REVIEW

Investigation of the potential relationship between DNA damage and Alzheimer's disease: a clinicobiological approach

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ABSTRACT

Introduction: DNA damage in humans is a common occurrence across various diseases and has garnered significant attention in scientific investigations in recent times. Alzheimer's disease (AD) is a form of dementia that affects a large number of elderly people and is characterized by memory loss, functional decline and behavioral disturbances. Research on DNA damage in Alzheimer's Disease (AD) has been gaining attention in the scientific community in recent years due to its potential association with the pathogenesis of the disease.

Aim: The aim of this mini review is to provide a short summary of the latest information on human DNA damage in (AD).

Material and methods: A brief review was performed based on a narrative synthesis of previously published literature. The material of the present study was exclusively Internet-based. A comprehensive electronic literature search in the databases PubMed and Google Scholar using the following terms/key words: "DNA damage" AND "Alzheimer's Disease" AND "humans".

Results: Numerous studies have been undertaken to investigate DNA damage in individuals with (AD). Researchers employed the Comet assay and ELISA techniques to quantify DNA damage levels in this population. It was consistently found that (AD) patients exhibited significantly elevated levels of DNA damage compared to controls. Moreover, heightened levels of the oxidative stress (and DNA damage) marker 8-OHdG in (AD) suggest a potential association between oxidative stress and (AD).

Conclusions: Research conducted in (AD) has shown a notable elevation in human DNA damage present in the blood or urine of patients when compared to healthy subjects. These results have been consistently observed across various case-control studies, indicating a potential association. To validate these findings and delve deeper into the potential therapeutic approaches, it is imperative to carry out additional studies with larger participant groups and varied demographics.

Keywords: DNA damage, Alzheimer's disease, humans

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INTRODUCTION

Human DNA alterations are classified into two main groups: mutations, which involve changes in the bases of both DNA strands that are unable to be recognized or repaired, and DNA damage, which entails

structural alterations in the DNA that can be identified by specific enzymes and repaired. The types of DNA damage can be further categorized based on their origin as endogenous, occurring during cell metabolism such as replication, or exogenous, caused by external factors like ultraviolet radiation, thermal decomposition, toxins, smoking, and chemical mutagens. The chemical mechanisms of DNA damage include errors in DNA polymerase during replication, base alterations like oxidations and methylations, DNA breaks (single-strand and double-strand), pyrimidine dimers, and the addition of bulky chemical molecules [1-4].

The single-cell gel electrophoresis assay, also known as the comet assay, is a widely utilized method for assessing DNA damage visually. When subjected to alkaline conditions, DNA molecules with different molecular weights and electric charges exhibit distinct behaviors in an electric field. Undamaged DNA molecules remain within the cell nuclei and show minimal migration during electrophoresis, whereas denatured DNA fragments migrate away from the nuclei. The increased migration of genetic material from the nucleus to the tail, termed "comet damage," is a measure of DNA damage. The comet assay essentially involves quantifying images obtained through light microscopy [5]. Additionally, the human 8-hydroxy-2-deoxyguanosine (8-OHdG) ELISA assay is a precise in vitro quantitative technique for the detection of 8-OHdG in human saliva, serum, urine, and plasma samples. 8-OHdG is a reactive oxygen species (ROS)-induced DNA base modification due to hydroxyl radical attack of guanine. The quantification of 8-OHdG concentrations through ELISA is gaining popularity due to its stability, sensitivity, and importance as an indicator of oxidative DNA damage [6].

Alzheimer's disease (AD) is a form of dementia that affects a large number of elderly people and is characterized by memory loss, functional decline and behavioral disturbances. Neuronal cell death, the formation of amyloid plaques and neurofibrillary tangles (NFTs) constitute the microscopic histopathological changes in AD. In particular, amyloid plaques are extracellular deposits of the peptide amyloid beta (Aβ) mainly in the gray matter of the brain ("plaques of β-amyloid"), while neurofibrillary tangles consist of hyperphosphorylated tau protein (a protein associated with the stabilization of microtubules) within neurons [7].

No single test can determine whether a person has Alzheimer's disease [8]. Diagnosis is made by determining the presence of certain symptoms and ruling out other causes of dementia. It involves a careful medical evaluation, including a thorough medical history, mental status testing, physical and neurological examination, and possibly cerebrospinal fluid (CSF) biochemical tests and brain imaging tests, including computed tomography (CT) of the head, magnetic resonance imaging (MRI) of the head, positron emission tomography (PET) of the head or the combined PET/CT scan [7-9]. Cerebrospinal fluid (CSF) biochemical tests for Alzheimer's disease (AD) include the quantification of total tau (T-tau) protein, phosphorylated tau (P-tau) protein, and amyloid beta peptide 42 (Aβ42). In a symptomatic patient, a low concentration of Aß42 peptide in CSF together with high levels of total tau protein reflect a possible onset of Alzheimer's disease. However, since these analyzes are still at the research level and

