Environmental Pollution 226 (2017) 118–124

Contents lists available at ScienceDirect

Environmental Pollution

journal homepage: www.elsevier.com/locate/envpol

Exposure to environmental noise and risk for male infertility: A population-based cohort study☆

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ARTICLE INFO

Article history:
Received 6 November 2016
Received in revised form
28 March 2017
Accepted 28 March 2017
Available online 12 April 2017

Keywords:
Noise
Residential exposure
Male infertility
Daytime and nocturnal
Endocrine
General population

ABSTRACT

Background: Noise is associated with poor reproductive health. A number of animal studies have suggested the possible effects of exposure to high noise levels on fertility; to date, a little such research has been performed on humans.
Objectives: We examined an association between daytime and nocturnal noise exposures over four years (2002–2005) and subsequent male infertility.
Methods: We used the National Health Insurance Service-National Sample Cohort (2002–2013), a population-wide health insurance claims dataset. A total of 206,492 males of reproductive age (20–59 years) with no history of congenital malformations were followed up for an 8-year period (2006–2013). Male infertility was defined as per ICD-10 code N46. Data on noise exposure was obtained from the National Noise Information System. Exposure levels of daytime and night time noise were extrapolated using geographic information systems and collated with the subjects' administrative district code, and individual exposure levels assigned.
Results: During the study period, 3293 (1.6%) had a diagnosis of infertility. Although there was no association of infertility with 1-dB increments in noise exposure, a non-linear dose-response relationship was observed between infertility and quartiles of daytime and night time noise after adjustment for confounding variables (i.e., age, income, residential area, exercise, smoking, alcohol drinking, blood sugar, body mass index, medical histories, and particulate pollution). Based on WHO criteria, adjusted odds for infertility were significantly increased (OR = 1.14; 95% CI, 1.05–1.23) in males exposed to night time noise ≥ 55 dB.
Conclusion: We found a significant association between exposure to environmental noise for four years and the subsequent incidence of male infertility, suggesting long-term exposure to noise has a role in pathogenesis of male infertility.

1. Introduction

Noise, “unwanted sound”, is major environmental pollutant and stressor for humans. Noise is widespread and imposes auditory and non-auditory consequences on health and quality of life (Basner et al., 2014; Ising and Kruppa, 2004). The health impact of noise includes annoyance, hearing impairment, interference with speech intelligibility, sleep disturbance, cardiovascular diseases, mental illness, interference with complex task performance, and modification of social behaviors (Basner et al., 2014; Ising and Kruppa, 2004). Noise stress is also reportedly associated with reproductive health and outcomes (Meyer et al., 1989; Ristovska et al., 2014). Some observational studies have suggested that subjects exposed to occupational or environmental noise are at increased risk for low birth weight infants, preterm birth, spontaneous abortion, and congenital malformations (Dzhambov et al., 2014; Gehring et al., 2014; Knipschild et al., 1981; Matsui et al., 2003; Nurminen, 1995; Wu et al., 1996). Animal data have demonstrated an effect of noise in inducing abnormalities in sex hormone regulation (i.e., testosterone and luteinizing hormone [LH]), reproductive organ morphology (i.e., testis and ovary), and decreases in breeding performance and pregnancy rates (Diab et al., 2012; Halfwerk et al., 2011; Ruffoli et al., 2006; Sato et al., 1982; Swami et al., 2007).

☆ This paper has been recommended for acceptance by David Carpenter.

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http://dx.doi.org/10.1016/j.envpol.2017.03.069
0269-7491/

