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REVIEW ARTICLE

Alzheimer's Disease-Like Neuropathology Following Exposure to Ambient Noise

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ABSTRACT

Many factors play a role in the risk of dementia, including the environment. Widespread and significant worldwide exposure to noise, the severity of related health consequences, and the limited tools available to the public to protect themselves strongly support the WHO's argument that 'noise pollution is not only an environmental nuisance but also a threat to public health'. Exposures to noise from industrial activities, airport noise, or occupational noise are very important. One of the limitations of such studies is the lack of information about lifestyle habits that can play a key role in a person's risk of dementia. This review suggests that people with more exposure to ambient noise are at higher risk of Alzheimer's Disease (AD) and dementia than other people and we examined how chronic noise exposure causes neuropathology such as AD and how it relates to ApoE4 activation. Further studies are essential to expanding global knowledge about the harmful health effects and costs of health care due to noise pollution.

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- Dementia

ABBREVIATIONS

Aβ: Amyloid-β; AD: Alzheimer's Disease; Apo E: Apo Lipoprotein; ECDK5: Cyclin Dependent Kinase; 5GFAP: Glial Fibrillary Acidic Protein; GSK-3β: Glycogen Synthase Kinase 3 Beta; HPA: Hypothalamic-Pituitary Adrenal; Iba1: Ionized Calcium Binding Adaptor Molecule; 1RAGE: Receptor for Advanced Glycation End Products; TNF-α: Tumor Necrosis Factor Alpha

INTRODUCTION

Experimental evidence in rodents has indicated that neurological damage such as Alzheimer's Disease (AD) can induce by environmental hazards [1,2]. The AD pathogenesis, characterized by a gradual cognitive decline, overproduction of β-amyloid (Aβ), and hyperphosphorylated tau in specific areas of the brain, is considered to involve several internal (individual) interactions and external environmental factors [3]. External environmental factors affecting the AD risk include chronic exposure to chemical, physical and psychosocial risks, as well as individual lifestyle factors. Previous studies have shown that environmental noise can lead to cognitive deficits and neuropathological stimulation similar to AD in the hippocampus and prefrontal cortex, which reduces spatial learning and memory [4,5]. In addition, other studies have shown that exposure to noise leads to impaired hippocampal neurogenesis and cognitive deficits [6,7].

Internal factors influencing AD include genetics, aging, and other factors that

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are mostly inherited and cannot be changed [8,9]. The Apolipoprotein E4 (ApoE4) gene is one of the strongest genetic risk factors for AD, encoding a protein that is essential for the catabolism of triglyceride-rich lipoprotein constituents and the regulation of lipoprotein metabolism [10]. Previous researches have shown that ApoE4 may mediate and lead to hippocampal-dependent memory and learning disorders [10]. Other researchers have reported that ApoE4 may lead to pathological accumulation and deposition by reducing A β clearance in the brain [11,12]. ApoE4 also plays an important role in tau pathology [13] degradation of the normal microtubule system, which leads to increased hyperphosphorylated tau and loss of normal biological function [14,15]. In addition, recent studies have shown that environmental factors such as lead and ethanol may activate the ApoE4 gene, which may contribute to cognitive deficits and impaired hippocampal neurogenesis [7,16]. Thus, overexpression of internal ApoE4 and the risks of external environmental noise accelerate hippocampal-related cognitive decline and can lead to the development of AD-like pathological changes that require further evaluation of the role of different signaling pathways in this process. In this present review, we examine how chronic noise exposure causes neuropathology such as AD and how it relates to ApoE4 activation.

