Journal of research in health science
2018 № 1 (3), May-August
www.journalofresearch.org; info@journalofresearch.org
DOI 10.26739/2523-1243
ISSN Print: 2523-1243; ISSN Online: 2523-1251

JOURNAL OF RESEARCH IN HEALTH SCIENCE

A Review: Brain glucose activity of Alzheimer's disease in neurodegenerative

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To cite this article:
Praveen N M, Manasa S, Kiran B Muchadi, VashniR, Abignan Gurukar, Sathish Kumar B Y. A Review: Brain glucose activity of Alzheimer's disease in neurodegenerative. *Journal of research in health science*. Vol. 1, No. 3, 2018, pp. 116-124. DOI 10.26739/2523-1243

http://dx.doi.org/10.26739/2523-1243/-2018-1-3-17

Abstract: Alzheimer's is progressive dementia that characterized diverse pathological markers in the brain due to large numbers of amyloid plagues surrounds by neurons containing neurofibrillary tangles, vascular damage from extensive plaque deposition, neuronal cell loss, they destroy mental memory function. It mainly expressed with gentle confusion and tricky remembering undergoes dramatic personality changes that intellectual with social skills.

It most common among mid-aged people that seriously affect brain cells which decline in mental functions through degenerative and die. Dementia seriously affects person's ability and their daily activities to suppress brain disorder that troubles in speaking, reading or writing behavioral extent which interferes person's daily life activity. The severity begins while affecting person's in multiple stages inversely depends on activities basic in daily life. The effects of Alzheimer's mainly involve controlling memory and language activity of the brain. Those suffering from Alzheimer's are correlated with mild cognitive impairment, effects memory problems for same age persons.

Alzheimer's disease temporally wipes memory and thinking dexterity in a progressive manner on brain cells. The contemporary framework has done to mimic its effects by performing certain medications and management that relates Alzheimer's disease by independence with longer maximizes function.

Key words: Alzheimer's, Apolipoprotein, Neurodegenrative, Brain Glucose, Phosphorylation

Introduction

Alzheimer disease associate progressive cognitive loss with neurodegenerative disorder affects the conventional pattern of autosomal dominant on Mendelian inheritance genetic aspects. Late-onset of AD affects major cognitively risk factors through autosomal domain on apolipoprotein E (ApoE) epsilon 4 genotype that contribute etiology and expression of disease. The epidemiology of AD affects mother to confer extent risk, whereas it affects through father revile minute cognitive performance that

may predictable to dementia offspring [1].

Alzheimer's are mainly evaluating with hereditary and non-genetic modifier of psychiatric or neurological disorder that susceptibility with endo-phenotype due to inheritable risk factors in unaffected persons. The cerebral metabolic rate for glucose (CMRgl) associated with abnormally low in CMRgl in posterior cingulate and frontal cortex, the reduction predict subsequent conversion of AD [2].

The similarity of Alzhemier's disease effects through neurodegenerative disease like Parkinson's, frontotemproal dementia, Lewy body disease and seldom syndrome occur in young or middle age individuals. Aging increased DNA damage mediates oxidative stress, mitochondrial dysfunction, and reduction of energy metabolism which is the production of ATP [3]. Abnormalities of AD occurs due to impaired or destroyed normal aging that is involved in corticolimbic and learning behavior which progressively damages DNA and triggers oxidative stress. The brain insulin impairment signals the core neurodegenerative cascade that proposes energy metabolism deficits, inhibits insulin gene response and required acetylcholine homeostasis [4].

AD associated with pathological lesions due to the presence of plaques and tangles that leads to clinical aspects of cellular changes which specify disrupted brain through thrashing synapse and neuronal death by a selective neuronal vulnerability. The extracellular amyloid plaques and intracellular neurofibrillary tangles are degenerative pathogenesis of AD, mainly because of abnormally hyperphosphorylated tau [5]. The uptake of glucose metabolism impaired in Alzheirem's brain consequence neurodegenerative attaches hydroxyl group of serine or threonine scum regulates inversely protein phosphorylation.