Infertility is the inability of the body to reproduce by natural means. Globally, one in six couples are affected by infertility at least once in their lifetime, with 20–30% due to male infertility, 20–35% to female infertility, and 25–40% attributable to both parties (European Society of Human Reproduction and Embryology, 2014). Genetics or lifestyle factors (i.e., older age, smoking, heavy drinking, unhealthy diet, sedentary habits, and over- or underweight) are implicated as risks for male and female infertility (Bunting and Boivin, 2008; Ferlin et al., 2006; Hart, 2016; Sharma et al., 2013; Sharpe and Franks, 2002). A lot of attention has been paid to the potential association between the endocrine-disrupting effects of environmental pollutants and male infertility (Goncharov et al., 2009; Knez, 2013; Mocarelli et al., 2008; Vested et al., 2014). Such substance can mimic or interfere with the biologic activity of natural hormones and can thus alter their ability to regulate reproduction (Goncharov et al., 2009; Knez, 2013; Mocarelli et al., 2008; Vested et al., 2014). In humans, noise stress has been shown to modify endocrine or neural systems responsible for maintaining the homeostasis of reproductive hormones (i.e., testosterone and LH) (Farzadinia et al., 2016; Jalali et al., 2013, 2012a, 2012b; Swami et al., 2007), suggesting its relation to male infertility. However, a little such research has been performed on humans so far (Eisenberg et al., 2015).

The aim of this study was to investigate whether residential exposure to noise is associated with risk of male infertility. Using a representative sample data from a cohort of South Koreans, we looked for an association between daytime and nocturnal noise exposures over four years (2002–2005) and subsequent male infertility.

2. Materials and methods

2.1. Data source and study population

The National Health Insurance Service (NHIS) is a compulsory social insurance program in Korea (Lee et al., 2016). The NHIS maintains a National Sample Cohort (NHIS-NSC) containing data from a population-based cohort extracted from the NHIS records, including medical claims data - personal information, medical examinations and treatment, prescription drugs, medical costs, and diagnostic codes as per the International Classification of Diseases (ICD). Beginning in 2002, a cohort of 1,025,340 participants (approximately 2.2% of the total eligible population) was selected by a stratified random sampling design and were followed up until 2013 (Lee et al., 2016).

For the current study, inclusion criteria were as follows: (1) males of reproductive age (20–59 years); (2) males who were available for personal information and medical examinations; and (3) males who had no history of congenital malformations of the male genital organs (ICD-10, Q55), malignant neoplasm of testis (ICD-10, C62), or injury to urinary or pelvic organs (ICD-10, S37).

Exclusion criteria were males (1) who were aged $\leq$ 19 years or $\geq$ 60 years; (2) who had missing personal information (i.e., address, exercise, smoking, and alcohol); (3) who had a history of previous infertility (ICD-10, N46); or (4) who had no health examination results for weight, height, and blood glucose.

From the NHIS-NSC (NHIS-2016-2-0081), the study population meeting all inclusion criteria with no exclusions consisted of 206,492 men. The study protocol was approved by the Institutional Review Board of the Seoul National University Hospital (IRB number: E-1604-003-750). Informed consent was exempted by the committee.

2.2. Outcome variables

Diagnosis of infertility included a medical history, genital examination, and semen analysis as standard assessment in all men (Park, 2007). Semen analysis measured the number of sperm in a man's ejaculate, abnormalities in shape (morphology) and movement (motility) of the sperm and semen parameters (i.e., volume, color, and PH). According to WHO criteria, if semen analysis results are within normal limits, one test is sufficient, otherwise at least two tests and further andrologic investigation are required (World Health Organization, 1999). Male infertility was defined as ICD-10 code N46.

