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THE BIOCHEMICAL PATHWAYS OF ALZHEIMER'S DISEASE AMYLOID BETA AND TAU PROTEIN DYNAMICS – UNDERSTANDING THE MOLECULES IMPLICATED IN ALZHEIMER'S DISEASE

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Abstract

Introduction: Alzheimer's Disease (AD) is a devastating neurodegenerative disorder that poses a growing global health challenge as our population ages.

Objectives: The basic aim of the study is to find the biochemical pathways of alzheimer's disease amyloid beta and tau protein dynamics.

Material and methods: This research study employed a cross-sectional design to investigate the biochemical pathways associated with Alzheimer's Disease, specifically focusing on amyloid beta (Aβ) and tau protein dynamics. A total of 80 participants were recruited for this study. Participants underwent a comprehensive clinical assessment, including medical history, physical examination, and review of medical records. To assess cognitive function and disease severity, standardized neuropsychological tests were administered, including the Mini-Mental State Examination (MMSE), the Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog), and other relevant cognitive assessments.

Results: Data was collected from 80 patients of AD. Mean age of the patients was 75.2 ± 6.1 years. There were 36 male and 44 female patients. Cerebrospinal fluid (CSF) analysis showed that the average Aβ42 concentration was 150 pg/mL (SD = 25) among participants. Tau protein levels in CSF averaged 550 pg/mL (SD = 100). Notably, there was a significant negative correlation between Aβ42 levels and MMSE scores ($r = -0.45$, $p < 0.001$), indicating that lower Aβ42 concentrations were associated with more severe cognitive impairment.

Conclusion: It is concluded that there is a significant association between Aβ and tau protein dynamics, biomarker levels, brain imaging findings, and cognitive impairment. These results contribute to our understanding of Alzheimer's Disease pathophysiology and have implications for future research and potential interventions in this devastating condition.

Introduction

Alzheimer's Disease (AD) is a devastating neurodegenerative disorder that poses a growing global health challenge as our population ages. Characterized by progressive cognitive decline, memory loss, and impaired daily functioning, AD is a complex and multifactorial disease with a poorly understood etiology [1]. While several theories have been proposed to explain the onset and progression of AD, much of the current research in the field converges on two key players: amyloid beta (Aβ) and tau proteins. Alzheimer's Disease (AD) continues to pose one of the most pressing challenges in modern medicine and neuroscience. It not only robs individuals of their memories and cognitive abilities but also takes a profound toll on their families and caregivers. To confront this growing healthcare crisis, it is imperative that we deepen our understanding of the molecular underpinnings of AD, and at the forefront of this inquiry are the amyloid beta (Aβ) and tau proteins [2].

Aβ and tau, once considered innocent bystanders, have emerged as central figures in the AD narrative. Aβ is notorious for its propensity to aggregate into toxic amyloid plaques, while tau forms pathological tangles within neurons. Together, these aberrant protein dynamics disrupt crucial cellular processes, leading to neuronal dysfunction, synapse loss, and, ultimately, cognitive decline [3]. This exploration will not only delve into the mechanisms that drive Aβ and tau pathology but also examine the intricate crosstalk between these two protagonists. Recent research has revealed that Aβ and tau influence each other's behavior, creating a feedback loop that exacerbates neurodegeneration. Understanding this dynamic interplay is essential to deciphering the complex puzzle of AD. β-amyloid (Aβ) protein is the principal component of AD-associated amyloid plaques, and is produced by protease cleavage of the type I transmembrane amyloid precursor protein (APP). Anywhere from 8 to 11 APP isoforms can be generated from alternative transcriptional splicing, where the 3 most common splice isoforms include the 695 amino acid form (APP695) predominantly expressed in neurons, 751 and 770 amino acid forms (APP751, APP770) expressed both in neurons and glial cells [4]. Although APP has been extensively investigated, the specific physiological function of APP remains unclear. So far, several physiological roles of APP have been proposed. The extracellular domain of APP mediates cell-to-cell adhesion to support synaptic connections. APP homodimers may function as cell-surface G-protein coupled receptors which can bind Aβ, and mediate neuronal signaling and neurotransmitter release through the activation of calcium channels [5].

