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Brooke Spillman, Student

Dr. Wayne Sanderson, Committee Chair

Dr. Sarah Wackerbarth, Director of Graduate Studies

Volatile Organic Compound Exposure and Hearing Loss in Children

**University of Kentucky College of Public Health
Master of Public Health, Preventative Medicine and Environmental Health
Capstone Project**

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Hearing loss is often associated with repeated exposure to noise levels above 85 decibels. While noise is noted as the largest contributor to hearing loss, some fail to consider the impacts of chemical exposure on the hearing health of children, specifically VOCs. Early detection and prevention of hearing loss in children is important due to the impacts that hearing has on the learning, behavior, speech, and language development of children. This study examined the relationship between VOC exposure and hearing loss in children using NHANES data collected from 2005-2006. This was analyzed with Chi-square analyses and a logistic regression taking other variables into account. Overall, no significant findings were found for the relationship between VOC exposure and hearing loss in this population. These findings have indicated the need for more in-depth data collection and analysis pertaining to this relationship.

Introduction

Hearing loss is often associated with repeated exposure to noise levels above 85 decibels. This is referred to as noise induced hearing loss and has been studied in children, specifically in relation to recreational activities such as headphone use (Roberts & Neitzel, 2019). While noise is noted as the largest contributor to hearing loss, some fail to consider the impacts of chemical exposure on the hearing health of children, specifically volatile organic compounds (VOCs). Common sources of VOC exposure for children include secondhand smoke, household cleaning products, soil, and home renovation items like paint, adhesives, varnish, and vinyl flooring (Choi et al., 2010). Due to higher respiratory rates caused by smaller lung capacity, children are breathing in contaminated air at higher rates than adults (International Programme on Chemical Safety, United Nations Environment Programme, International Labour Organization, World Health Organization, & Commission of the European Communities, 1987).

VOCs are chemicals that easily evaporate under normal indoor conditions (World Health Organization, 1989). With this broad definition many chemicals are encompassed by this term. VOCs can be found in household cleaning products, paint, cigarette smoke, fingernail polish, and countless other products children are exposed to daily. Numerous VOCs are naturally occurring and only hazardous to health in extreme circumstances while others can have immediate impacts at small doses (Environmental Protection Agency, 2017a). Issues such as asthma, eczema, and rhinitis have been studied as a result of VOC exposure in children (Choi et al., 2010). However, there is a lack of literature pertaining to VOC exposure and hearing loss in children, an outcome most often being associated with occupation.

Some VOCs are considered to be ototoxicants, such as styrene and xylene (Environmental Protection Agency, 2017b). Ototoxicants, (substances that damage the inner ear),

are categorized as neurotoxicants, cochleotoxicants, or vestibulotoxicants depending on where and how they damage the ear (Fabelova et al., 2019; Teixeira, da Silva Augusto, & Morata, 2002). Auditory systems continue to develop through the age of 18 making exposures to these substances a potential cause of decreased or damaged hearing development in children (Litovsky, 2015).

Hearing loss is related to increased disability adjusted life years (DALYs), years of productive life lost due to disability (Saunders et al., 2015). Due to the greater number of potential years of life, DALYS disproportionately impact children in comparison to adults (World Health Organization, 2019). The lack of literature pertaining to the VOC exposures of children, and the potential life years lost due to this disability creates a need for the understanding of how VOCs impact children and their hearing.

Literature Review

Volatile Organic Compounds

As mentioned earlier, VOCs are compounds that evaporate easily, specifically they are organic compounds with a boiling point lesser than or equal to 250° C at standard atmospheric pressure (WHO, 1989). With only these two characteristics needed to be considered a VOC, many chemicals fall into this category. This leads to a plethora of ways in which generalized VOC exposure can impact one's health, but inhalation is still the main pathway of exposure for VOCs, followed by ingestion of contaminated drinking water (Montero-Montoya, López-Vargas, & Arellano-Aguilar, 2018; Sexton et al., 2005). VOC exposure has been heavily studied in relation to respiratory health issues, and occupation (Alabdulhadi, Ramadan, Devey, Boggess, & Guest, 2019; Lamplugh et al., 2019). Some are known to cause cancer, liver damage, kidney damage, and central nervous system degradation (WHO, 1989).