2.3. Residential exposure to noise during the daytime and night time

Environmental noise is the summary of noise pollution in our communities caused by transport, industrial, and recreational activities, excluding that which originates in the workplace (Goines and Hagler, 2007). This study used data on environmental noise exposure from the National Noise Information System (NNIS). The NNIS was established to identify the noise level of each region in the country to provide secure reliable noise measurement data and implement the noise reduction policy. Measurement of environmental noise level falls under the Act on Environmental Testing and Inspection and observes the Official Test Standard for Noise and Vibration, which specifies the necessary matters to maintain accuracy and uniformity of noise measurement (Environmental Testing and Inspection Act, 2015). The measurement area of environmental noise was selected from cities having the greatest influence on the maintenance of citizens' normal living conditions, by considering population and city size. Outdoor measurement was, in principle, classified into “general area” and “roadside area”. “General area” was defined as a location representative of the noise of the concerned area, while “roadside area” was defined as a location where it is a possibility that noise will cause problems. When choosing a measurement point, sites such as factories, workplaces, aerodromes, and railways that are expected to have a significant impact on the local noise evaluation should be avoided. The measurement period of environmental noise was weekdays (Monday to Friday) with small noise fluctuations depending on the day of the week in months 2–3, 5–6, 8–9, and 11–12. Noise values were determined by the arithmetic average value of the measured noise levels: daytime noise was measured at least four times at intervals of $\geq$2 h at each measurement point, and nighttime noise was measured at least two times at intervals of 2 h at the same measurement sites measured during the daytime. The noise measurement equipment was to be of Class 2 noise level or equivalent performance, as defined in Korea standard C 61672-1 International Electrotechnical Commission, allowing units of decibels (dB). The measurable range was 35–130 dB. Sound level meters were set to the A-weighting scale to account for the relative loudness perceived by the human ear.

The NNIS provided national environmental noise level data measured either automatically or manually. Automatic noise measurement was conducted in relatively few areas (i.e., 64 sites in 2002); thus, most noise data obtained were based on manual testing at 1286–1372 monitoring sites during the study period. We downloaded environmental noise data from 2002 to 2005 and calculated noise levels during the day (07:00–19:00) and night (23:00–07:00).

Noise levels at unmeasured regions were estimated using geographic information systems (GIS) tools. The Kriging geostatistical method was used for spatial interpolation of data; this methodology has been used in a range of epidemiological studies to assess environmental exposure (Liao et al., 2006; Nuckols et al., 2004; Tsai et al., 2009). GIS zonal statistics were used to calculate the annual daytime and night time noise for each region (Fig. 1). We matched extracted regional levels of noise with individual