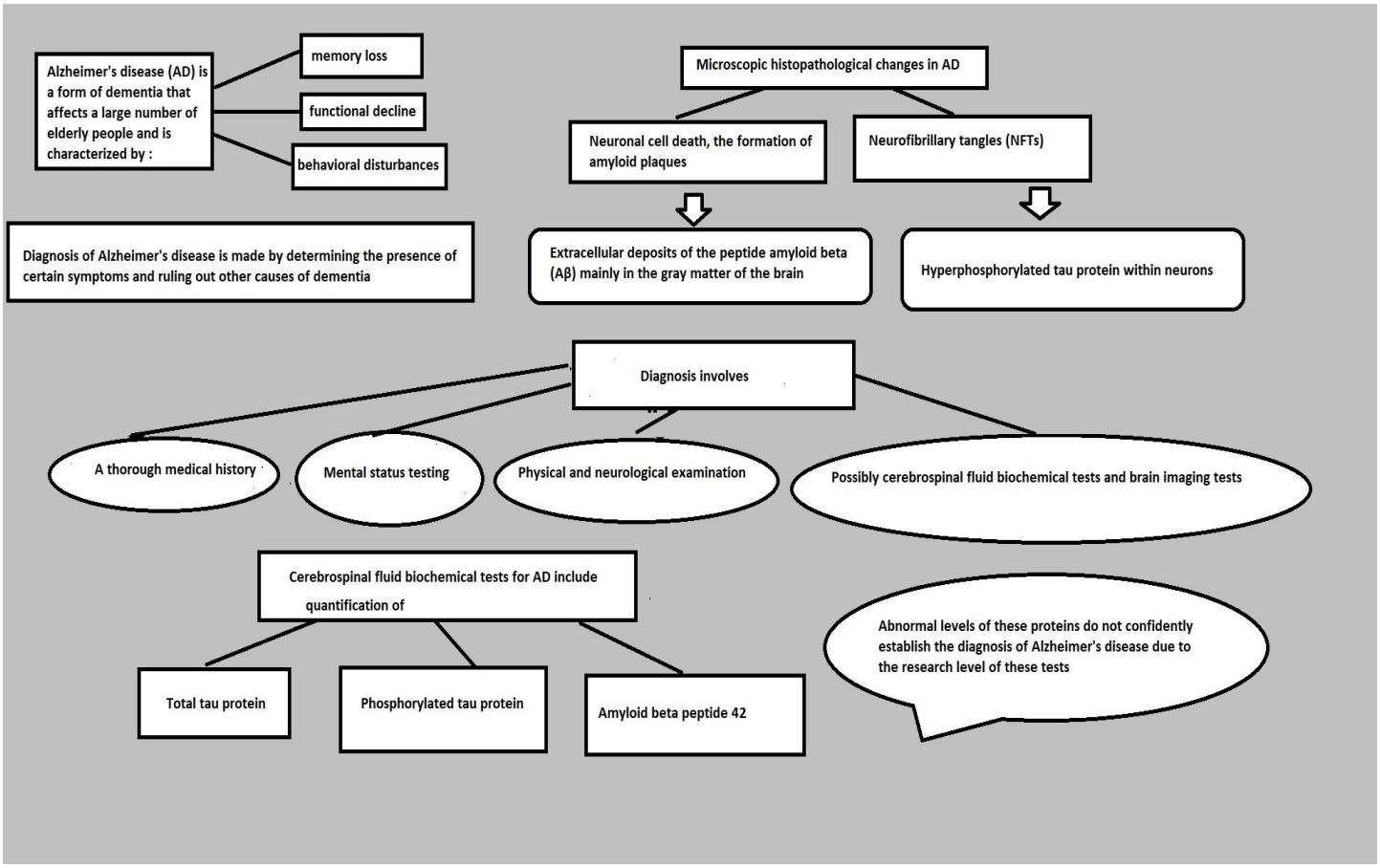

Figure 1. Diagram showing factors/parameters related to the diagnosis of Alzheimer's disease (AD).

are not part of routine clinical laboratory tests, abnormal levels of these proteins do not confidently establish the diagnosis of Alzheimer's disease [10]. Also, in clinical practice, the determination of Aβ42 and total tau biomarkers in plasma is not currently recommended. Their results have limited clinical value as their evaluation is still at research level [8] (Figure 1).

According to recent studies, more than 18 million people are affected by AD worldwide and this number will almost double by 2050 [11]. The prevalence of AD is 4% in people in the community over 60 years of age, while the incidence is 15.8 per 1000 person-years [12]. AD risk factors can be divided into two broad categories, modifiable and non-modifiable. Modifiable risk factors include diabetes mellitus, high blood pressure, dyslipidemia, excess body weight, sleep-wake cycle disorders, and smoking. Non-modifiable risk factors include age, gender (women appear to be at greater risk of developing AD than men) and genetic predisposition. There is currently no cure for AD, but several treatments can slow its progression and relieve symptoms. [12,13]. Many medicinal substances, of various categories, have been used and tested, without completely successful results at the level of prevention and treatment. In particular, medical treatment includes the use of acetylcholinesterase inhibitors (donepezil, galantamine and rivastigmine) and the N-methyl-D-aspartic acid (NMDA) receptor antagonist memantine, aiming to increase cholinergic neurotransmission and

NMDA receptor activation, respectively [14]. The non-pharmacological treatment of AD includes physical exercise, the Mediterranean diet and activities that stimulate the mental process such as leisure activities and improving knowledge (puzzles, crosswords, etc.) [12,15].