Though few studies have been conducted on overall VOC exposure and the connection to hearing loss, some have studied pesticides, smoking, and secondhand smoke, all containing VOCs, and found an increased risk of hearing loss with each of these exposures (Choochouy et al., 2019; Dawes et al., 2014; Morata & Dunn, 1994). These include VOCs that are known ototoxicants such as carbon disulfide, ethylbenzene, and toluene (Arlie-Søborg, Zilstorff, Grandjean, & Milling Pedersen, 1981; Wilson, 1943; World Health Organization, 1979).

Children and Hearing Loss

Previous studies have focused on the effect that specific VOCs have in relation to the prevalence of hearing loss in an *adult* population, but this issue is not unique to adults. VOC exposure is likely to happen for a child due to the common occurrence of new parents updating or renovating their home in preparation for a newborn (Herberth et al., 2013). What differentiates children from their adult counterparts is that they are often limited to indoor activity for the first few months of life, and it has been found that indoor areas tend to have higher concentrations of VOCs than outdoor areas (Sexton et al., 2005). The implications of these studies also indicate that more child specific research needs to be conducted to identify particular differences in the loss of hearing in children compared to their adult counterparts (Herberth et al., 2013; Sexton et al., 2005).

While hearing loss may not be evident by the affected child initially, early detection of hearing loss in children is important due to the impacts that hearing has on the learning, behavior, speech, and language development of children (Paterson et al., 2019; Rosemann & Thiel, 2018). These issues stem from the difficulty in hearing words with multiple syllables, word endings such as -s and -ed, and hearing their own voice when speaking (Pittman, Stewart, Odgear, & Willman, 2017). With the difficulty in hearing, an understanding of language is

decreased which can then cause decreased vocabulary development, complexity of sentence structure, sociability, and academic achievement (Pittman et al., 2017).

The developmental impacts have not yet been studied in children with VOC exposures specifically, but these issues are a driving force in the effort to develop and integrate hearing conservation programs, and increasing hearing loss education in this population (Pittman et al., 2017). The regulations and standards for VOC exposure for adults in the workplace could potentially be modified to create recommendations and regulations for children in the home (Niskar et al., 2001). Developing these regulations can provide future children with safer environments and decrease impacts of hearing loss due to VOC exposure (Niskar et al., 2001; Pittman et al., 2017).

Previous Methodology

Many of the studies referenced above use a cross sectional study design. While this allows for many variables such as age, race, gender, and hearing loss to be compared, it lacks longitudinal data which would be helpful in determining developmental changes associated with VOC exposure over time (Choi et al., 2010; Lalwani, Liu, & Weitzman, 2011; Pittman et al., 2017). Another commonality in the methods of the mentioned studies, is the data source. NHANES is a common source for the data analyzed as it contains a large, nationally representative study sample, and includes questionnaire and biometric data. For many of the studies above, adults are examined in depth, and much more invasive biometric data is available for analysis, in comparison to the studies including children. While the findings of the adult focused research are relevant, it is difficult to apply them to children without further evaluation. For all of the studies above that include children, there are limitations to data collection due to

children being considered a protected population and the special requirements that accompany this classification.

Methods

Study Sample

The original data source used for this study was extracted from the 2005-2006 National Health and Nutrition Examination Survey (NHANES) results. For this study only certain variables captured in the survey were used, and some were transformed for the chosen analyses.

