Effects of Chronic Urban Noise Pollution on the Brain

Anya Verma

SPECIFIC AIMS

Since the Industrial Revolution, many technological advancements have been made, including factories, automobiles, and more. The introduction of new machines has significantly affected the world, either by contributing to global warming or increasing noise pollution. In this study, urban noise pollution is characterized by the sounds of sirens, cars, trains, and other traffic. It can be a nuisance to the average person during their commute. Noise pollution is a prevalent environmental issue that contributes to the suffering of millions of people globally (United Nations Environment Programme, 2020; Soundproof Cow, 2017). Several diseases and negative mental states have been linked to excessive noise, such as cardiovascular disease and increased annoyance (Münzel et al., 2018; Jafari et al., 2019). However, while the physical effects of noise have been investigated thoroughly, the biochemical effects are yet to be studied. Specifically, this means analyzing the effects of persistent noise on neurogenesis and hormone, neurotransmitter, and oxidative stress signaling in the brain.

The first specific aim of this study is to analyze the chemical changes in the brain in response to varying amplitudes of noise. Currently, it is known that noise increases variability in neurotransmitter release (Faisal et al., 2008). Additionally, response to noise results in an increase in the stress hormone cortisol (Spreng, 2000). However, there is a significant lack of studies on other hormones and neurotransmitters released during exposure to unwanted noise. Therefore, this is an area of investigation for this study.

The second specific aim of this study is to determine what chronic noise exposure does to oxidative stress in the brain. Specifically, it aims to determine whether levels of oxidative stress vary as the time of exposure increases, or remains the same during the whole period, including during levels after exposure has concluded. Jafari et al. have suggested the existence of transient oxidative stress when trying to induce sensorineural hearing loss in model organisms. However, this experiment wants to simulate chronic noise that many people around the world have and see what effects it may have on oxidative stress in the brain.

The third specific aim of this study is to analyze what happens to the rate of hippocampal neurogenesis during exposure to chronic noise. It has been established that noise exposure negatively affects visual and auditory attention span (Jafari et al., 2019). However, not much is known about what happens to the neurons involved in these processes during exposure. Since noise affects cognitive functions such as learning and memory, this study wants to determine whether hippocampal neurogenesis rates slow down to explain this phenomenon. This study will analyze the amount of mature and proliferating neurons in the hippocampus to identify specific patterns.

With more research about the effects of noise on the nervous system, future generations can work on improving current machines and technology to preserve human health. This will improve urban planning in the future and provide more discoveries for the world of science.

INTRODUCTION AND SIGNIFICANCE

Urban noise pollution is a major environmental issue, contributing to health issues for people of all age groups (United Nations Environment Programme, 2020). It is characterized by the sound of cars, sirens, trains, and other common noises in urban areas (*Urban Noise - an Overview | ScienceDirect Topics*, n.d.). Around 1 in 5 people living in an urban population are exposed to harmful levels of road traffic noise (*Noise*, 2023). Current bustling cities, including New York City, Mumbai, and Tokyo, average around 90-100 dB of noise, which, when exposed to humans for a mere 8-hour period, is likely to cause damage to the ear (Soundproof Cow, 2017). With the advent of rapid urbanization and development, noise pollution has become even more prevalent.

Until the 1960s, neuroscientists were unaware of nor did they accept the human brain's ability for neurogenesis (Kumar et al., 2019). When evidence for neurogenesis first emerged, it was ignored because of its implausibility to the scientists of the time. However, over the years, scientists have identified the dentate gyrus of the hippocampus as one of the major sites for neurogenesis, yielding functional neurons important for memory storage (Eriksson et al., 1998).

Neurogenesis is essential for integrating cognitive processes in aging adults, including understanding patterns and encoding memory (*Neurogenesis - an Overview | ScienceDirect Topics*, n.d.). A decline in neurogenesis directly removes these capabilities from an organism, leading to dementia and numerous other cognitive issues (Mathews et al., 2017). Various factors, including nutrition and environmental conditions, can influence neurogenesis. For example, diets high in fat and sugar, alcohol, and opioids have been shown to affect this process negatively (Poulose et al., 2017). Some environmental factors, on the other hand, have the opposite effect. Introduction to an enriched environment consisting of abundant sensory stimuli and physical activity has been found to have a positive impact on the rate of neurogenesis in model organisms (Grońska-Pęski et al., 2021). However, increased age and oxidative stress significantly decline the rate of neurogenesis (Gemma et al., 2013).

