Insulin present in adult CNS is primarily derived from pancreatic β-cells and is transported by CSF into the brain [3–5, 9, 10]. Once bound to α subunits of the neuronal IR or IGF-1R, insulin (or IGF-1) promotes autophosphorylation of the β subunit at Tyr residues 1158, 1162, and 1163, triggering its intrinsic Tyr kinase activity [5, 39, 40, 44–46] and phosphorylating insulin receptor substrate (IRS) docking proteins (IRS1-4) at Tyr residues [1]. Then, Src homology-2 (SH2). An alternative pathway for insulin to provide energy for neurons involves inhibition of neuronal norepinephrine uptake, with subsequent activation of glial β-adrenoreceptors and glucose extrusion from glial glycogen stores, namely, in astrocytes [2, 120]. Neuroprotective astrocyte-derived insulin/IGF-1 stimulates endocytic processing and extracellular release of neuron-bound Aβ oligomers. Authors: Jason Pitt University of Washington United States. In contrast, neurons in the presence of astrocytes showed markedly reduced AβO binding and synaptopathy. Results identified the protective factors released by astrocytes as insulin and insulin-like growth factor-1 (IGF1). The protective mechanism involved release of newly bound AβOs into the extracellular medium dependent upon trafficking that was sensitive to exosome pathway inhibitors. Delaying insulin treatment led to AβO binding that was no longer releasable.