Pathophysiological of AD

Alzheimer's is a progressive form of extracellular and intracellular dementia with neuron due to amyloid plaques, neurofibrillary tau in the brain plays essential in Alzheimer's pathogenesis. Accumulation of ?-amyloid peptides (A?) sequentially cleaved with ?-secretase and ?-secretase. If tau protein is prevented binding to promote microtubule that inhibits neuronal transport [6, 7]. The ?-amyloid peptides plays related to age alteration due to the synaptic, metabolic, inflammatory, and neuronal and cytoskeletal pathogenesis of AD. The sequestration of A? into fibrillar forms oligomeric species against protective mechanism on Alzheimer's. The autosomal dominant leads to amyloid precursor protein production or cleavage that plays a crucial role in genetic impact on amyloid trafficking and plaque clearance [8,9].

Genetically late-onset shows metabolic disruption in atrophy neuropathy in cortical regions in the amyloid deposition that correlates with a posterior cortical region of amyloid deposition, atrophy, and hypo-metabolism that directly disrupt in an early stage of an AD during this conditions they act as passive control in young adults amyloid deposition. The posterior network involved in retrieval memory prominently affects through default cognitive mode [10]. The sporadic AD onset apolipoprotein E (ApoE) gene produces microglia and astrocytes in the brain by scavenging peptide from extracellular space they carry a significant risk of cerebral hemorrhagic which process anti-amyloid therapies by less effective.

They intracellular aggregation of tau protein that becomes self-perpetuating found in a neurodegenerative disease that modifies tau to accumulate neurotoxic insult [11]. The neurotoxic effects act as reservoir soluble oligomers through brain parenchyma from individual amyloidogenic protein as amyloid β-protein (Aβ), tau, prion protein (PrP), and α-synuclein.

Epidemiology

The main cause of Alzheimer's due to dementia in presence of neuritic plaque in the neuropil of cerebral cortex and hippocampus, the amyloid peptide has 40-42 amino acids that contribute neurodegenerative occurs in the brain on Alzheimer's[12]. The inherited autosomal dominant associated with a mutation in amyloid precursor proteins accumulate neurofibrillary tangles in pyramidal neurons diminished glucose uptake and utilization in the brain [13]. The AD is aging brain or disease responsible for protein cross-linking and inflammation reacts carbonyl compound leads to the formation of glycation end-products or lipoxidation end-products [14, 15]. An augmented risk in cognitive declined by AD owed vascular menace in hypertension, hypercholesterolemia, and diabetes associated with increased peril of dementia in the brain. They specify environmental exposure activities include cognitive, physical, leisure and social activity with decreased risk of AD dementia. They invoked extent AD in histopathological changes ability to tolerate the higher level of brain injury with great synaptic density represent reserve ability for alternating brain network [16].

Increased risk of aging associate in AD and diabetes wheredeterioration shows mitochondrial and oxidative capacity. Caloric restriction has shown neurodegenerative, diabetes, and heart disease associated with excessive energy body fat intake.

Clinical manifestations

Alzheimer's are neurodegenerative that shrinks supplementary brain cells die through initial behavioral memory defects impaired judgment and modify in traits. The molecular mechanism of AD involved in oxidative stress, mitochondrial dysfunction, and tainted gene expression [17]. Sporadic AD mainly occurs through genetic factors that affect cerebrovascular disease and typical brain inflammation [18]. Aging process in AD onset metabolic influence in oxidative and inflammatory risk with free radicals that originate in apolipoprotein E gene, these APOE genes are a carrier of lipid transport in repairingbrain [19, 20]. AD and diabetes are degenerative bug involve neuronal loss and cell destruction leads to neurodegenerative and cognitive damages impaired insulin signaling in tau hyperphosphorylation, equally AD and diabetes[21,22] split a common pathway in growth factor receptor and abnormalities in protein phosphorylation, glycogen synthase kinase[23,24,25].