Overall, there were 10,348 participants in the survey. Only participants between the ages of 12 and 18 were included in this study; children below the age of 12 were not included in this study due to exclusion from the NHANES questionnaires. The poverty income ratio, as determined by NHANES, was a continuous variable, but to create a cohesive data set to analyze, this was transformed into a poverty binary variable. If, in the NHANES data, an individual was less than or equal to 1, the poverty binary was 1, indicating the subject was impoverished. If the poverty income ratio variable was greater than 1, the poverty binary was 0, indicating not impoverished.

Hearing Loss Categories

Hearing loss was determined through self-reported hearing status in the NHANES questionnaire. The participants were asked, "Which statement best describes your hearing status?" Originally, the options were grouped as, "Excellent", "Good", "A Little Trouble Hearing", "Moderate Trouble Hearing", "A lot of Trouble Hearing", and "Deaf." For this study the first two original NHANES categories and the last four categories were combined, respectively, to create the outcome groups "No Hearing Loss to Normal Hearing Loss" and "Moderate Hearing Loss to Deaf."

VOC Exposure Categories

VOC exposure data was ascertained by blood sample. The blood was tested for 33 VOCs by solid phase microextraction, gas chromatography, and bench top quadrupole mass spectrometry. The results were reported as “detectable result” and “below detectable result”, with most detection limits set at 50 ppt (pg/mL). Those with any detectable result were labeled as the “VOC Exposure” group, and the participants with a “below detectable result” were in the “No VOC Exposure” group for this study.

Statistical Analysis

All statistical analyses performed were conducted using R version 3.6.2 (R Core Team, 2019). First, chi square tests were used to compare the hearing groups by exposure and demographic variables to determine if VOC exposure was associated with hearing status. Next, VOC exposure was stratified by ear infection, to further investigate any confounding variables. A simple logistic regression was then utilized to determine if there is an association between hearing loss and VOC exposure in children when accounting for all variables of interest. All tables reflecting the above information were created in Microsoft Excel using data output from R.

Results

Table 1: Study Sample Characteristics

Out of 4,575 participants in this age range only 961 were surveyed for hearing loss and VOC exposure. These 961 participants were first compared by sex, age, race, poverty status, and job status. All variables for this table were used from NHANES unaltered, except for the variable “Poverty Status.”

Of the 961 individuals analyzed, 908 had normal to no hearing loss (95%) and 53 ranged from moderate hearing loss to deaf (5%). Out of the 53 with hearing loss, 44 were exposed to VOCs, and 9 were not. Of those with normal or no hearing loss, 786 were exposed to VOCs and 122 were not. Overall, males accounted for 48.3% of the study population and females 51.7%. Thirteen-year-olds reported the lowest percentage of VOC exposure among age groups (12.3%). Sixteen-year-olds reported the highest percentage of VOC exposure among age groups (15.3%). All other age groups percent of exposure fell within this range (12.3% - 15.3%). When observing race, Non-Hispanic Black individuals account for the majority at 326 participants. Following is Mexican American at 315, Non-Hispanic white with 247, and Other Hispanic and Other/Multi-racial at 25 and 48 participants respectively. Lastly, poverty status was observed to be 630 non-impooverished, and 277 impooverished participants, and the remaining 54 were missing data for this variable.

Following the initial demographic comparison, a Chi square analysis was performed for variables known to impact hearing health and the variables of interest in this study. This included VOC exposure, gender, poverty status, ear infection data, and hearing protection use. The only variable studied which appeared to have an association with hearing loss was having three or more ear infections. Almost 9% of study participants who had three or more ear infections had moderate hearing loss to deaf, while only 5% of participants with less than three ear infections had such hearing loss ($p=0.004$).