Recent research has focused on investigating the phenomenon of human DNA damage in individuals affected by (AD), as there is a growing interest in understanding its potential implications for the pathophysiology of this disease [11,16,17]. The aim of this mini (brief narrative) review is to provide a short summary of the latest information on human DNA damage in (AD) via a clinicobiological approach. Mini (brief narrative) reviews play a crucial role in expediting the dissemination of newly emerging evidence, thereby promoting timely communication of recent discoveries to influence future research endeavors. These concise reviews offer flexibility in addressing a wide range of research questions without being limited by strict inclusion criteria. Furthermore, they serve the purpose of pinpointing gaps in existing knowledge and suggesting potential directions for future research investigations. Moreover, by encouraging critical thinking through the presentation of various perspectives, mini reviews have the capacity to stimulate novel insights and discoveries within the scientific domain [18,19]. The importance and implications of the concise literary assessment in the domain of molecular neurology pertain to its examination of the correlation between DNA damage and (AD). Exploring the potential pathways through which DNA damage influences the pathophysiology of (AD) can offer valuable perspectives into the onset and advancement of this neurological disease. This synthesis of existing literature on human DNA damage in (AD) enhances the comprehensive clinicobiological comprehension of the disease, consequently facilitating the advancement of research methodologies in the field of molecular neurology.

MATERIAL AND METHODS

Design

A brief review was performed based on a narrative synthesis of previously published literature.The material of the present study was exclusively Internet-based. A comprehensive electronic literature search in the databases PubMed and Google Scholar was performed (from 10 April 2024 to 30 May 2024) using the following terms/key words: “DNA damage” AND “Alzheimer's disease” AND “humans”. In addition, a search in the reference lists was carried out.

Criteria for inclusion of studies were:

- Literature written in English.
- Literature published from 1990 to 2024.
- Studies that involved men and women with Alzheimer's disease.
- Studies that had keywords in the title and/or abstract.

Criteria for exclusion of studies were:

- Reviews
- Conference papers
- Book chapters

- Books
- Short surveys
- Articles and documents written in languages other than English

The search process is shown in Figure 2.

Selection of studies

All references obtained from the search were organized and duplicates were excluded. The titles and abstracts were screened for content and relevance to the topic with focus on the inclusion criteria. The integral text of selected titles was read, and the reference list of selected articles was consulted in order to find out other relevant publications. Additionally, studies which failed to adequately describe human DNA damage in arterial hypertension were excluded.

Data extraction and analysis

The essential data from each published study were extracted and synthesized. The results are presented in a brief narrative form.

