Alzheimer's disease (AD) is the most common form of dementia in the elderly. Despite decades of intense research, the etiology of AD remains mostly unknown. A new potential pathophysiological mechanism arises from the knowledge that insulin is synthesized also in the central nervous system and is involved in the regulation of several cell processes including memory formation. Upon this knowledge as well as the pathological similarities with diabetes mellitus type 2 (T2DM), some hypotheses propagate AD meanwhile as insulin resistance brain state (IRBS). In this study, we focused especially on the insulin-receptor β subunit (IRβ) expression in human post-mortem tissue. Using immunohistochemical staining against IRβ in brain tissue originating from AD, AD combined with T2DM, T2DM patients and aged matched controls, we evaluated the alterations of IRβ in frontal cortex, dorsal and ventral part of the hippocampus. Significant lower IRβ protein expression in AD cases compared to the other groups was observed in all investigated brain regions. Additionally we investigated the amount of phosphorylated peroxisome proliferator-activated-receptor-γ (PPARγ) producing cells. PPARγ is a prototypical ligand-activated nuclear receptor that coordinates glucose and energy metabolism, and is found in elevated levels in brains of individuals with AD. In all investigated brain region we could show that phosphorylated PPARγ level was significantly higher in each patient group compared to control group. These results point to the contribution of IRβ, PPARγ to AD and show an ample link between AD and T2DM. Further investigations are necessary to enlighten the exact mechanism.