



## **“IMPACT OF INSULIN RESISTANCE ON THE CENTRAL NERVOUS SYSTEM”**

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### **ABSTRACT**

Insulin resistance is one of the most widespread metabolic disorders in modern medicine and has traditionally been studied primarily in association with type 2 diabetes mellitus and cardiovascular diseases. In recent years, scientific research has demonstrated that insulin resistance also exerts adverse effects on the functioning of the central nervous system. This article analyzes the mechanisms through which insulin resistance affects the central nervous system, particularly disruptions in insulin signaling pathways, neuroinflammation, oxidative stress, and alterations associated with neurotransmitter imbalance. The findings indicate that early detection of insulin resistance and its management based on a comprehensive therapeutic approach are of critical importance in preventing central nervous system–related complications.

**Keywords:** Insulin resistance, central nervous system, neuroinflammation, cognitive dysfunction, Alzheimer’s disease.

### **INTRODUCTION**

In recent decades, metabolic disorders, particularly insulin resistance (IR), have been recognized as a significant global public health issue. Insulin resistance is a condition characterized by a decreased biological response of peripheral tissues to insulin and represents a major pathogenic factor in the development of type 2 diabetes, obesity, and cardiovascular diseases. However, recent research has revealed that insulin resistance not only affects metabolic processes but also significantly impacts the central nervous system (CNS). Under conditions of insulin resistance, disruptions in these signaling pathways lead to reduced glucose utilization in neurons, impaired synaptic plasticity, and disturbances in neurotransmitter balance. Moreover, insulin resistance has been associated with depression, cognitive decline, and other psychoneurological disorders. Therefore, a detailed investigation of the mechanisms by which insulin resistance affects the CNS—particularly its influence on neuroinflammation, energy metabolism, and neurotransmitter systems—is of both theoretical importance and practical relevance for developing strategies to prevent and treat these pathological conditions.

According to the World Health Organization (WHO), over 500 million people worldwide live with this disease, the majority of whom have type 2 diabetes. Type 2 diabetes is characterized by reduced tissue sensitivity to insulin, i.e., insulin resistance. In this condition, although insulin is present, it cannot exert its full physiological effect, leading to impaired glucose metabolism.

Genes S.G. emphasizes that hyperglycemia in diabetes, as a compensatory protective mechanism, accelerates glucose uptake by tissues, ultimately causing diabetic angiopathy. Consequently, blood vessels supplying the retina, kidneys, and nerves are damaged, leading to vision loss, numbness in the legs, and stroke. In parallel, insulin resistance has significant effects on the central nervous system. Insulin receptors are highly concentrated in brain tissues, particularly in the hippocampus, hypothalamus, and cortical regions. Insulin signaling in these areas is essential for



cognitive functions, memory, learning processes, and neuronal survival. In conditions of insulin resistance, disruptions in these signaling pathways reduce glucose consumption in neurons, impair synaptic plasticity, and disturb neurotransmitter balance. High blood glucose levels, along with thickened and narrowed vascular walls, damage blood vessels and deprive neurons, particularly in the hypothalamus, of oxygen and nutrients. The hypothalamus regulates the body's energy status (fat and glucose metabolism), and its damage disrupts food intake and energy homeostasis. As a result, the pancreatic islets of Langerhans increase insulin production.

Furthermore, the development of type 2 diabetes is influenced by genetic factors, poor nutrition, physical inactivity, obesity, and chronic stress. At the molecular level, disturbances in insulin signaling pathways—such as IRS-1, PI3K/Akt, and GLUT4 translocation—play a critical role in the progression of insulin resistance. Without detailed study of these mechanisms, effective treatment and prevention strategies remain limited. Initially, insulin resistance manifests as increased hepatic gluconeogenesis, reduced glucose utilization in muscle tissue, and enhanced lipolysis in adipose tissue. This leads to hyperinsulinemia and hyperglycemia. During early stages, pancreatic beta cells attempt to compensate by producing more insulin; however, over time, these compensatory mechanisms fail, and chronic hyperglycemia develops.