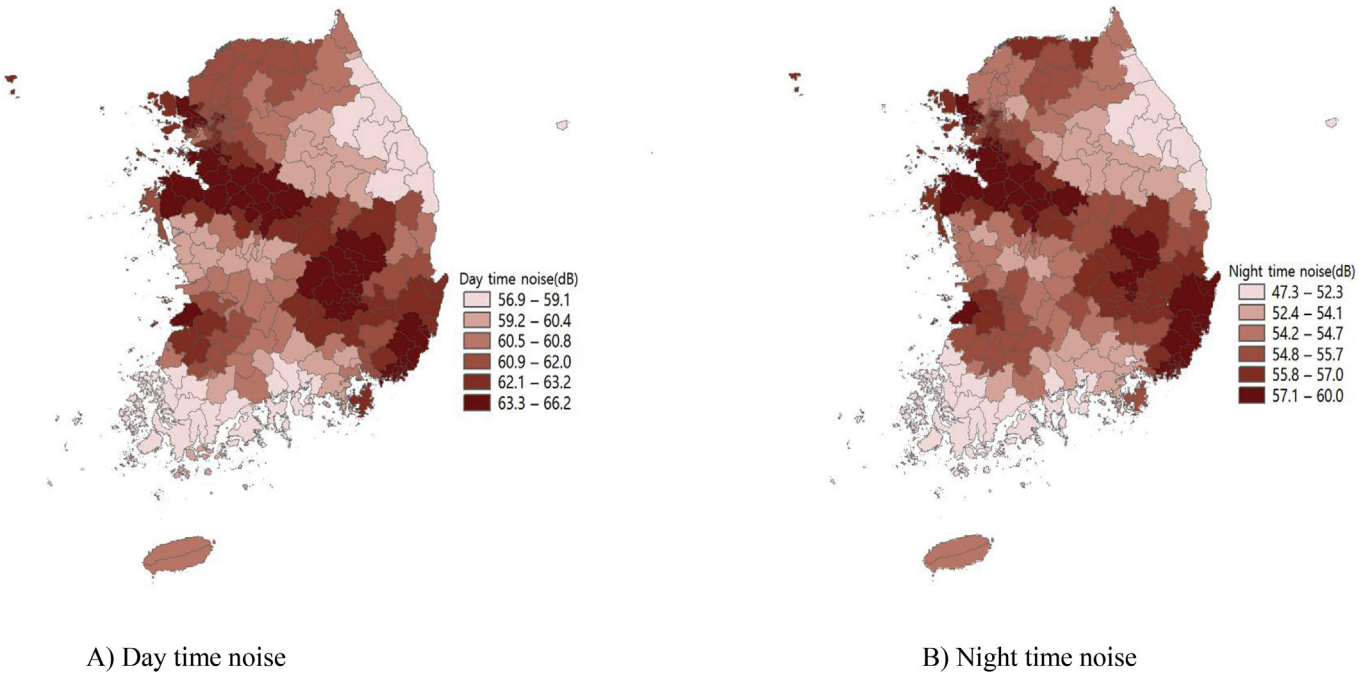

Fig. 1. Mean distribution of daytime and nocturnal noise levels in 2002–2005.

administrative district codes to assign individual noise exposure levels based on the addresses of subjects.

Noise levels were treated as continuous (per 1 dB increase) and quartile variables (Q1 –Q4). In addition to this, nocturnal noise was categorized in two levels, ≤55 dB vs. >55 dB based on WHO recommendations for Europe (World Health Organization, 2009). The threshold of daytime noise applied was that for which no observed adverse health effect (NOAEL) has been demonstrated for the association between noise and myocardial infarction, i.e., ≤60 dB vs. >60 dB (Babisch, 2002; World Health Organization, 2009).

2.4. Other variables

Baseline characteristics obtained from the NSC database were from health examinations and questionnaires and included age stratified in five-year increments (20–24 years, 25–29 years, 30–34 years, 35–39 years, 40–44 years, 45–49 years, 50–54 years, or 55–59 years), income by quartile, residence area (urban or rural), smoking history (current, former, or never smoked), exercise (yes or no), alcohol consumption (yes or no), and body mass index (BMI, recorded as underweight [<18.5 kg/m^2], normal weight [18.5–24.9 kg/m^2], overweight [25.0–29.9 kg/m^2], or obesity [≥30.0 kg/m^2]). Blood glucose levels were reported in two levels, ≤125 mg/dL or >125 mg/dL. A history of diseases that could affect fertility included mumps (ICD-10: B26), hydrocele and spermatocele (ICD-10: N43), scrotal varices (ICD-10: I861), undescended testicle (ICD-10: Q53), gonorrhea or syphilis (ICD-10: A51-54), and thyroid disease (ICD-10: E01_E06). Particulate matter 10 μm or less in diameter (PM10) was included as air pollution exposure.

2.5. Statistical analysis

Statistical differences in variables of interest in males with and without infertility were examined using the chi-square test. We performed unadjusted and multivariate-adjusted logistic regression analyses to estimate the odds of male infertility. Odds ratio (OR) and 95% confidence interval (CI) for infertility were generated for each 1-dB increase in noise level. We also divided the noise levels into quartiles and calculated the OR for male infertility considering the lowest quartile (Q1) as the reference group throughout the analysis. Furthermore, a threshold of daytime and night time noise was applied based on WHO criteria (night time: ≤55 dB vs. >55 dB) and NOAEL (daytime: ≤60 dB vs. >60 dB). We constructed a logistic regression model to find the OR for infertility according to each criterion. OR and the corresponding 95% CI were calculated using the likelihood of infertility with exposure to higher than recommendation levels of daytime and night time noise. In the adjusted regression model, age, income, residence area, smoking history, exercise, alcohol use, blood glucose levels, BMI, history of diseases, PM10 were included as potential confounding variables. All analyses were performed using the SAS 9.2 software (SAS Institute, Cary, NC, USA), and the statistical significance level was set at $p = 0.05$.

