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The Effects of Noise Pollution on the Cell Senescence

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Abstract

Noise pollution, primarily caused by human activities, refers to unwanted ambient noise that adversely affects quality of life and health. The World Health Organization (WHO) and the Environmental Protection Agency (EPA) suggest a safe noise exposure level of 70 dB. Noise pollution can lead to significant health issues. It is supposed that noise pollution accelerates cellular senescence, characterized by cell cycle arrest, metabolic changes, inducing inflammation. Although there is no direct evidence to show the relation of noise exposure and induction of cell senescence, the noise pollution often mediated some key proteins involve in cell senescence like p53 and AMPK. It also affects mitochondrial function, leading to increased reactive oxygen species (ROS), reduced telomerase activity and change in pro-inflammatory cytokines. Chronic noise exposure alters cellular signaling pathways and metabolic responses, highlighting the need for further understanding of its impact on health and aging. Overall, noise pollution poses significant risks to human health and cellular dynamics, necessitating attention to environmental noise levels.

Keywords: noise pollution, cellular senescence, health impact, mitochondrial function, chronic exposure

1 Introduction

Noise pollution refers to an increase in the environmental ambient and unwanted noise. Noise pollution is anthropogenic and makes by the human activities (1), and may interfere with normal human activities and life quality. However, based on the WHO guidelines, the safe level of noise varies in different situations and times (2), 70 db has been suggested by Environmental Protection Agency's (EPA's) for public as safe level of noise exposure (3). Noise pollution has many detrimental effects on human health. Noise-induced hearing loss is one of the most important side effects of noise pollution that affects 5% of the population around the world (4). Noise pollution also increase the chance of diseases in different organs such as heart (5, 6), vessels (7), kidney (8, 9), and brain (10). Noise pollution also increases the risk of hypertension (11), and hypertension depended diseases such as preeclampsia (12). It also leads to an increase in the prevalence of the metabolic disorders (13, 14, 15). Structural changes in some organs such as chick inner ear hair cells (16), rat adrenal gland (17) and mice developing heart (18) have been also reported by noise exposure.

Animal studies showed that noise pollution has many impacts on the embryo development as well. Exposure of the chick embryo to 110 dB noises led to a reduction in body weight, brain size and weight through a decrease in neuronal density (19), and changes in metabolite concentrations in the auditory cortex (20). The prenatal administration of 126 dB noise to the pregnant mouse showed embryotoxicity as well as a decrease in the pregnancy rate (21). Histochemical changes in developing heart (22), cochlea (23) and spiral ganglion (24) have been reported in mouse embryos by noise pollution. It supposed that the adverse effects of noise exposure can be due to releasing the glucocorticoid hormones by noise stress (25), activation of inflammatory factors (26), reactive oxygen species (ROS) production (27). The cells in the body can be influence by noise-induced oxidative stress. ROS and antioxidant imbalance may lead to change in differentiation and self-renewal capacity of stem cells (28). Aging has been defined as the progressive reduction in the tissue functional that leads to dead of organism (29). The process of aging is multifactorial, and can be impacted by environmental, social, and psychosocial factors. It has been shown that the noise pollution can promote aging process (30). Cellular senescence happens throughout in the life in different tissues and leads to stable cell cycle arrest in response to DNA damage or the environmental stressors. Although, cell senescence is one the regressive processes in the aging, it has some benefits for organisms (31). The senescence cells can be considered as postmitotic fully differentiated cell (32).

The objective of the current review is to discuss the evidence that shows the possible influence of noise pollution on the different aspects cell senescence physiology.

2 Noise impact on metabolism, oxidative stress and inflammation

Animal studies showed that in response to noise stress, the releasing glucocorticoids led to an increase in gluconeogenesis and hepatic glycogenolysis and the level of glucose. It also can act as antagonist of insultin. Noise pollution interrupts the hypothalamo-pituitary adrenal axis (25). Short and long term exposure to noise led to producing ROS, and increasing in the Malondialdehyde (MDA), nitric oxide (NO) and glutathione peroxidase (26) and decreasing in the superoxide dismutase (33) in rats and human. Noise pollution also reduces the level of superoxide dismutase in blood serum (27). ROS production in turn elevated the level of factors including nuclear factor erythroid 2-related factor 2 (Nrf2), nuclear factor-κB (NF-κB), and peroxisome proliferator-activated receptor (PPAR) that

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induce the inflammation. The noise exposure leads to morphological changes and induces apoptosis in spleen (26), rat testicular tissue (34) and hair cells of inner ear (35). Mitochondrial destruction has been also reported by noise exposure (26). Noise mediates apoptosis through elevation of the p53 expression level, and therefore, p53 inhibitors have been suggested to prevent noise-induced cell death (35).