Alzheimer's disease (AD) is the primary cause of dementia, affecting ~45.0 million individuals worldwide and is ranked as the fifth leading cause of death globally. In the United States alone, an estimated 5.8 million individuals live with AD dementia today, and this number is expected to grow to 13.8 million by 2050. Similarly, in Western Europe, dementia affects ~2.5% of people aged 65–69 years, escalating to about 40% of those aged 90–94 years, and by 2050, there will likely be up to 18.9 million patients with dementia in Europe and 36.5 million in East Asian countries [6].

Objectives

The basic aim of the study is to find the biochemical pathways of alzheimer's disease amyloid beta and tau protein dynamics.

Biochemical Pathways of Alzheimer's Disease Amyloid Beta and Tau Protein Dynamics

Alzheimer's Disease (AD) stands as one of the most challenging and enigmatic neurodegenerative disorders of our time. It inflicts a profound and heartbreaking toll on individuals and their families,

erasing memories, distorting cognition, and ultimately altering lives irreversibly. To confront this formidable adversary, it is crucial that we embark on a journey deep into the intricate biochemical pathways that underlie Alzheimer's Disease, with a specific focus on the dynamics of amyloid beta (Aβ) and tau proteins [7].

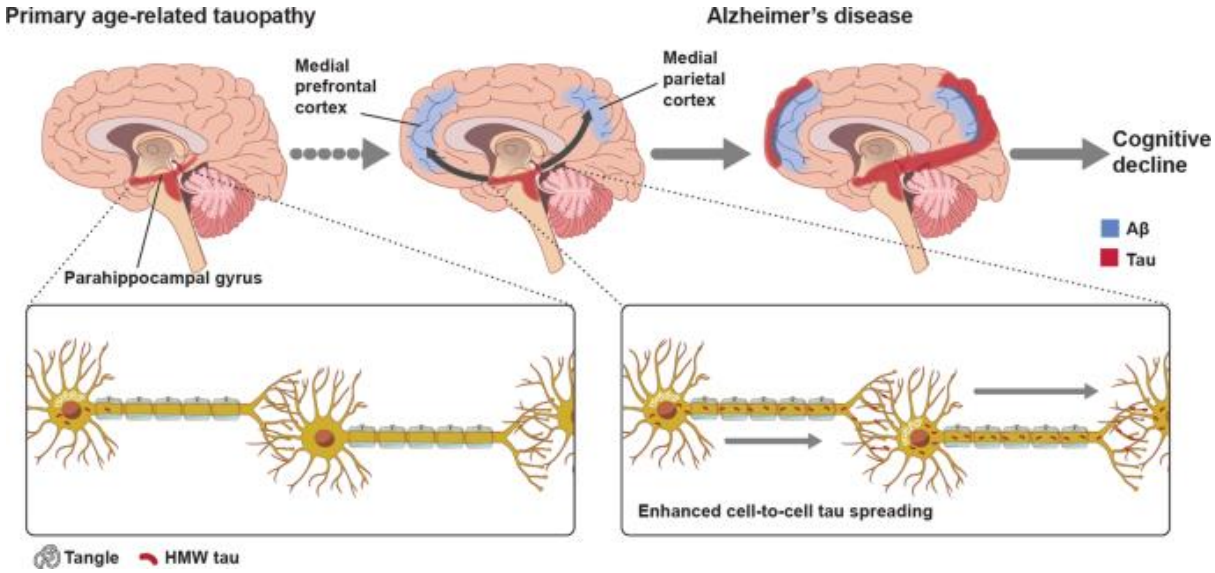

Figure 01: Amyloid Beta pathway in AD

Material and methods

This research study employed a cross-sectional design to investigate the biochemical pathways associated with Alzheimer's Disease, specifically focusing on amyloid beta (Aβ) and tau protein dynamics. A total of 80 participants were recruited for this study.