Ambient noise and ApoE4 causes AD-like neuropathology

Studies have shown that exposure to sound impairs cognitive function. The results of studies have shown that dual exposure to chronic noise and ApoE4 intensifies A β accumulation and tau hyperphosphorylation. Significantly, tau hyperphosphorylation was associated with an increase in AKT-GSK-3 β and calpain-CDK5 signaling following combination exposure. Previous studies have also shown that chronic noise exposure and ApoE4 activation may indicate a gene-environment interaction that accelerates AD development [5,17]. The ApoE4 expression accelerates hippocampal-related cognitive deficits [18]. The hippocampus is prone to damage from environmental stress and is involved in integrating cognitive and emotional information and modulating Hypothalamic-Pituitary-Adrenal (HPA) responses to sound stress. Therefore, chronic noise exposure and ApoE4 activation are synergistically effective in accelerating the risks of cognitive dysfunction [6]. Therefore, noise exposure and ApoE4 activation may be attributed to neuropathological changes in the hippocampus. A β deposition and tau hyperphosphorylation are prominent pathological features of AD [19]. Findings have also indicated A β accumulation and tau hyperphosphorylation in the hippocampus after noise exposure as well as related cognitive deficits [4,20]. Result of recent studies have shown that ApoE4 may increase A β expression and A β load in the hippocampus and play an important role in tau pathology, thereby accelerating neuropathological damage [8,12].

Neuroinflammation is associated with the pathophysiology of stress-induced [21-25] and increases A β production while decreasing its clearance, which may accelerate the occurrence and development of AD [26,27]. Significant increases in A β expression and tau hyperphosphorylation in the rat hippocampus have also been reported following chronic noise exposure and ApoE4 transfection, which supports the hypothesis that these factors have a cumulative effect on the onset and progression of AD-like neuropathological injury and shows that the synergistic interaction of these genetic and environmental factors underlies the development of AD-related pathological changes [26,27].

Neuroinflammation following exposure to chronic noise and ApoE4

Proinflammatory cytokines are elevated in several neuropathological conditions associated with cognitive deficits and can exacerbate disorders induced by additional cytokines, glutamate, and oxidative stress [25,26,28,29]. In addition, active microglia and reactive astrocytes are the main source of inflammation in AD, and up-regulation of these cells in the inflammatory response has been observed in brain regions related with AD including the limbic system and frontal cortex. Researchers have reported that exposure to noise increased the expression of Iba1, GFAP, TNF- α , and RAGE, suggesting that neuroglial activation due to chronic noise exposure can play an important role in initiating neuroinflammation [5,27].

Other studies have shown that increased TNF- α expression induced by ApoE4 can lead to synaptic dysfunction and neuronal loss [30]. Also, a significant increase in Iba1, GFAP, RAGE and TNF- α levels in the hippocampus of rats exposed to chronic noise and ApoE4 has been reported, which is consistent with an increase in the combination exposure of A β and tau hyperphosphorylation and indicates an increase in neuroinflammation and related AD-like neuropathology in the primary brain structure involved in memory and learning. In addition, according to the studies finding, increases in inflammatory effects are greater for a combination exposure than a single exposure, highlighting the synergistic effect of chronic noise and ApoE4 on hippocampal structure and function.

The combined effect of chronic noise and ApoE4 activation on the AKT-GSK-3 β and calpain-CDK5 signaling pathways

The signaling pathways AKT-GSK-3 β and calpain-CDK5 play an important role in the development of AD [31,32]. The GSK-3 β has been shown to be involved in A β formation, tau protein phosphorylation, neuronal apoptosis, and the inflammatory response, which are closely related to AD development, through regulating multiple signal transduction pathways. β GSK-3 activity was also regulated

by phosphorylation, and β GSK-3 activity was inhibited by serine site phosphorylation (ser9) [33].

Research findings have shown that ApoE4 may increase GSK-3 β activity, thereby resulting in abnormal tau phosphorylation [34]. Previous findings have shown that noise exposure leads to abnormal tau phosphorylation, which also provides evidence for GSK3 β involvement in these processes. The P35 is specifically expressed in nerve cells and can bind directly to and activate Cdk5. P25 is the residual carboxy terminal part of p35 that is cleaved by the calpain [5]. This review shows that chronic noise exposure and ApoE4 activation can have a synergistic effect on tau hyperphosphorylation and a β accumulation in the hippocampus. This synergy may be associated with β -CDK5 / GSK-3 signaling pathways and contribute to cognitive deficits characteristic of neurodegenerative diseases such as AD.

CONCLUSION

Further studies are needed to further elucidate the underlying mechanisms of such synergy. Our results can have a significant effect on the prevention and delay of AD. In everyday life, we can delay the onset of AD predisposed genes, and reducing noise exposure can delay the onset of AD disease or prevent noise in normal people. At the same time, we can delay the course of AD patients or prevent the occurrence of normal people by controlling environmental factors and genetic factors.

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