3 Cellular Senescence

Although, there are different type of cellular senescence, they are characterized by cell division arrest, resistance to apoptosis, change in cell secretome, (36) deregulation of metabolism, inflammation and regressive changes in tissue (37, 38). Cell cycle regulators such as P53, P21 and P16 play some roles in senescence processes (36). Cell division arrest by these regulators inhibits inherited damaged DNA to the daughter cells (39). Transcriptional heterogeneity also increases in senescence cells (40). Age-related shortening of telomere and decrease in telomerase activity are the other senescence features in some type of cellular senescence (29). Shortening of the telomere led to cell division arrest, and increase in the number of senescence cells in tissues is related to aging and development of age related diseases (41).

The mammalian target of rapamycin (mTOR) is a kinase that has important roles in cellular senescence. It regulates cellular metabolism, immune responses, autophagy, survival, and proliferation. In non-senescence cells, it inhibits autophagy. Autophagy activation by m-TOR in senescence cells leads to providing amino acids that activates mTOR complex 1. M-TOR, and changes the transcriptome of the cells toward senescence associated secretory phenotype (SASP) (42). mTOR complex 1 can be inhibited by AMP-activated protein kinase (AMPK), and therefore, the activation of AMPK represses m-TOR (43). Cells use m-TOR signaling pathway as a strategy for survival by regulating metabolism (44). Environmental stressors can be sensed by m-TOR signaling pathway and change the cell growth and metabolism in a species-dependent manner (45, 46).

Another parameter in cell aging is mitochondrial dysfuction. In senescent cells, respiratory capacity per mitochondrion and mitochondrial membrane potential (MMP) diminish. Due to decrease in mitophagy, these dysfunctional mitochondria accumulate in the cells leads to an increase in total mass on mitochondria in senescence cells. The damaged mitochondria produce a higher amount of ROS. A reduction in nicotinamide adenine dinucleotide (NADH) to NAD+ ratio has been shown in cell senescence (47).

4 Noise pollution and cellular senescence

Noise exposure leads to immunological changes. It also changes the protein content of the plasma. Noise exposure elevates the level of the enzymes involves in oxidative stress such as inducible nitric oxide synthase (*iNOS).* Immuno cell activation causes oxidative stress induction and ROS formation (48). It is one of the major factors that promotes cell senescence (49, 50, 51). Traffic noise exposure has been also shown to accelerate aging process (52,53), and one of the potential mechanisms is through oxidative stress induction. Noise exposure has been shown to reduce telomerase activity in sex-depended manner. The noise stress reduce telomere length in the female brain but not male. However, noise exposure led to a decrease in telomerase activity in male gonads of mature stone sculpins (53). Traffic noise also reduced the telomere length in blood cells of the house sparrows (54). Noise also reduced the functionality and size of mitochondria in the blood cells of this species as well (55). Exposure of the peled to 176-186 dB noise led to a reduction in the number of active mitochondria in the red blood cells without changing in telomeres (56). Accumulation of damaged mitochondria may accelerate the processes of cellular senescence (57).

In one study, the mice were exposed to sound intensity with average 85db (aircraft noise). This noise pollution leads to endothelial dysfunction, blood pressure, and oxidative stress. Detrimental effects of noise stress have been reported in hair cells. Also, nuclear import of the caspase-independent cell death marker, Endo G, has been shown in outer hair cells after 1-3 h post-exposure. Traumatic noise temporary reduces intracellular ATP concentration and activates Rho GTPase pathways in mouse outer hair cells. (58). Both ATP depletion and Rho GTPase signaling pathways have roles in the induction of cell senescence. In senescence cells, the ATP generation by mitochondria decreases (59). Reduction of ATP triggers cell senescence by upregulating P21 and P16 (60, 61). Cell senescence has been shown to induce in rat peripheral annulus fibrosus cells (62), human foreskin fibroblast (63), mouse embryo fibroblasts (64), primary fibroblasts (65), and HeLa cell clones (66) through the RhoA/ROCK pathway. Administration of one of the AMPK activator (5-Aminoimidazole-4-carboxamide-1-β-D-ribofuranoside) caused normalization of the oxidative stress and protected the detrimental impact of noise pollution (67). Activation of the AMPK inhibits m-TOR, the regulator of senescence processes (68).

