

## **New horizons of diabetes: Type 3 diabetes**

**Madhukar Saxena**

**Department of Biotechnology, Babasaheb Bhimrao Ambedkar University (A Central University) Vidya Vihar,**

**Rai Bareilly Road, Lucknow-226025, (INDIA)**

**E-mail: madhukarbio@gmail.com**

**Received: 24<sup>th</sup> September, 2013 ; Accepted: 27<sup>th</sup> October, 2013**

The present knowledge of diabetes has been enhanced and been explored day by day. Till now, most of the researchers are gearing about the Type 1 (T1DM) and Type 2 diabetes (T2DM). However, new doors of are open called Type 3 diabetes. Insulin is also produced in brain apart from pancreas. For the survival of brain cells insulin and its growth factors are necessary, failure may contribute to the progression of Alzheimer's disease. This secreted brain insulin and its related proteins with reduced levels in brain are directly or indirectly associated with Alzheimer's disease. This is now become as "Type 3 diabetes" (T3DM).

This reduced level of insulin production in brain cells impairs the proper function of brain cells initiates the symptoms of Alzheimer's. These abnormalities in the brain cells do not revealed by T1DM and T2DM as well as their associated complications. This point of improper function focused a new and more complex disease that originates in the central nervous system (CNS)<sup>[1-3]</sup>. The defect lies in the gene that blocks insulin signaling in the brain where insulin and insulin growth factors (IGFI and IGFII) are all expressed in the neurons. Alzheimer's disease (AD) has characteristic histopathological, molecular and biochemical abnormalities, including cell loss; abundant neurofibrillary tangles; dystrophic neurites; amyloid precursor protein, amyloid- $\beta$  (APP-A $\beta$ ) deposits; increased activation of prodeath genes and signaling pathways; impaired energy metabolism; mitochondrial dysfunction; chronic

oxidative stress and DNA damage. The recent contribution of researchers showed that AD represents a form of diabetes mellitus that selectively afflicts the brain. The human and experimental animal model studies also showed that CNS impairments in insulin/IGF signaling mechanisms can occur in the absence of T1DM or T2DM. However, obesity with T2DM causes brain insulin resistance with some features of AD-type neurodegeneration, the effects are relatively modest, not associated with significant histopathological lesions and lack most of the critical abnormalities that typify AD. Therefore, T2DM was deemed not sufficient to cause AD, although it could possibly serve as a cofactor in its pathogenesis or progression. Altogether, the data provide strong evidence that AD is intrinsically a neuroendocrine disease caused by selective impairments in insulin and IGF signaling mechanisms, including deficiencies in local insulin and IGF production. At the same time, it is essential to recognize that T2DM and T3DM are not solely the end results of insulin/IGF resistance and/or deficiency, because these syndromes are unequivocally accompanied by significant activation of inflammatory mediators, oxidative stress, DNA damage and mitochondrial dysfunction, which contribute to the degenerative cascade by exacerbating insulin/IGF resistance. Referring to AD as T3DM is justified, because the fundamental molecular and biochemical abnormalities overlap with T1DM and T2DM rather than mimic the effects of either one. Some of the most relevant

data supporting this concept have emerged from clinical studies demonstrating cognitive improvement and/or stabilization of cognitive impairment in subjects with early AD following treatment with intranasal insulin or a PPAR agonist<sup>[4,5]</sup>. Impaired insulin signaling has already been linked to increased oxidative stress and mitochondrial dysfunction in neuronal cells<sup>[6-8]</sup>. Additional studies demonstrated that the AD-associated abnormalities in insulin/IGF-I signaling mechanisms were not accompanied by reduced expression of GLUT4 or IDE. Altogether, the results suggest that impaired insulin/IGF-I stimulated survival signaling and attendant chronic oxidative stress represent major abnormalities in AD. From the standpoint of therapeutic intervention, treatment with ligands that specifically enhance insulin/IGF-I signaling mechanisms may help to improve viability and function of neuronal cells at risk for AD-type neurodegeneration.

This relatively new wave of enthusiasm is being fueled by reports showing interest in T3DM. In conclu-

sion the term “type 3 diabetes” accurately reflects the fact that AD represents a form of diabetes that selectively involves the brain cell impairment and has molecular and biochemical features that overlap with both forms of diabetes.

## REFERENCES

- [1] S.M.De La Monte; J.of Alzheimer’s Disease, **10**, 89-109 (2006).
- [2] M.Saxena; J.of Appl.Biosci., **34**, 139-151 (2008).
- [3] E.Steen; J.of Alzheimer’s Disease, **7**, 63-80 (2005).
- [4] G.Landreth; Curr.Alzheimer Res., **4**, 159-164 (2007).
- [5] M.A.Reger; Neurobiol.Aging, **27**, 451-458 (2006).
- [6] S.M.De La Monte; Cell Mol.Life Sci., **59**, 882-893 (2002).
- [7] S.Hoyer; Ann N.Y.Acad Sci., **893**, 301-303 (1999).
- [8] S.Hoyer; Ann N.Y.Acad Sci., **920**, 256-258 (2000).