3. Results

Of the 206,492 males, 3293 (1.6%) had a diagnosis of infertility (Table 1). Infertile men were more likely to be in aged 25–29 years, have low income, live in an urban area, drink alcohol, have a high BMI, and have blood glucose levels below 125 mg/dL. Infertile men had a significantly more frequent history of diseases such as hydrocele and spermatocele ($p = 0.012$), scrotal varices ($p < 0.0001$), undescended testicle ($p < 0.0001$), and gonorrhea or syphilis ($p < 0.0001$), compared to male without infertility. No differences in exercise, cigarette smoking, and exposures to PM10 were detected between the two groups.

Table 2 shows the ORs (95% CIs) for male infertility against noise exposure levels with continuous (increment per 1-dB increase) and quartile scales (Q1-Q4). In the unadjusted model, 1-dB increases were associated with significantly increased odds for infertility during both daytime (OR = 1.03, 95% CI: 1.01–1.05, p-trend = 0.0206) and nighttime (OR = 1.02, 95% CI: 1.01–1.04, p-trend = 0.0327). Following multiple adjustments (i.e., age, income, residential area, exercise, smoking, alcohol drinking, blood sugar,

Table 1
Characteristics of study population by the presence of infertility (n = 206,126).

	Without infertility (n = 202,833)		With infertility (n = 3293)		p-value
Age (years)-n (%)					
20-24	21,588	(98.4)	355	(1.6)	<0.0001
25-29	24,759	(95.9)	1073	(4.2)	
30-34	28,488	(96.0)	1203	(4.1)	
35-39	30,659	(98.6)	446	(1.4)	
40-44	30,199	(99.5)	143	(0.5)	
45-49	29,039	(99.9)	43	(0.2)	
50-54	21,144	(99.9)	21	(0.1)	
55-59	16,957	(99.9)	9	(0.1)	
Income-n (%)					
Quartile 1	56,760	(98.4)	920	(1.6)	<0.0001
Quartile 2	42,749	(98.0)	854	(2.0)	
Quartile 3	49,359	(98.3)	851	(1.7)	
Quartile 4	53,965	(98.8)	668	(1.2)	
Residential area-n (%)					
Urban	97,099	(98.3)	1700	(1.7)	<0.0001
Rural	105,734	(98.5)	1593	(1.5)	
Exercise-n (%)					
Yes	106,266	(98.4)	1760	(1.6)	0.2288
No	96,567	(98.4)	1533	(1.6)	
Cigarette smoking-n (%)					
Current smoker	75,995	(98.4)	1268	(1.6)	0.3823
Past smoker	23,015	(98.4)	379	(1.6)	
Never smoked	103,823	(98.4)	1646	(1.6)	
Alcohol drinking-n (%)					
Yes	137,970	(98.3)	2353	(1.7)	<0.0001
No	65,163	(98.6)	940	(1.4)	
Blood glucose levels (mg/dL) -n (%)					
≤125	189,540	(98.3)	3213	(1.7)	<0.0001
>125	13,293	(99.4)	80	(0.6)	
Body mass index (kg/m^2) -n (%)					
Underweight (<18.5)	4557	(98.9)	51	(1.1)	0.0310
Normal (18.5–24.9)	122,603	(98.4)	2004	(1.6)	
Overweight (25.0–29.9)	67,665	(98.4)	1093	(1.6)	
Obesity (≥30.0)	8008	(98.2)	145	(1.8)	
History of disease -n (%)					
Mumps	244	(97.6)	6	(2.4)	0.3110
Hydrocele and spermatocel	526	(97.1)	16	(3.0)	0.012
Scrotal varices	347	(76.5)	107	(23.5)	<0.0001
Undescended testicle	37	(86.1)	6	(14.0)	<0.0001
Gonococcal or syphilis history	4154	(97.2)	121	(2.8)	<0.0001
Thyroid disease	19,730	(98.5)	295	(1.5)	0.1317
PM10 (μg/m^3)-mean (+SE)	51.37	(4.12)	51.10	(4.05)	0.4137

P-value was calculated by the chi-square test.
PM10: particulate matter 10 μm or less in diameter.
SE: standard error.