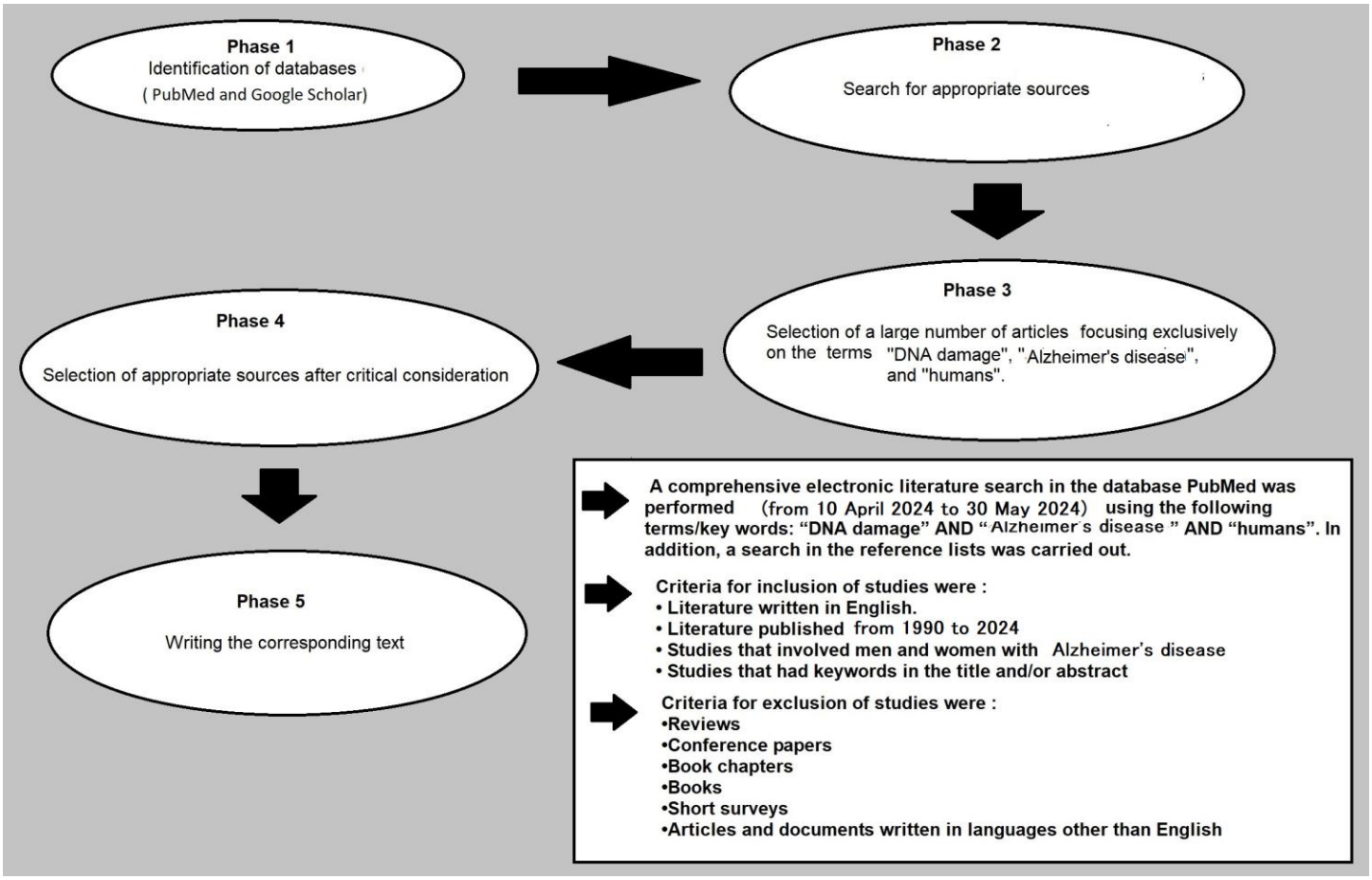

Figure 2. Flow chart demonstrating the search strategy of the mini (brief narrative) review.

RESULTS

Human DNA damage in Alzheimer's disease

In the research of Moslemnezhad et. al. (2016) [11] studied 30 AD patients and 30 healthy subjects matched for gender and age. The diagnosis of AD was based on the National Institute of Neurological and Communicative Disorders and Stroke/Alzheimer's Disease and Related Disorders Association (NINCDS/ADRDA) criteria. Also, AD patients underwent the psychometric test of short mental evaluation (MMSE), computed tomography (CT) and magnetic resonance imaging (MRI) of the brain. Plasma levels of 8-OHdG and total antioxidant capacity (TAC) were measured by competitive ELISA and the Fe3+ complex reduction reaction (FRAP) antioxidant power assay, respectively. The results showed that plasma 8-OHdG levels were significantly higher in AD compared to controls ($p<0.001$), while total antioxidant potential was significantly lower in patients compared to controls ($p=0.002$). The area under the ROC curve value for 8-OHdG and TAC to discriminate AD patients from controls was 0.87 and 0.32, respectively. In conclusion, the results indicated an association between oxidative stress and AD, indicating the possible contribution of these markers to the development of AD and as a marker to distinguish AD patients from healthy controls [11].

Also, Mórocz et. al. (2002) [16] performed a case–control study of 27 AD patients and 12 (age-matched) controls in which the level of oxidative damage and DNA repair capacity of peripheral lymphocytes of AD patients and controls was determined by the comet assay. Statistically significant increases ($p < 0.05$) were observed in the levels of oxidized purines in the nuclear DNA of peripheral lymphocytes from AD patients, compared to age-matched controls, both at basal level and after oxidative stress-induced from H_2O_2. AD patients also showed reduced repair of H_2O_2-induced oxidized purines. It was hypothesized that increased levels of oxidized purines in AD patients may be due to either increased oxidative stress or impaired antioxidant mechanisms [16].

In the work of Kadioglu et. al. (2004) [17] determined levels of oxidative damage in peripheral lymphocytes of 24 AD patients and 21 healthy controls (age-matched) by the comet assay, applied to freshly isolated blood samples using oxidative damage-specific DNA repair endonucleases (endonuclease III for oxidized pyrimidines, formamidopyridine glycosylase for oxidized purines). The work showed that AD patients had increased levels of oxidized pyrimidines and purines ($p<0.0001$) compared to age-matched healthy controls. The comet assay was also shown to be useful as a biomarker of oxidative DNA damage when used with enzymes specific for oxidative damage [17].

Additionally, in the research of Mullaart et. al. (1990) [20] directly compared the levels of DNA damage in neural tissue of AD patients and healthy controls (control group). More specifically, the study determined the levels of DNA breaks and alkali-labile sites (DNA sites sensitive to alkaline conditions expressed as single-strand breaks via the alkaline comet assay) in cerebral cortex tissue samples from AD patients and healthy controls, which were obtained from rapid autopsies. Study data in 11 AD patients and 8 control subjects indicated at least two-fold

higher levels of DNA damage in the cortex of AD patients compared to controls ($p<0.05$) [20].

Furthermore, in the study by Wang et. al. (2005) [21] quantified multiple oxidized bases in DNA (nuclear and mitochondrial) of frontal, parietal and temporal lobes and cerebellum from brains obtained at a short postmortem interval (PMI: the time that has elapsed since a person's death) of patients with AD and healthy controls (age-matched) using gas chromatography/mass spectrometry with selective ion monitoring (GC/MS-SIM) and stable labeled internal standards. In particular, nuclear and mitochondrial DNA (mtDNA) were extracted from 8 AD patients and 8 age-matched control subjects. It was found that the levels of multiple oxidized bases in AD brain samples were significantly higher ($p < 0.05$) in the frontal, parietal and temporal lobes compared to control subjects, and that mtDNA had approximately 10-fold higher levels of oxidized bases than nuclear DNA. These data indicate higher levels of oxidative stress in mitochondria and that mtDNA damage is more extensive than nuclear DNA damage. The presence of increased mtDNA damage could be due to continued ROS production from lipid peroxidation and/or damage within the electron transport system. The concentration of 8-hydroxy-2'-deoxyguanosine (8-OHdG) was approximately 10-fold higher than other oxidized base adducts in both AD and control subjects. DNA from the temporal lobe showed the most oxidative damage, while the cerebellum was only slightly affected in AD patient brains. The results suggest that oxidative damage to mitochondrial DNA may contribute to the neurodegeneration seen in AD [21].