Augmented oxidative anxiety and induced glyceraldehydes sophisticated glycation end products with AD and diabetes.

The APOE gene identify major risk factors in elevated blood pressure, soaring cholesterol and head trauma by reversing metabolic abnormality in Type 2 Diabetes with absence of insulin resistance evenly reaches in rigorous phase, pancreatic beta cells in require insulin signaling that results in diabetes.

Brain metabolism

The human brain has most metabolically active organ used glucose oxidation to CO2 and H2O under typical conditions to contribute fatty acids by complete oxidation of glucose. The glucose is oxidative tainted for ATP synthesis used in energy degenerative from glucose to neuronal gesture from "evasion network" activity. The brain increases blood flows that consume energy produced ATP generation used for neuronal signaling which performs specific tasks activates default network [26]. The brain depends on glucose circulation stores energy from glycogen initiate glucose transporter 1 (GLUT1). The brains encoded GLUT1 and GLUT3 gene for facilitative transporter prominently expressed in endothelial cells of cerebral micro-vascular in GLUT1protein. Glucose concentration in cerebrospinal featured in GLUT1 includes seizures, hypotonia, ataxia, language deficits, and microcephaly [27].

Brain glucose metabolism formed in arterio-venous in multiple cerebral blood flow approach by PET using tracer-FDG stimulates combination of glucose transport and subsequent phosphorylation. FDG phosphorylated by glycolytic enzyme that cannot metabolize, fructose-6-phosphate in glucose phosphate isomerase[28, 29].They associated with neurons, fibers which disrupt in cortical-laminar architecture and neuroinflammatory retort, exclude microglial cell activation by overlapping neurodegenerative disease.

Glucose metabolism

The glucose consumed by the brain maintains pre-synaptic and post-synaptic ion gradients for neurotransmission of glutamate that transports neurotransmitting signals in phospholipid remodeling which stimulates the brain basal energy consumption. Under regular circumstances, the brain glucose completely oxidized to CO2 and water cooperate an energetic responsibility in normal brain function [30].The conversion of glycolysis to lactate is observed in the production of pyruvate that contributes to astrocytes neuronal activity. The brain activation rivet inhibitory and excitatory pathway by restricted cerebral blood flow to the integrity of oxygen and fuel convey from capillary neuron to replace ATP brain activation [31].The abnormalcerebral metabolic rate of glucose show subsequent cingulated, parietal, secular and prefrontal cortex. The increased glucose metabolism utilize by conducive hypometabolism, plaque authentication, and cell atrophy. The metabolic rate of cerebral glucose reduction showed the activity of terminal neuronal fields or glial cells, the homozygotes help to decline glucose metabolism in an AD. In cerebral glucose, they utilize deficits insulin which helps to express insulin-responsive gene particular in acetyltansferase, tau and glyceraldehydes-3-phosphate dehydrogenase which mediates neuronal cytoskeletal and metabolic activity that suppressed in AD [32, 33]. Insulin resistance escort to oxidative stress, reactive oxygen species, DNA damage and mitochondrial dysfunction in AD brain manifested reduced insulin receptor level in polypeptide gene expression in brain and cerebrospinal fluid [34].

Glucose uptake may impaired brain glucose to the functional defect of GLUT mediate glucose uptake may responsible for defective neurodegenertation or type 2 diabetes was excluded.

Brain insulinin Alzheimer's disease

The reduction of cerebral blood flow of glucose utilization expressed in the later stage of metabolic and physiological deformity [35] resembles in T2DM in abnormal energy metabolism caused insulin resistance or abridged insulin exploit in the brain [36]. The human brain reduction expressed in insulin dementia and neurodegenerative express effectively activate downstream pathway represent the major abnormality in an AD [33, 37]. The insulin receptor substrate (IRS) molecules exhibit reduction in brain weight with genetic depletion of impairs neuronal proliferation promoted intra-neuronal gathering of phosphorylated tau [38].