Increasing noise pollution has been proven to have adverse effects on physical well-being. In a study conducted in Toronto, Canada, increased exposure to traffic noises was linked to an elevated chance of congestive heart failure and acute myocardial infarction (Bai et al., 2020). Furthermore, exposure to noise at high volumes (>95 dBA) heavily reduces cognitive functions such as mental workload and attention, which are associated with the cerebrum (Jafari et al., 2019). However, these studies do not shed light on the biochemical effects of chronic noise exposure on neurons. Thus, it is important to investigate the effects excessive noise has on the nervous system.

There is a gap in research regarding the effects of noise pollution on neurogenesis, especially in the absence of sensorineural hearing loss. Sensorineural hearing loss caused by excessive noise has been shown to decrease neurogenesis in the hippocampus (Liu et al., 2016). However, an investigation into whether the effects of persistent noise pollution without hearing loss on neurogenesis is yet to be conducted, underlying the importance of such research as it

could have important implications for future urban planning to maintain the health of the human population.

This study wishes to identify the mechanisms by which constant noise influences neurogenesis. It aims to identify biochemical markers associated with noise and its effects on the brain and neurogenesis. Specifically, as proposed by Liu et al., it is hypothesized that oxidative stress induced by noise may contribute to the erosion of synapses, thus leading to cognitive decline.

Understanding these mechanisms is crucial for informing public health strategies and urban planning to mitigate the effects of noise pollution on brain health.

RESEARCH STRATEGY

Specific Aim 1: Determine chemical changes in the brain in response to varying amplitudes of the same noise

While it is understood that continually increased amplitude of noise results in a decrease in visual and auditory attention span (Jafari et al., 2019), there is a lack of thorough research on the chemical basis of these changes. The decrease in attention span suggests an impairment of signaling in the cerebral cortices of the brain. This experiment aims to explain this impairment chemically using groups of mice exposed to varying noise levels. Using five groups of 5 mice each, each group will be placed into separate sound-controlled chambers. The first chamber, serving as the control, will experience no noise (0dBA) playing. The second chamber will play a persistent 45 dBA noise consisting of sounds of sirens, cars, and traffic, emulating typical urban ambient noise. The third, fourth, and fifth chambers will play increasingly loud levels of the same noise at 75 dBA, 85 dBA, and 95 dBA, respectively, simulating more extreme urban environments.

Before each group of mice is placed into its chamber, a preliminary cerebral microdialysis will be employed near the frontal, occipital, and temporal lobes of the mice to examine extracellular levels of all neurotransmitters and stress hormones. After each mouse is placed into its designated chamber, microdialyses will be taken at the following intervals: 1 hour, 1 day, 2 days, 1 week, 2 weeks, and 1 month. Then, the noise will be shut off for all mice after 1 month, and another microdialysis will be taken. Microdialyses of the mice will be tested for levels of all chemicals (stress hormones and neurotransmitters) and analyzed to show varying levels across different groups.

As time increases, it is expected that the levels of stress hormones in the mice increase, specifically corticotropin-releasing-factor (CRH) and adrenocorticotropin-releasing-hormone (ACTH), as well as markers of oxidative stress such as reactive oxygen species (ROS) (Münzel et al., 2018). Current studies have shown that exposure to noise leads to annoyance, which is linked to a higher level of stress hormones such as cortisol (Zare et al., 2019). However, as time keeps increasing, it is expected that levels of stress hormones decline as the mice acclimate to the sound. It is also expected that dopamine levels rise as a stress response, and acetylcholine levels rise in response to auditory stimulation.

Specific Aim 2 and 3: Understand the changes in oxidative stress (Aim 2) and the rate of neurogenesis (Aim 3) in the hippocampus in response to prolonged noise exposure

The second specific aim of this project is to understand the effect of persistent noise on levels of oxidative stress. Oxidative stress is caused by an inability to detoxify the free radical ROS accumulated due to an imbalance between its accumulation and production (Pizzino et al., 2017). While free radicals have some benefits, such as creating cell structures, they also cause much harm, and in this form, they are known as oxidative stress. In an organism with high levels of oxidative stress, lipid peroxidation is highly likely to occur, destroying cell membranes and other vital cell structures. It has even been implicated in cancer and diseases of multiple organ systems.

In the nervous system, it is known that oxidative stress and inflammation result in cognitive disabilities (Harman, 1981). Transient oxidative stress during noise exposure has been identified in the experiments by Jafari et al. on sensorineural hearing loss affecting hippocampal neurogenesis. However, while the mentioned study investigates neurogenesis after hearing loss is induced, this study investigates the effects on neurogenesis without causing hearing loss.