BMI, medical history, and PM10), results showed that 1-dB increases in daytime (p = 0.9414) and nighttime (p = 0.6089) noise levels no longer had a significant effect; furthermore, characteristics of study populations including personal and lifestyle variables and medical history, adjusted for the regression model, were possibly modified the effect by attenuating the effect of noise on infertility. On the contrary, significant, non-linear dose-response relationships (p < 0.05) were observed between infertility and the quartiles of daytime and nighttime noise levels, regardless of whether or not participants' characteristics were adjusted statistically. In the unadjusted model, compared with males exposed to the lowest noise levels (Q1), those exposed to mid to high (Q2 - Q4) noise levels had significantly higher odds for infertility. After adjusting for confounding variables (i.e., age, income, residential area, exercise, smoking, alcohol drinking, blood sugar, BMI, medical histories, and PM10), the OR (95% CI) for infertility was reduced but remained significant in terms of the quartiles of noise levels. Specifically, for daytime noise, the ORs (95% CI) for infertility were 1.30 (95% CI: 1.16–1.46) in Q2, 1.23 (95% CI: 1.10–1.38) in Q3, and 1.15 (95% CI: 1.02–1.29) in Q4. For nighttime noise, the ORs (95% CI) were 1.26 (95% CI: 1.13–1.40) in Q2, 1.18 (95% CI: 1.06–1.32) in Q3, and 1.12 (95% CI: 1.01–1.25) in Q4.

Fig. 2 shows percentages of male infertility against the WHO and NOAEL noise criteria. The incidence of male infertility was significantly increased in those exposed to higher vs. lower recommended noise levels in above the recommended noise levels: daytime, 1.8% vs. 1.4% (p < 0.0001) and night time, 1.5% vs. 1.2% (p = 0.0002).

Table 3 shows the ORs (95% CIs) for male infertility according to recommended noise criteria. In the unadjusted model, the likelihood for infertility was significantly increased in both high daytime (>60 dB) (p = 0.0002) and nighttime (>55 dB) (p < 0.0001) noise levels. After adjustment for confounding variables (i.e., age, income, residential area, exercise, smoking, alcohol drinking, blood sugar, BMI, medical histories, and PM10), high daytime noise did not affect male infertility. In other words, the high daytime noise effect on infertility could be modified by confounding variables, such as personal and lifestyle characteristics and medical history. Conversely, results showed that the likelihood of male infertility was not significantly increased by high daytime noise levels (>60 dB). However, a significantly increased likelihood for infertility was observed in males exposed to nighttime noise levels of >55 dB (OR = 1.14; 95% CI: 1.05–1.23) (p = 0.0002) compared to those exposed to ≤55 dB, after adjustment for confounding variables, which are less likely to affect the daytime noise-infertility link.

Table 2
Odds (95% CI) for male infertility against noise exposure levels.

Noise	no. of event/total	Unadjusted model			Adjusted model[a]		
		OR	(95% CI)	p-trend	OR	(95% CI)	p-trend
Day time							
Increment per 1 dB increase		1.03	(1.01–1.05)	0.0206	1.00	(0.98–1.03)	0.9414
Quartiles (dB)							
Q1 (<61.1)	602/48,443	Reference			Reference		
Q2 (61.1–62.1)	958/50,376	1.53	(1.38–1.70)	<0.0001	1.30	(1.16–1.46)	0.0001
Q3 (62.1–63.3)	928/51,983	1.44	(1.30–1.59)		1.23	(1.10–1.38)	
Q4 (≥63.3)	805/52,031	1.24	(1.12–1.38)		1.15	(1.02–1.29)	
Night time							
Increment per 1 dB increase		1.02	(1.01–1.04)	0.0327	1.01	(0.99–1.03)	0.6089
Quartiles (dB)							
Q1 (<54.6)	636/49,687	Reference			Reference		
Q2 (54.6–55.9)	942/49,199	1.50	(1.35–1.66)	<0.0001	1.26	(1.13–1.40)	<0.0001
Q3 (55.9–57.3)	911/51,235	1.39	(1.25–1.54)		1.18	(1.06–1.32)	
Q4 (≥57.3)	804/52,712	1.19	(1.07–1.32)		1.12	(1.01–1.25)	

[a] Adjusted by age, income, residential area, exercise, smoking, alcohol drinking, blood sugar, BMI, medical histories, and PM10.