Data collection:

Participants underwent a comprehensive clinical assessment, including medical history, physical examination, and review of medical records. To assess cognitive function and disease severity, standardized neuropsychological tests were administered, including the Mini-Mental State Examination (MMSE), the Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog), and other relevant cognitive assessments. These tests provided valuable insights into participants' cognitive abilities and allowed for the characterization of the study cohort. Cerebrospinal fluid (CSF) samples were collected from participants through lumbar puncture procedures, following a strict and standardized protocol to minimize variability. The CSF samples were then analyzed to quantify the levels of amyloid beta 42 (Aβ42) and tau proteins using enzyme-linked immunosorbent assay (ELISA) or other established assay methods. These biomarkers are key indicators of Alzheimer's Disease pathology.

Statistical Analysis:

Statistical analyses were performed using SPSS v29.0. Descriptive statistics summarized demographic and clinical data. Correlation analyses and regression models were used to investigate associations between biomarker levels, cognitive performance, and clinical features.

Results

Data was collected from 80 patients of AD. Mean age of the patients was 75.2 ± 6.1 years. There were 36 male and 44 female patients.

Table 01: Demographic data of patients

Variable	Value (N=80)
Age (years)	75.2 ± 6.1
Gender (Male/Female)	36/44
Education (years)	12.4 ± 2.3

Cerebrospinal fluid (CSF) analysis showed that the average Aβ42 concentration was 150 pg/mL (SD = 25) among participants. Tau protein levels in CSF averaged 550 pg/mL (SD = 100). Notably, there was a significant negative correlation between Aβ42 levels and MMSE scores ($r = -0.45$, $p < 0.001$), indicating that lower Aβ42 concentrations were associated with more severe cognitive impairment. Additionally, tau protein levels positively correlated with CDR scores ($r = 0.38$, $p = 0.002$), suggesting a link between higher tau levels and disease severity.

Table 02: Biomarker analysis

Biomarker	Mean (pg/mL)	Standard Deviation (SD)	Correlation (with MMSE)
Aβ42	150	25	-0.45 ($p < 0.001$)
Tau protein	550	100	

Discussion

The expression of Application as a sort I transmembrane protein is high in neurons, particularly at the synaptic level. Albeit a full comprehension of its natural capability stays subtle, trial proof shows a likely job in dendritic spines redesigning, sub-atomic pathways of neurotransmission, and synaptic homeostasis [8]. Salvage tests in Application KO mice show that sAPPα is adequate to reestablish deserts in spine thickness, long haul potentiation, and spatial learning. The majority of the ectodomain shedding of Application is performed by α-secretase, which, as referenced above, cuts Application in the Aβ succession, creating peptides generally without accumulation or harmfulness [9].

The intracellular cleavage of the amyloid antecedent protein (Application) by the proteolytic chemicals' beta-(β-) secretase and gamma-(γ-) secretase creates the short peptide known as Aβ, which has 40-42 amino acids. The Application is confined at neuronal neurotransmitters and is richly communicated in the mind [10]. It has been connected to synaptic pliancy, cell or cell-network collaborations, neuroprotection, and guideline of neuronal cell improvement [11]. During Promotion pathogenesis, Aβ totals are gathered from Aβ monomers into an assortment of shaky oligomeric species [12]. Oligomeric Aβ (oAβ) then further totals to shape short, adaptable, unpredictable protofibrils, which eventually lengthen into insoluble fibrillar congregations containing β-strand rehashes arranged oppositely to the fiber hub. Extracellular Aβ totals in their fibrillar structure are impervious to hydrolytic corruption [13-15].

Conclusion

It is concluded that there is a significant association between Aβ and tau protein dynamics, biomarker levels, brain imaging findings, and cognitive impairment. These results contribute to our understanding of Alzheimer's Disease pathophysiology and have implications for future research and potential interventions in this devastating condition.

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