According to the research of Mecocci et. al. (2002) [22] studied 40 AD outpatients and 39 age- and sex-matched healthy controls. In particular, the levels of 8-OHdG and the levels of vitamin C, vitamin A, vitamin E and carotenoids (zeaxanthin, β-cryptoxanthin, lycopene, lutein and α- and β-carotene) in plasma were determined by high-performance liquid chromatography. 8-OHdG concentration was significantly higher and plasma antioxidant levels (with the exception of lutein) were significantly lower in AD patients compared to controls ($p<0.001$). In AD patients, a significant inverse relationship was observed between 8-OHdG concentration and plasma lycopene, lutein, α-carotene and β-carotene levels, respectively. In other words, markers of oxidative damage were found to be elevated in AD and were associated with reduced plasma antioxidant levels. These findings suggested that the concentration of 8-OHdG in AD patients reflects a state of increased oxidative stress, which is associated with a reduced antioxidant capacity [22].

At the same time, Migliore et. al. (2005) [23] conducted a case-control study with AD patients (20 subjects) and patients with mild cognitive impairment (MCI) (15 subjects). In addition, 15 healthy subjects, comparable in terms of age, sex, and smoking habit, were selected as healthy controls in the study population. As for the laboratory part, the alkaline version of the comet assay was performed to detect oxidized pyrimidines and purines, respectively. In particular, the analysis was performed on human peripheral leukocytes of three groups of subjects: the first two groups with MCI and AD and the last group with healthy subjects who were used as controls (with an age range comparable to the patient groups). Multivariate analysis of

variance revealed highly significant differences in primary DNA damage, considering single-strand and double-strand breaks, in AD and MCI patients compared to healthy controls ($p < 0.001$). The AD and MCI patient groups showed higher DNA damage at both pyrimidine and purine levels than controls ($p < 0.002$ and $p < 0.001$, respectively) [23].

Furthermore, in the research of Gabbita et. al. (1998) [24] isolated nuclear DNA from frontal, temporal and parietal lobes and cerebellum from 9 AD subjects and 11 healthy controls, while quantifying oxidized purine and pyrimidine bases using gas chromatography/mass spectrometry. Also, stable isotope-labeled oxidized base analogues were used as internal standards for the quantification of 5-hydroxyuracil, 5-hydroxycytosine, 8-hydroxyadenine, and 8-hydroxyguanine. Statistically significant increases in the levels of 5-hydroxycytosine, 5-hydroxyuracil, 8-hydroxyadenine and 8-hydroxyguanine were found in the brains of AD patients compared to control subjects ($p < 0.05$). Higher levels of oxidative DNA damage were found in the neocortical regions of the brain compared to the cerebellum. No statistically significant correlation was observed between the levels of oxidized bases and the number of neurofibrillary tangles (NFTs) and plaque. The results demonstrated that nuclear DNA damage by free radicals is increased in AD and support the idea that the brain is under increased oxidative stress in AD [24].

Also, in the research of Mecocci et. al. (1994) [25] quantified 8-hydroxy-2'-deoxyguanosine from three regions of the cerebral cortex and cerebellum in 13 AD patients and 13 age-matched healthy controls. A significant threefold increase in OH8dG levels in mitochondrial DNA was found in the parietal cortex of AD patients compared to controls ($p < 0.001$). In the whole group of samples there was a statistically significant small increase in oxidative damage to nuclear DNA ($p < 0.05$) and a statistically significant threefold increase in oxidative damage to mitochondrial mtDNA in AD patients compared to age-matched healthy controls ($p < 0.001$). These results confirm that mitochondrial DNA is particularly sensitive to oxidative damage and show that there is increased oxidative DNA damage in AD, which may contribute to the neurodegenerative process [25].

Additionally, in the study by Peña-Bautista et. al. (2019) [26] determined different oxidized products of proteins and DNA in urine samples from patients with mild cognitive impairment (MCI) due to AD (MCI-AD, $n = 53$) and healthy controls ($n = 27$) by high-performance liquid chromatography analysis combined with ultra-performance liquid chromatography-tandem mass spectrometry analysis. A multivariate model developed by partial least squares produced a diagnostic model for AD with an AUC-ROC (Area Under the Curve-Receiver Operating Characteristic) equal to 0.843 ($p = 0.0001$). Of the molecules determined, 8-OHdG ($p=0.0001$) and the 8-OHdG/2dG (2'-deoxyguanosine) ratio ($p =0.019$) were able to discriminate between AD and healthy controls, showing statistically significant differences between groups and indicating DNA oxidation as a molecular pathway involved in early AD. According to the study, determination of 8-oxoG levels may be an important biomarker for AD (high value of the AUC parameter) [26].