The expression of insulin reduction in AD impairs ligand-receptor binding by increased cholesterol content in the brain with secondary ApoE genotype receptor binds with alternative lipid membrane composition that represents brain confidential form of diabetes mellitus [39, 40]. Accumulation of amyloid protein associated with cerebral vasculature found in senile plaque cores in neurotoxicity with a high concentration of peptide emerges dimmers and small aggregates toxic [41, 42]. The insulin-degrading enzyme associated with AD glucose metabolism in the brain,[43]autosomal dominant mutation genes are amyloid precursor protein (APP), and presenilin genes 1 and 2 are commonly encoded with APOE for late onset of an AD in complex and heterogeneous personality of the disease[44].The proteolytic dispensation of APP production on b-amyloid, Ab peptides in the brain cumulative microtubule tau protein that drives neuro-fibrillary tangle pattern within neurons that enhance Ab into neurotoxic oligomer and senile plaque. This antibody oligomers disruption leads to synaptic neurotransmission, and cerebral cortex cause cognition dysfunction [45]

AD type neurodegenerative and cognitive impairment induce brain insulin in T2DM and allied to chronic hyperglycemia, peripheral insulin resistance and increased fabrication of pro-inflammatory cytokines[46], in micro-vascular disease as complicating or hasten constituent of an AD [41,47].Insulin resistance syndrome or diabetes and AD evidence abnormal glucose regulation associates cerebrovascular disease responsible for increased risk in advanced glycation end products (AGEs) transpire in diabetes, may play a vital role in vascular complications and neurodegenerative disorder of includes AD. Insulin receptors contribute commencement of explicit signaling pathway with long-term reminiscence configuration [48].

By directive of Ab proteolytic squalor as the insulin-degrading enzyme that collapse multiple peptides, Ab, glucagon, and amylin[49].

Diet persuade insulin resistance promotes amyloidogenic Ab in the brain secretes decreased IDE activities in hyperinsulinemia, may affect insulin binding receptors of sAPP secretion, and Ab insulin binding can inhibit its effect[50,51].Insulin regulates neuronal function throughout existence from embryonic and in fetal development, results in phosphorylation and commencement of intrinsic receptor tyrosine kinase. Insulin adapts cerebral functions with large unexplored risk factors that feature endothelial dysfunction and vascular damage in both DM and AD.

Conclusion

Insulin signaling plays pathological interaction between Alzheimer's and diabetes mellitus affect synaptic neuronal senescence besides increasing tau phosphorylation involves in the mechanism of aging in minimal brain glucose supply in T2DM and insulin resistance are predispose to the AD. The brain glucose metabolism donates in the maturity of an AD with impaired glucose transport by targeting neurotransmitter by improved brain fuel supply.

Abbreviations

AD: Alzheimer's disease; Ab: Antibody; AGEs: Advanced Glycation End Products; APP: Amyloid Precursor Protein; ApoE: Apolipoprotein; Aβ: β Amyloid Peptide; ATP; Adenosine Tri Phosphate; CMRgl; Cerebral Metabolic Rate for Glucose; DM; Diabetes Mellitus; DNA; Deoxyribonucleic Acid; FDG: Fludeoxyglucose; GLUT; Glucose Transporter; IRS: Insulin Receptor Substrate; PET: Polyethylene Terephthalate; PrP: Prion Protein; T2DM: Type 2 Diabetes Mellitus.

Consent for publication

The authors declare that this article is original, has never been published, and has not been submitted to any other journal.

Ethics approval and consent to participate

Not applicable

Authors' contribution

PNM,MS, KBM and RV wrote the manuscript, SKBY edited and finalized the manuscript. All authors read and approved the final manuscript.

Funding

There is no funding for this review.

Competing interests

The authors declare that they have no competing interest.

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