Merings and Mingovskiy (1889) demonstrated that removal of 9/10 of the pancreas in experimental models reproduces all human diabetic symptoms, including ketonemia, hepatic steatosis, and ultimately diabetic coma. Complete pancreatic removal results not only in insulin deficiency but also in impaired digestive enzyme production, leading to elevated blood glucose that cannot enter cells. Although this model was established in animals, it contributed significantly to understanding the pathogenesis of diabetes and to the discovery of insulin.

Recent studies have linked insulin resistance not only to metabolic dysfunction but also to inflammation, oxidative stress, mitochondrial dysfunction, and epigenetic changes. Therefore, in-depth study of type 2 diabetes requires not only clinical but also molecular and genetic approaches.

This article examines the molecular basis, clinical manifestations, and diagnostic challenges of insulin resistance. Additionally, it analyzes therapeutic strategies targeting this mechanism based on recent research. The article provides insights into better understanding type 2 diabetes and opens new prospects for its prevention and treatment.

## METHODS

In this study, the principles of selecting and analyzing scientific literature were adopted as the main methodological approach. Specifically, articles published between 2015 and 2025 in international scientific databases such as PubMed, ScienceDirect, Google Scholar, and Scopus were analyzed. The reviewed sources focused on insulin signaling pathways (IRS-1/PI3K/Akt, MAPK), glucose transport (GLUT4), inflammatory markers (TNF- $\alpha$ , IL-6), mitochondrial dysfunction, oxidative stress, epigenetic modifications, and their effects on the central nervous system (CNS). Additionally, socio-demographic and lifestyle factors contributing to type 2 diabetes were considered.

## RESULTS

Insulin resistance is directly associated not only with metabolic disturbances but also with immunological and inflammatory processes. Chronic low-grade inflammation—particularly elevated levels of TNF- $\alpha$  and IL-6—negatively affects insulin signaling pathways. Such inflammatory conditions are closely linked to obesity, with abdominal (central) obesity being one of the major contributors to insulin resistance. Furthermore, disruptions in adipokine balance (increased leptin, decreased adiponectin) contribute to metabolic dysregulation. It should be emphasized that mitochondrial dysfunction and oxidative stress are increasingly recognized as key mechanisms impairing insulin signaling. Reactive oxygen species (ROS) not only block insulin pathways but also



impair the function of intracellular organelles, especially mitochondria, which in turn leads to decreased energy metabolism and diminished cellular responsiveness to insulin.

### DISCUSSION

Literature analysis indicates that insulin resistance in type 2 diabetes is a complex, multifactorial pathophysiological condition, involving multiple interrelated molecular mechanisms. Research suggests that the primary cause of insulin resistance is disruption of the insulin signaling pathway.

In many cases, the effects of insulin resistance on the central nervous system are mistakenly attributed to Alzheimer's disease. Alzheimer's disease is a progressive brain disorder characterized by gradual cognitive decline affecting memory, thinking, and social abilities. It is the most common cause of dementia and leads to significant impairment in daily functioning. A hallmark feature of Alzheimer's disease is memory loss, particularly for recent events or conversations. As the disease progresses, cognitive deficits become more severe. These two pathologies—insulin resistance and Alzheimer's disease—share similarities in the CNS, including disrupted energy metabolism, impaired insulin signaling, neuroinflammation, oxidative stress, and cognitive and emotional disturbances. Studies indicate that insulin resistance may impair brain metabolism and increase susceptibility to Alzheimer's disease. Disruption of normal insulin activity in the CNS affects A $\beta$  accumulation and neuronal signaling. Conversely, Alzheimer's development may also contribute to impaired insulin signaling. Although Alzheimer's disease and insulin resistance each have distinct pathophysiological mechanisms, they share interconnected pathways, which are important for developing prevention and therapeutic strategies.

In summary, insulin resistance is a multifaceted condition requiring a systemic approach. Its in-depth study remains a key area of research for early prevention and effective treatment of type 2 diabetes. In type 2 diabetes, insulin resistance is a major pathophysiological component, influenced by molecular, genetic, epigenetic, inflammatory, and oxidative stress mechanisms. In clinical practice, assessment of insulin resistance using HOMA-IR, HbA1c, and other laboratory indicators plays a crucial role. Therefore, genetic and epigenetic studies, as well as the development of individualized treatment strategies based on omics technologies, have become a priority in modern diabetology.

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