Three groups of mice, each with 5 mice, will be used for this experiment. Groups will be placed into separate chambers similar to the last experiment. The control group will not be exposed to any urban noise (0dBA) to assess for natural changes in neurogenesis and oxidative stress. The second group will be placed in a chamber with 75 dBA of consistent noise to simulate normal urban noise levels. The third group will be placed in a chamber with 95 dBA of consistent urban noise to simulate extremely loud cities. For 4 weeks, the mice will be continually exposed to their respective noises.

Levels of oxidative stress in the brain will be measured indirectly by using Thiobarbituric Acid Reactive Substances (TBARS). TBARS works by measuring levels of malondialdehyde (MDA), which is overproduced in areas of high oxidative stress (Gaweł et al., 2004). This will be assessed once before the experiment, and every subsequent week of the duration of the experiment.

Neurogenesis in the mice will be measured using Bromodeoxyuridine (BrdU). This is a thymidine analog that identifies cell proliferation, and it is instrumental in identifying hippocampal neurogenesis (Taupin, 2007). BrdU immunohistochemistry will be used to mark proliferating neurons in the dentate gyrus, signifying areas of neurogenesis.
Next, to identify already mature neurons in the hippocampus, neuronal nuclei (NeuN) will be used as a marker. NeuN has been used to identify the functionality of differentiated cells (Gusel'nikova & Korzhevskiy, 2015). In this experiment, it will be used to identify stagnant, shrinking, or growing areas of functional neurons in the hippocampus at the measured points in the study.

It is hypothesized that increased noise exposure will result in higher levels of oxidative stress, leading to an increase in MDA marked by TBARS. However, it may also be possible that the

levels of oxidative stress remain the same for as long as the exposure to noise, indicating a constant and sustained biochemical alteration in the brain due to chronic noise. Additionally, it is expected that with more noise, there is less neuronal proliferation, and therefore a lower number of BrdU-positive cells and a stagnant, if not decreasing, amount of NeuN-positive cells in the hippocampal tissue.

References

1. Babcock, K. R., Page, J. S., Fallon, J. R., & Webb, A. E. (2021). Adult Hippocampal Neurogenesis in Aging and Alzheimer's Disease. *Stem Cell Reports*, *16*(4), 681–693. https://doi.org/10.1016/j.stemcr.2021.01.019
2. Bai, L., Shin, S., Oiamo, T. H., Burnett, R. T., Weichenthal, S., Jerrett, M., Kwong, J. C., Copes, R., Kopp, A., & Chen, H. (2020). Exposure to Road Traffic Noise and Incidence of Acute Myocardial Infarction and Congestive Heart Failure: A Population-Based Cohort Study in Toronto, Canada. *Environmental Health Perspectives*, *128*(8), 087001. https://doi.org/10.1289/ehp5809
3. Eriksson, P. S., Perfilieva, E., Björk-Eriksson, T., Alborn, A.-M., Nordborg, C., Peterson, D. A., & Gage, F. H. (1998). Neurogenesis in the adult human hippocampus. *Nature Medicine*, *4*(11), 1313–1317. https://doi.org/10.1038/3305
4. Faisal, A. A., Selen, L. P. J., & Wolpert, D. M. (2008). Noise in the nervous system. *Nature Reviews Neuroscience*, *9*(4), 292–303. https://doi.org/10.1038/nrn2258
5. Gaweł, S., Wardas, M., Niedworok, E., & Wardas, P. (2004). [Malondialdehyde (MDA) as a lipid peroxidation marker]. *Wiadomosci Lekarskie (Warsaw, Poland: 1960)*, *57*(9-10), 453–455. https://pubmed.ncbi.nlm.nih.gov/15765761/#:~:text=Malondialdehyde%20(MDA)%20is%20one%20of
6. Gemma, C., Vila, J., Bachstetter, A., & Bickford, P. C. (2013). *Oxidative Stress and the Aging Brain: From Theory to Prevention*. Nih.gov; CRC Press/Taylor & Francis. https://www.ncbi.nlm.nih.gov/books/NBK3869/
7. Grońska-Pęski, M., Gonçalves, J. T., & Hébert, J. M. (2021). Enriched Environment Promotes Adult Hippocampal Neurogenesis through FGFRs. *The Journal of Neuroscience*, *41*(13), 2899–2910. https://doi.org/10.1523/jneurosci.2286-20.2021
8. Gusel'nikova, V. V., & Korzhevskiy, D. E. (2015). NeuN As a Neuronal Nuclear Antigen and Neuron Differentiation Marker. *Acta Naturae*, *7*(2), 42–47. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4463411/
9. Harman, D. (1981). The aging process. *Proceedings of the National Academy of Sciences of the United States of America*, *78*(11), 7124–7128. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC349208/
10. Huang, T.-T., Zou, Y., & Corniola, R. (2012). Oxidative stress and adult neurogenesis – effects of radiation and superoxide dismutase deficiency. *Seminars in Cell & Developmental Biology*, *23*(7), 738–744. https://doi.org/10.1016/j.semcdb.2012.04.003
11. Jafari, M. J., Khosrowabadi, R., Khodakarim, S., & Mohammadian, F. (2019). The Effect of Noise Exposure on Cognitive Performance and Brain Activity Patterns. *Open Access Macedonian Journal of Medical Sciences*, *7*(17), 2924–2931. https://doi.org/10.3889/oamjms.2019.742
12. Kumar, A., Pareek, V., Faiq, M. A., Ghosh, S. K., & Kumari, C. (2019). ADULT NEUROGENESIS IN HUMANS: A Review of Basic Concepts, History, Current Research, and Clinical Implications. *Innovations in Clinical Neuroscience*, *16*(5-6), 30–37. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6659986/#:~:text=The%20first%20evidence%20of%20adult
13. Liu, L., Shen, P., He, T., Chang, Y., Shi, L., Tao, S., Li, X., Xun, Q., Guo, X., Yu, Z., & Wang, J. (2016). Noise induced hearing loss impairs spatial learning/memory and