There are a contradictory data about the effects of noise exposure and glycocorticoid level, and, it seems to be species specific. Some studies indicate that the exposure to traffic noise in birds such as the white-crowned sparrows (69), and free-living house sparrows (70) lowered or had no impact on the level of glucocorticoids, and the other showed that it elevated in white-crowned sparrows (71). A correlation has been detected between the traffic noise exposure and glucocorticoid metabolism in human newborns (72). Exposure of mice to 90 dB noise increased the cortisol and glucose level (73). Both cortisol and high glucose level induce cell senescence. Stress induced glucocorticoids increased the ROS by mitochondrial activity. ROS in turn, damaged telomere and reduces the telomerase activity (74). Also, glucocorticoides induces the expression of pre-inflammatory cytokines (75), and these cytokins can induce cell senescence (76). In contrast, glucocorticoid administration has been reported to elevate the activity of beta-galactosidase, senescence marker, without decrease in cell proliferation or increase in DNA damage in mesenchymal stem cells, but not in fibroblasts isolated from synovial membrane (77). High glucose exposure induces cell senescence by upregulation of p16, p21, and p53 (78), telomere shortening and proinflammatory cytokine release (79, 80). Also high glucose level elevates the m-TOR level and as a result, cell senescence in mesenchymal stem cells and human vascular endothelial cells (81, 82, 83).

Calcium overload in the cells such as outer hair cells has been shown after noise exposure (84, 85). Intracellular calcium elevation has been also demonstrated in senescence cells. The calcium accumulation in the mitochondria interferes with their normal function (86).

Studies have demonstrated that noise-induced stress causes pro-inflammatory cytokines elevation, including interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) in different organs (87, 88, 89). Both these cytokines increase in older adults (90). Besides, long term exposure of MCF-7 cell line and human umbilical vein endothelial cells to IL6 and TNF-α induces senescence phenotype (91, 92).

There is a controversy about the effect of noise on cholesterol and HDL levels. While one study showed that occupational exposure to noise has been reported to decrease the cholesterol level (93), the other study revealed any correlation between serum cholesterol and HDL and noise exposure (94). In contrast, occupational noise exposure to human workers had no impact on the cholesterol level (95). On the other hand, a study showed that administration of mice to intermittent noise with level of 70–100 dB for 50 days reduced the HDL and cholesterol levels in serum (96). HDL has been reported to reduce the cell senescence in endothelial progenitor cells. HDL also activates telomerase through phosphatidylinositol-3-kinase/Akt (PI3K/Akt) signaling pathway (97). Therefore, noise may influence cellular senescence by decreasing HDL. In senescence cells, the metabolism of lipids is also disregulated (99, 100). Cholesterol may regulate human cellular senescence positively. Mevalonate kinase and phosphomevalonate kinase pathway, that induces premature cell senescence, promotes the Estrogen-Related Receptor alpha (ERRα). ERRα induces mitochondrial dysfunction, increase ROS production, DNA damage and leads to a p53-dependent cell senescence. Cholesterol biosynthesis has been hypothesized to activate ERRα during PMVK-induced cell senescence (101).

5 Conclusion

Exposure to traffic or traumatic noise may be linked to significant changes in cellular signaling pathways associated with AMPK, mTOR, telomerase activity, and tumor suppressor proteins like p53, p21, p16, and pro-inflammatory cytokines. Noise pollution also may induce cell aging by increase in the level of glycocorticoides and glucose. These pathways illustrate a complex response to environmental stressors, wherein cells attempt to manage energy balance, growth, and survival amid the detrimental effects of chronic noise exposure. This growing body of research underscores the importance of understanding how environmental factors like traffic noise can influence cellular dynamics and contribute to health problems.

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