Moreover, in the study by Sliwinska et. al. (2016) [27] evaluated biomarkers of oxidative DNA damage from peripheral blood, such as 8-oxo-guanine (8-oxoG, a product of guanine oxidation in DNA) and the enzyme (protein) DNA 8-oxoguanine glycosylase 1 (OGG1, repairs damage resulting from guanine base oxidation in DNA) by comparing their levels between AD patients and healthy controls. Specifically, the study analyzed DNA and serum isolated from peripheral blood obtained from 100 AD patients and 110 controls. The ELISA method was used for the quantitative determination of 8-oxoG and the OGG1 enzyme. The results showed that the levels of 8-oxoG were significantly higher in AD patients compared to the control group ($p = 0.0001$). Also, the levels of OGG1 protein, which was determined in serum, were significantly lower in AD patients than in the control group ($p < 0.0001$). The findings led to the conclusion that: a) biomarkers of oxidative DNA damage detected in peripheral blood could reflect changes occurring in the brain of AD patients, b) peripheral blood samples may be useful for measuring oxidative biomarkers stress in AD [27].

DISCUSSION

The studies reviewed demonstrate a potential association between oxidative stress and Alzheimer's disease (AD). Various markers of oxidative damage, including 8-hydroxy-2'-deoxyguanosine (8-OHdG) and oxidized purines and pyrimidines, were consistently found to be elevated in AD patients compared to healthy controls. This oxidative damage was observed in both nuclear and mitochondrial DNA, with higher levels of damage found in regions of the brain affected by AD pathology. Reduced antioxidant capacity was also observed in AD patients, suggesting an imbalance between oxidative damage and antioxidant defenses. Additionally, the levels of proteins and enzymes involved in repairing oxidative DNA damage were found to be altered in AD patients [11, 16,17, 20-27].

Particularly, the study by Moslemnezhad et. al. (2016) showed significantly higher plasma 8-OHdG levels in AD patients compared to controls, whereas total antioxidant capacity was significantly lower in patients compared to controls [11]. In contrast, Mórocz et. al. (2002) found statistically significant increases in the levels of oxidized purines in the nuclear DNA of peripheral lymphocytes from AD patients compared to controls [16]. Kadioglu et. al. (2004) determined that AD patients had increased levels of oxidized pyrimidines and purines compared to age-matched healthy controls [17]. Mullaart et. al. (1990) found at least two-fold higher levels of DNA damage in the cortex of AD patients compared to controls [20]. Wang et. al. (2005) observed significantly higher levels of multiple oxidized bases in AD brain samples compared to control subjects, with mtDNA having approximately 10-fold higher levels of oxidized bases than nuclear DNA [21]. Mecocci et. al. (2002) reported significantly higher 8-OHdG concentration and lower plasma antioxidant levels in AD patients compared to controls [22]. In contrast, Migliore et. al. (2005) observed higher DNA damage levels in AD and MCI patients compared to healthy controls [23]. Gabbita et. al. (1998) found statistically significant increases in the levels of oxidized purine and pyrimidine bases in the brains of AD patients compared to control subjects [24]. Additionally, Mecocci et.

al. (1994) identified a significant threefold increase in OH8dG levels in mitochondrial DNA in parietal cortex of AD patients compared to controls [25]. Peña-Bautista et. al. (2019) found that 8-OHdG and the 8-OHdG/2dG ratio were able to discriminate between AD and healthy controls, indicating DNA oxidation as a molecular pathway involved in early AD [26]. Sliwinska et. al. (2016) observed significantly higher levels of 8-oxoG and lower levels of OGG1 protein in AD patients compared to healthy controls, suggesting a potential role of peripheral blood biomarkers in measuring oxidative stress in AD [27].

The studies by Moslemnezhad et. al. (2016) [11], Mórocz et. al. (2002) [16], Kadioglu et. al. (2004) [17], Mullaart et. al. (1990) [20], Wang et. al. (2005) [21], Mecocci et. al. (2002) [2], Migliore et. al. (2005) [23], Gabbita et. al. (1998) [24], Mecocci et. al. (1994) [25], Peña-Bautista et. al. (2019) [26], and Sliwinska et. al. (2016) [27] all explored the relationship between oxidative stress and Alzheimer's disease. These studies all investigated levels of oxidative damage and DNA repair capacity in AD patients compared to healthy controls. The researchers found increased levels of oxidative damage markers, such as 8-OHdG, 8-oxoG, and various oxidized bases, in AD patients compared to control subjects. Additionally, decreased levels of antioxidants and impaired repair of oxidized DNA were observed in AD patients. These findings suggest a link between increased oxidative stress and AD pathology, indicating that oxidative damage to DNA may be a contributing factor in the development and progression of the disease (Figure 3) [11, 16,17, 20-27].