hippocampal neurogenesis in mice. *Scientific Reports*, *6*(1). https://doi.org/10.1038/srep20374
14. Mathews, K. J., Allen, K. M., Boerrigter, D., Ball, H., Shannon Weickert, C., & Double, K. L. (2017). Evidence for reduced neurogenesis in the aging human hippocampus despite stable stem cell markers. *Aging Cell*, *16*(5), 1195–1199. https://doi.org/10.1111/acel.12641
15. Münzel, T., Schmidt, F. P., Steven, S., Herzog, J., Daiber, A., & Sørensen, M. (2018). Environmental Noise and the Cardiovascular System. *Journal of the American College of Cardiology*, *71*(6), 688–697. https://doi.org/10.1016/j.jacc.2017.12.015
16. *Neurogenesis - an overview | ScienceDirect Topics*. (n.d.). Www.sciencedirect.com. Retrieved July 16, 2024, from https://www.sciencedirect.com/topics/medicine-and-dentistry/neurogenesis#:~:text=Neurogenesis%20occurring%20in%20the%20dentate
17. *Noise*. (2023, October 4). Www.eea.europa.eu. https://www.eea.europa.eu/en/topics/in-depth/noise?activeTab=fa515f0c-9ab0-493c-b4cd-58a32dfaae0a
18. Pizzino, G., Irrera, N., Cucinotta, M., Pallio, G., Mannino, F., Arcoraci, V., Squadrito, F., Altavilla, D., & Bitto, A. (2017). Oxidative Stress: Harms and Benefits for Human Health. *Oxidative Medicine and Cellular Longevity*, *2017*(8416763), 1–13. https://doi.org/10.1155/2017/8416763
19. Poulose, S. M., Miller, M. G., Scott, T., & Shukitt-Hale, B. (2017). Nutritional Factors Affecting Adult Neurogenesis and Cognitive Function. *Advances in Nutrition: An International Review Journal*, *8*(6), 804–811. https://doi.org/10.3945/an.117.016261
20. Soundproof Cow. (2017, July 21). *Top 10 Loudest Cities in the World to Live*. Soundproof Cow; Soundproof Cow. https://www.soundproofcow.com/top-10-loudest-cities-world-live/
21. Spreng, M. (2000). Possible health effects of noise induced cortisol increase. *Noise & Health*, *2*(7), 59–64. https://pubmed.ncbi.nlm.nih.gov/12689472/
22. Taupin, P. (2007). BrdU immunohistochemistry for studying adult neurogenesis: Paradigms, pitfalls, limitations, and validation. *Brain Research Reviews*, *53*(1), 198–214. https://doi.org/10.1016/j.brainresrev.2006.08.002
23. United Nations Environment Programme. (2020). *Frontiers 2022: Noise, Blazes and Mismatches – Emerging Issues of Environmental Concern*. https://www.unep.org/resources/frontiers-2022-noise-blazes-and-mismatches
24. *Urban Noise - an overview | ScienceDirect Topics*. (n.d.). Www.sciencedirect.com. https://www.sciencedirect.com/topics/earth-and-planetary-sciences/urban-noise
25. Zare, S., Baneshi, M. R., Hemmatjo, R., Ahmadi, S., Omidvar, M., & Dehaghi, B. F. (2019). The Effect of Occupational Noise Exposure on Serum Cortisol Concentration of Night-shift Industrial Workers: A Field Study. *Safety and Health at Work*, *10*(1), 109–113. https://doi.org/10.1016/j.shaw.2018.07.002