Table 2: VOC Exposure Stratified by Ear Infection and Hearing Loss

Out of the 961 study participants included, 289 reported ever having three or more ear infections and 661 reported having fewer than three. Both ear infection categories were found to have 22 study participants with VOC exposure and self-reported as having moderate to severe

hearing loss. For the less than three ear infections category, 548 had VOC exposure and no to normal hearing loss, 86 had no VOC exposure and no to normal hearing loss, and lastly 5 had no VOC exposure and moderate to severe hearing loss. Among the participants with three or more ear infections, 229 had VOC exposure and no to normal hearing loss, 35 had no VOC exposure and no to normal hearing loss, and 3 had no VOC exposure and moderate to severe hearing loss. A chi square test was then calculated for both ear infection groups. This analysis demonstrated that there was no effect modification occurring from the ear infection variable, as differences among each stratum were not present.

Table 3: Logistic Regression

Finding at least one significant difference among the variables, a logistic regression was then generated to see if there was a relationship between VOC exposure and hearing loss when adjusting for other factors in the model, as seen in **Table 3**.

If a child was exposed to VOCs, they were found to be slightly less likely to have hearing loss with an odds ratio of 0.95 ($p=0.91$), which was not statistically significant. Therefore, hearing loss was not found to be associated with VOC exposure. Females were slightly more likely ($OR = 1.03$) to have hearing loss than males. All races, in comparison to Mexican Americans, were more likely to have hearing loss. These ORs range from 1.04 (Non-Hispanic Black) to 2.86 (Other/Multiple Race) times more likely to have hearing loss.

Once again, statistically significant differences were only found between the “Ever Had \geq 3 Ear Infections” groups. With this analysis, it was found that individuals who reported 3 or more ear infections had a statistically significant odds ratio of 2.26 at the nominal alpha level of .05 ($p < .01$). This indicates an increased odds of hearing loss among individuals ever having three or more ear infections when accounting for all other variables of interest.

No additional significant differences were found with the logistic regression analysis.

Discussion

While some VOCs are known ototoxicants, general VOC exposure was not found to have any correlation with hearing loss in the studied population. Out of the seven variables of interest, “Ever Had ≥ 3 Ear Infections” was the only variable found to have a significant difference in hearing loss among the groups. Those that self-reported as ever having three or more ear infections were found to have a 2.26 increased likelihood of having hearing loss. This is consistent with previous studies (World Health Organization, 2018). Due to this finding a stratified comparison of the ear infections groups was calculated to determine if effect modification was present due to ear infection. No differences were found among these groups.

VOC exposure was not found to have any statistically significant correlation with hearing loss. While it is possible that general, low-level VOC exposure does not impact hearing loss in children, there are limitations within this study that may have impacted the outcomes. First, to understand true exposure, the blood would need to be measured over a period of time in this population. While a longitudinal study is preferred for following changes and development in hearing health, the NHANES data used in this study was cross-sectional collected at one time point (2005-2006). The specific sources of the exposures are not documented in the questionnaire, which could have provided further insight to overall VOC exposure and length of exposure. Also, hearing loss was determined by self-reported hearing status. With self-reporting, response bias becomes an issue due to a plethora of reasons including social desirability (Althubaiti, 2016)

While there are limitations of this study, there are strengths that support the findings as well. Age is one of the biggest predictors of hearing loss in adult studies, as our auditory function

decreases over time naturally due to the aging process as well as loud noise exposure, or long-term exposure to ototoxicants (Hoffman, Dobie, Losonczy, Themann, & Flamme, 2017). As referenced above in previous studies, NHANES is a common data source for research pertaining to this topic. This can be attributed to the reliable, and accurate data they provide for analysis in combination with the yearly release of their datasets. Loud noise exposure is one of the biggest impacts on hearing health, so to account for any impacts that may have on our findings, we accounted for hearing protection use in the final model.

Overall, considering the findings of this study and the lack of published research related to hearing loss and VOC exposure in children it is recommended that further research be conducted to characterize this relationship in more detail.

Conclusion

Overall, this study found no significant relationship between hearing loss and VOC exposure in the studied population. It was found that children who have had three or more ear infections are more prone to hearing loss, confirming previous published findings. What this study may show is the need for longitudinal research which includes actual noise and VOC exposure monitoring and hearing acuity testing.