The strengths of the above studies lie in their comprehensive approach to studying the link between oxidative stress and Alzheimer's disease (AD). Each study utilized specific methodologies to measure markers of oxidative stress, such as 8-OHdG levels and comet assay (single cell gel electrophoresis, SCGE), in various tissues and biological fluids. The inclusion of both AD patients and age-matched healthy controls in the studies allowed for direct comparison and identification of differences in oxidative stress markers. Additionally, the use of established diagnostic criteria for AD diagnosis ensured the accuracy of patient selection. The results of these studies consistently demonstrated significant increases in markers of oxidative stress and DNA damage in AD patients compared to healthy controls, providing strong evidence of the association between oxidative stress and AD. The use of advanced techniques such as gas chromatography/mass spectrometry and ELISA assays further enhanced the reliability and accuracy of the findings. These findings contribute valuable insights into the potential role of oxidative stress in the development and progression of AD, highlighting the importance of oxidative stress biomarkers as potential diagnostic and prognostic tools for the disease [11, 16,17, 20-27].

However, there are limitations to consider in these studies. First, the sample sizes were relatively small in most studies, which may limit the generalizability of the findings. Additionally, the studies relied on biomarkers of oxidative stress in blood samples, which may not accurately reflect the oxidative damage occurring in the brain. Furthermore, the cross-sectional design of many studies does not allow for causal

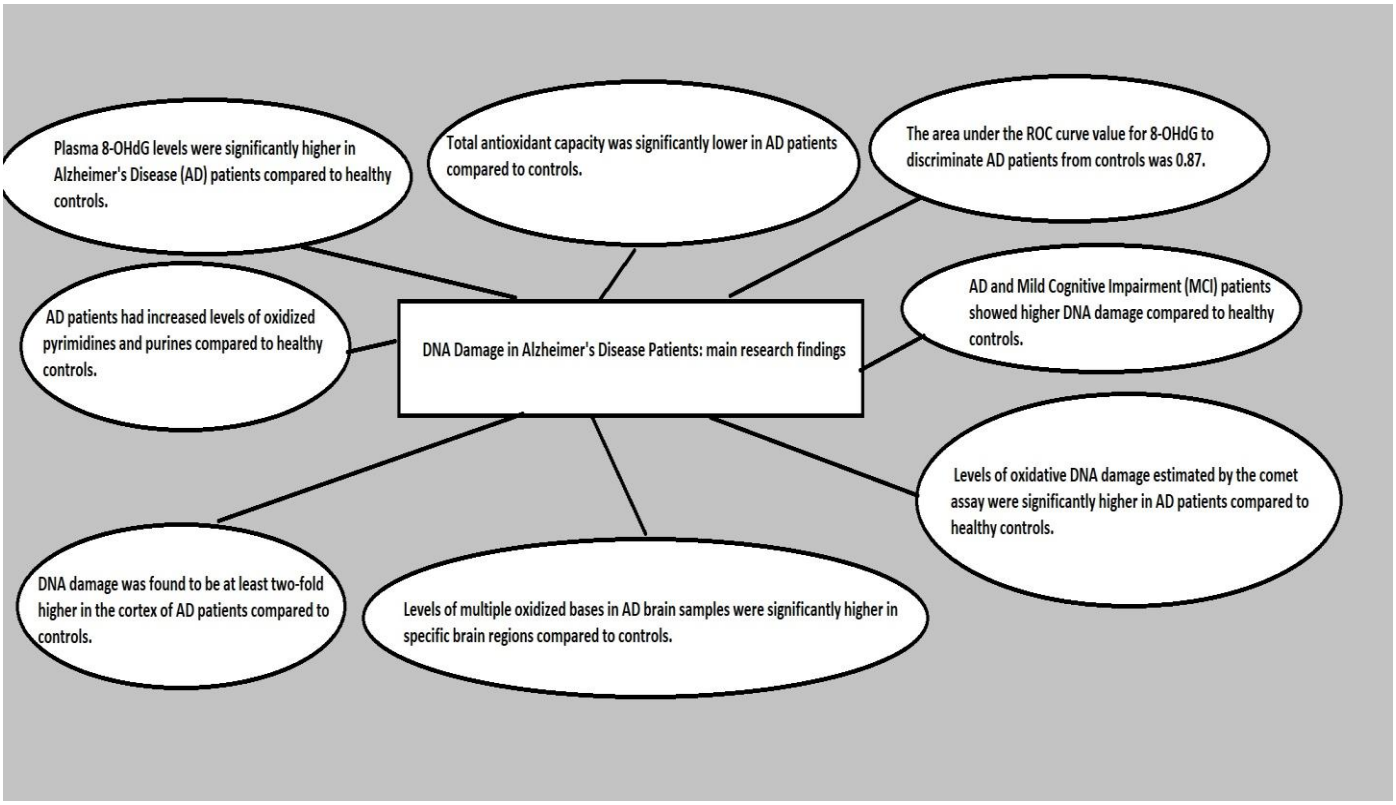

Figure 3. Diagram demonstrating the main research findings regarding DNA Damage in Alzheimer's Disease patients.

relationships to be established between oxidative stress and Alzheimer's disease. Finally, the studies did not always take into account potential confounding factors, such as lifestyle factors, medication use, and comorbidities, which could impact the results. Overall, while these studies provide valuable insights into the role of oxidative stress in Alzheimer's disease, further research with larger sample sizes, longitudinal designs, and consideration of confounding factors is needed to strengthen the evidence base [11, 16,17, 20-27].