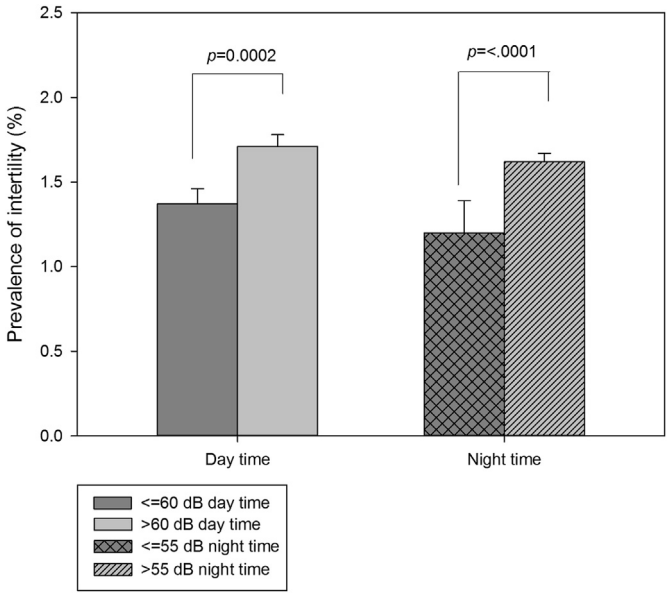

Fig. 2. Percentages of male infertility against recommended noise criteria.

4. Discussion

We found that residential exposure to noise for four years was significantly associated with a reported diagnosis of male infertility. Although there was no association of infertility with 1-dB increments in noise exposure, a non-linear dose-response relationship was observed between infertility and quartiles of daytime and night time noise. Specifically, compared with the lowest (Q1) exposures to both daytime and night time noise, males exposed to higher noise levels (Q2 – Q4) were significantly more likely to have a diagnosis of infertility. Based on WHO criteria, adjusted odds for infertility were significantly increased (OR = 1.14; 95% CI, 1.05–1.23) in males exposed to night time noise $\geq$ 55 dB. This study extends the previous findings on the potential effect of noise exposure in damaging male reproductive health (Farzadinia et al., 2016; Jalali et al., 2013, 2012a, 2012b; Swami et al., 2007). It provides evidence on the association between noise exposure and infertility in humans, suggesting that noise stress has a role in pathogenesis of male infertility.

To date, many animal studies have suggested an effect of noise exposure on male fertility (Farzadinia et al., 2016; Jalali et al., 2013, 2012a, 2012b; Swami et al., 2007). Swami et al. (2007) compared reproductive parameters among male rats according to duration of exposure to traffic noise (100 dB) in three groups (acute group, chronic group, and control). They found that serum testosterone levels decreased in both acutely and chronically exposed animals compared with controls. Additionally, structural changes in testicular tissue and maturation arrest in proliferating testis germinal cells, suggestive of infertility, were observed (Swami et al., 2007). Diab et al. (2012) reported greater reductions in serum sexual hormones (i.e., testosterone, LH, and follicle-stimulating hormone [FSH]) with moderately abnormal histological changes in male albino rats treated with 100 dB noise for six hours daily for 30 days (Diab et al., 2012). Jalali et al. (2012a,b) also found that noise exposure significantly decreased weights of testes, epididymis, seminal vesicles, ventral prostates, and sperm counts and mobility (Jalali et al., 2012a). A recent study by Farzadinia et al. (2016) demonstrated that noise stress altered hormone levels –adrenocorticotropic hormone (ACTH) and cortisol levels were increased and testosterone decreased – and induced atrophy in germinal epithelial cells and the abnormal dilation of seminiferous tubules (Farzadinia et al., 2016). Furthermore, noise exposure in rats negatively affected *in vivo* fertilization capacity, such that in normal female rats mated with noised-stressed male rats, the rate of pre-implantation loss (corpora lutea minus implantation sites) and post-implantation loss (implantation sites minus live fetuses) was significantly higher than in females mated with males not exposed to noise (Jalali et al., 2012a). Taken together, these studies provide evidence on noise-induced changes in testis morphology and hormonal levels that could affect male infertility. However, given the danger of extrapolating data from animal studies, further research on the effect of noise on human fertility is needed.