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Appendix

Table 1

Characteristics of Children Ages 12 to 18 in the National Health and Nutrition Examination Survey (NHANES) who Reported Hearing Loss and Volatile Organic Chemical (VOC) Exposure

	Total N (%)	No to Normal Hearing Loss N (%)	Moderate Hearing Loss to Deaf N (%)	p-value
VOC Exposure				0.60
No	131 (13.6)	122 (93.1)	9 (6.9)	
Yes	830 (86.4)	786 (94.7)	44 (5.3)	
Gender				0.76
Male	464 (48.3)	440 (94.8)	24 (5.2)	
Female	497 (51.7)	468 (94.2)	29 (5.8)	
Age (Years)				0.32
12-15	526 (54.7)	501 (95.2)	25 (4.8)	
16-18	435 (45.3)	407 (93.6)	28 (6.4)	
Race				0.43
Mexican American	315 (32.8)	300 (95.2)	15 (4.8)	
Other Hispanic	25 (2.6)	23 (92.0)	2 (8.0)	
Non-Hispanic White	247 (25.7)	231 (93.5)	16 (6.5)	
Non-Hispanic Black	326 (33.9)	311 (95.4)	15 (4.6)	
Other/Multi Racial	48 (5.0)	43 (89.5)	5 (10.5)	
Poverty Income Ratio				.94
<1	630 (65.6)	596 (94.6)	34 (5.4)	
>1	277 (28.8)	261 (94.2)	16 (5.8)	
Missing	54 (5.6)	51 (94.4)	3 (5.6)	
Ever Had ≥ 3 Ear Infections				< 0.01
Yes	289 (30.1)	264 (91.3)	25 (8.7)	
No	661 (68.8)	634 (95.9)	27 (5.1)	
Hearing Protection Use				0.83
Most of the Time	36 (3.7)	32 (88.9)	4 (11.1)	
Sometimes	128 (13.3)	124 (96.9)	4 (3.1)	
Rarely/Seldom	56 (5.8)	53 (94.6)	3 (5.4)	
Never	739 (76.9)	697 (94.3)	42 (5.7)	
All Participants	961 (100)	908 (94.5)	53 (5.5)	

Table 2

VOC Exposure Stratified by Ear Infection and Hearing Loss Categories of Children Ages 12 to 18 in NHANES

VOC Exposure	< 3 Ear Infections			≥ 3 Ear Infections		
	No to Normal Hearing Loss N (%)	Moderate Hearing Loss to Deaf N (%)	p-value	No to Normal Hearing Loss N (%)	Moderate Hearing Loss to Deaf N (%)	p-value
No	86 (13.0)	5 (0.8)	0.66	35 (12.1)	3 (1.0)	> 0.99
Yes	548 (82.9)	22 (3.3)		229 (79.2)	22 (7.6)	
Total	634 (95.9)	27 (4.1)		264 (91.3)	25 (8.7)	

Table 3

Logistic Regression Analysis of Hearing Loss by Select Patient Characteristics

Value of Interest	Odds Ratio	p-value
VOC Exposure		
Not Exposed	<i>Ref.</i>	-
Exposed	0.95	0.91
Gender		
Male	<i>Ref.</i>	-
Female	1.05	0.87
Race/Ethnicity		
Mexican American	<i>Ref.</i>	-
Other Hispanic	1.45	0.64
Non-Hispanic White	1.13	0.78
Non-Hispanic Black	1.05	0.90
Other/Multiple Race	2.90	0.06
Age (12-18)	1.38	0.28
Poverty Status		
Not Impoverished	<i>Ref.</i>	-
Impoverished	1.12	0.73
Ever Had ≥ 3 Ear Infections		
No	<i>Ref.</i>	-
Yes	2.28	0.01
Hearing Protection Use		
Most of the Time	<i>Ref.</i>	-
Sometimes	0.33	0.13
Rarely/Seldom	0.49	0.38
Never	0.58	0.36