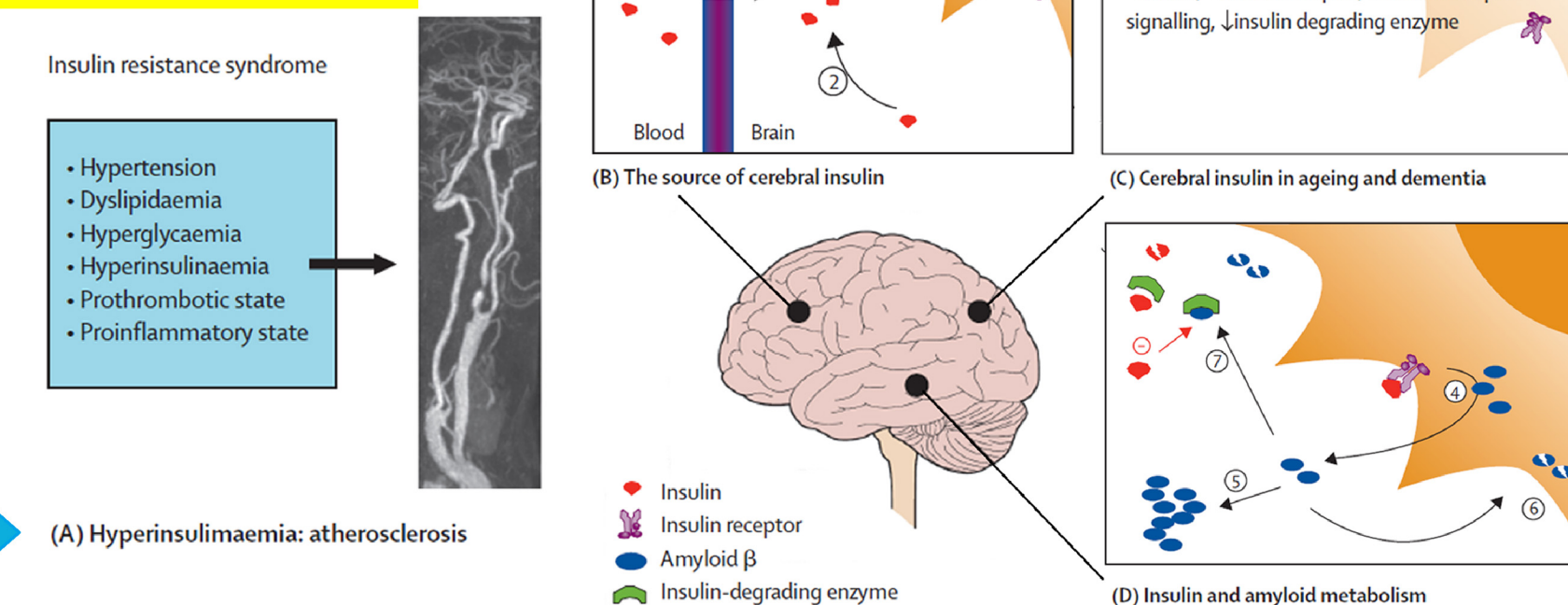
The investigation confirmed that increasing the amount of blood sugar in people with diabetes and those without diabetes causes dementia, including Alzheimer's disease. The brain is the organ of the body is hurt by an increase in blood glucose. given that the cure for Alzheimer's disease had not been reported, Can control blood sugar levels by techniques that are causing it to prevent early detection and control. You can also disrupt communication path of these two diseases by reducing free radicals, resulting in oxidative stress pathways is activated, preventing the formation of amyloid plaques and even hoped to cure diseases.



Evaluating the progress of diabetes

Investigation of AGE albumin in diabetic patients by isoelectric focusing and fluorescence to evaluate the progress of diabetes. (a) The relative percentage changes in immunization, albumin, glycated albumin, serum albumin, glucose incubation period of seven weeks, (b) Changes in the relative fluorescence of AGE compounds in sterile incubation period of 70 days with negative quantities of sugar to reduce the amount of added sugars compared to zero, (c) Changes during 49 days of incubation at increased electrophoretic mobility of albumin in sterile glucose change in isoelectric focusing isoelectric pH, (d) Comparison of serum samples from diabetic sera of healthy isoelectric focusing.

The potential role of insulin in the pathogenesis of dementia



Conclusion

Now, to better recognize the link between diabetes and Alzheimer's and also step forward on the path of their relationship the science of biophysics and biophysical tools can be great assistance.

References:

1. Butterfield, D.A., Di Domenico, F. and Barone, E., 2014. Elevated risk of type 2 diabetes for development of Alzheimer disease: a key role for oxidative stress in brain. *Biochimica et Biophysica Acta (BBA)-Molecular Basis of Disease*, 1842(9), pp.1693-1706.
2. Zhao, W.Q. and Townsend, M., 2009. Insulin resistance and amyloidogenesis as common molecular foundation for type 2 diabetes and Alzheimer's disease. *Biochimica et Biophysica Acta (BBA)-Molecular Basis of Disease*, 1792(5), pp.482-496.
3. Pugazhenthil, S., Qin, L. and Reddy, P.H., 2016. Common neurodegenerative pathways in obesity, diabetes, and Alzheimer's disease. *Biochimica et Biophysica Acta (BBA)-Molecular Basis of Disease*.
4. Goldsby, C., Kistler, J., Aebi, U., Arvinte, T. and Cooper, G.J., 1999. Watching amyloid fibrils grow by time-lapse atomic force microscopy. *Journal of molecular biology*, 285(1), pp.33-39.
5. Vivekanandan, S., Brender, J.R., Lee, S.Y. and Ramamoorthy, A., 2011. A partially folded structure of amyloid-beta (1-40) in an aqueous environment. *Biochemical and biophysical research communications*, 411(2), pp.312-316.