Moving forward, future studies should focus on exploring the potential of the quantification of 8-OhdG (in human blood or urine) using ELISA and the comet assay (for human lymphocytes) in understanding the pathophysiology Alzheimer's disease (AD). Further investigations should aim to elucidate the underlying mechanisms linking oxidative stress to the pathogenesis of AD. Additionally, research should delve into the role of oxidized purines and pyrimidines as markers of DNA damage in AD patients. Moreover, studies should seek to identify potential therapeutic targets that may mitigate oxidative stress-induced damage in AD. Overall, further research in this field holds promise for advancing our recognition of the relationship between oxidative stress and AD, ultimately paving the way for novel diagnostic and treatment strategies for this debilitating neurodegenerative disease [11, 16,17, 20-27].

CONCLUSIONS

In conclusion, the reviewed studies demonstrate a potential association between DNA damage (which is a marker of oxidative stress) and Alzheimer's disease (AD). Elevated levels DNA damage (estimated by the determination of 8-OhdG using ELISA and the comet assay) were observed in AD patients compared to healthy controls across multiple studies. While the findings seem to provide evidence of the link between DNA damage and AD pathology, limitations such as small sample sizes and reliance on peripheral biomarkers highlight the need for further research. Future studies should focus on exploring novel diagnostic and therapeutic approaches, including the use of specific oxidative stress biomarkers, mechanisms linking DNA damage (as a marker of oxidative stress) to AD pathogenesis, and potential therapeutic targets to mitigate DNA damage in AD. Therefore, continued research in this area is vital for advancing our understanding of the role of DNA damage in AD and developing innovative strategies to diagnose and treat this complex neurodegenerative disease.

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ΑΝΑΣΚΟΠΗΣΗ

Διερεύνηση της πιθανής σχέσης μεταξύ των βλαβών του DNA και της νόσου Αλτσχάιμερ: μια κλινικοβιολογική προσέγγιση

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ΠΕΡΙΛΗΨΗ

Εισαγωγή: Οι βλάβες του DNA στον άνθρωπο είναι συχνά εμφανιζόμενες σε διάφορες ασθένειες και ερευνώνται εντατικά τα τελευταία χρόνια. Η νόσος Alzheimer (AD) είναι μια μορφή άνοιας που επηρεάζει έναν μεγάλο αριθμό ηλικιωμένων και χαρακτηρίζεται από απώλεια μνήμης, λειτουργική έκπτωση και διαταραχές συμπεριφοράς. Η έρευνα για τις βλάβες του DNA στη νόσο του Αλτσχάιμερ (AD) έχει κερδίσει την προσοχή στην επιστημονική κοινότητα τα τελευταία χρόνια λόγω της πιθανής συσχέτισής της με την παθογένεια της νόσου. Σκοπός: Ο σκοπός αυτής της βραχείας ανασκόπησης είναι να παράσχει μια σύνοψη των πιο πρόσφατων δεδομένων σχετικά με τις βλάβες του ανθρώπινου DNA στην (AD).

Υλικό και μέθοδοι: Πραγματοποιήθηκε μια σύντομη ανασκόπηση βασισμένη σε περιγραφική σύνθεση παλαιότερα δημοσιευμένης βιβλιογραφίας. Το υλικό της παρούσας μελέτης ανακτήθηκε αποκλειστικά από το διαδίκτυο. Ειδικότερα, διεξήχθη μια ολοκληρωμένη ηλεκτρονική βιβλιογραφική αναζήτηση στις βάσεις δεδομένων PubMed και Google Scholar χρησιμοποιώντας τους ακόλουθους όρους/λέξεις-κλειδιά: «βλάβη DNA» ΚΑΙ «νόσος Alzheimer» ΚΑΙ «άνθρωποι».

Αποτελέσματα: Έχουν διεξαχθεί πολυάριθμες μελέτες για τη διερεύνηση της βλάβης του DNA σε άτομα με (AD). Οι ερευνητές χρησιμοποίησαν τη δοκιμασία comet assay και τεχνικές ELISA για να ποσοτικοποιήσουν τα επίπεδα βλάβης του DNA σε αυτόν τον πληθυσμό. Διαπιστώθηκε σταθερά ότι οι ασθενείς (AD) εμφανίζουν σημαντικά αυξημένα επίπεδα βλάβης του DNA σε σύγκριση με τους μάρτυρες. Επιπλέον, τα αυξημένα επίπεδα δεικτών του οξειδωτικού στρες (και της βλάβης του DNA) 8-OHdG σε ασθενείς (AD) υποδηλώνουν πιθανή συσχέτιση μεταξύ οξειδωτικού στρες και (AD).

Συμπεράσματα: Η παρούσα ανασκόπηση καταδεικνύει μια αξιοσημείωτη αύξηση στις βλάβες του ανθρώπινου DNA σε δείγματα από αίμα ή στα ούρα ασθενών με (AD) σε σύγκριση με υγιή άτομα. Ωστόσο, για να επικυρωθούν περαιτέρω αυτά τα ευρήματα και να εμβαθύνουμε στις πιθανές θεραπευτικές προσεγγίσεις, είναι επιτακτική ανάγκη να πραγματοποιηθούν πρόσθετες μελέτες με μεγαλύτερες ομάδες συμμετεχόντων και ποικίλα δημογραφικά στοιχεία.

Λέξεις ευρετηρίου: βλάβες DNA, νόσος Alzheimer, άνθρωποι

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