A recent study indicated the association between noise and fertility in an occupational setting (Chamkori et al., 2016). Compared with those working in quite environments, men with prolonged exposure to a noisy environment (119 dB) had significantly lower testosterone, LH, FSH, prolactin levels, and poor semen quality in terms of volume, number, and type of motility of sperm (Chamkori et al., 2016). Admittedly, it is hard to compare this study directly with ours because of differences in methodologies, for example, study population (workers vs. general population) and duration or levels of noise exposure. However, the findings are broadly consistent with ours, demonstrating a possible relationship between noise-exposure and male infertility.

By comparison with the previous literature on the health effects of noise in the general population (Eriksson et al., 2014; Franssen et al., 2004; Jarup et al., 2008), the noise levels in our study were considerably higher, even though exposure was to residential noise. In the daytime, mean (min-max) noise exposure was 62.19 dB (57.00–67.47 dB), in which more than 90% of subjects were exposed to higher than the recommended NOAEL level (>60 dB). Mean (min-max) noise at night was 55.90 dB (49.18–60.18 dB), and approximately 68% of subjects experienced levels above the WHO criteria limit of 55 dB. Indeed, both this study and that of Chamkori et al. (2016) indicate that long-term exposure to high noise levels appears to increase the risk of infertility in men, even though much remains to be learned about the extent and severity of noise effects on human reproduction (Chamkori et al., 2016).

How then might noise affect male reproductive health? Plausible biological explanations for male infertility focus on the disruption of neuroendocrine homeostasis (Nargund, 2015).

Table 3
Odds (95% CI) for male infertility according to recommended noise criteria.

Noise	no. of event/total	Unadjusted model			Adjusted model[a]		
		OR	(95% CI)	p-trend	OR	(95% CI)	p-trend
Day time							
≤60 dB	152/12,539	Reference			Reference		
>60 dB	3141/190,294	1.36	(1.16–1.60)	0.0002	1.05	(0.88–1.25)	0.6224
Night time							
≤55 dB	892/64,439	Reference			Reference		
>55 dB	2401/138,394	1.25	(1.16–1.35)	<0.0001	1.14	(1.05–1.23)	0.0020

[a] Adjusted by age, income, residential area, exercise, smoking, alcohol drinking, blood sugar, BMI, medical histories, and PM10.

Exposure to noise can create stress responses (Westman and Walters, 1981) and activate the hypothalamic-pituitary-adrenal (HPA) and the hypothalamic–pituitary–gonadal (HPG) axes (Nargund, 2015). Activation of the HPA axis stimulates the release corticotropin-releasing hormone and arginine vasopressin, leading to increased secretion of ACTH and glucocorticoids, which in turn inhibit testosterone levels necessary for spermatogenesis (Kalantaridou et al., 2010; Whirledge and Cidlowski, 2013). The HPG axis comprises the interaction between the hypothalamus, pituitary gland, and the gonads. Gonadotropin-releasing hormone is released from the hypothalamus and acts on the pituitary gland to stimulate the synthesis and release of gonadotrophins (LH and FSH), leading to secretion of testosterone (Asimakopoulos, 2012; Kirby et al., 2009). Too much testosterone, however, inhibits secretion of LH via a negative feedback effect on the hypothalamus and pituitary gland, resulting in low testosterone levels (Asimakopoulos, 2012; Nargund, 2015). Thus, stress due to noise exposure may modify the HPA and HPG signaling cascades responsible for testosterone and sperm production, potentially contributing to suppression of male reproductive potential.

To our knowledge, this is the first study to demonstrate that long-term exposure to high residential noise levels may contribute to male infertility in humans. The most critical limitation is the estimation of environmental noise exposure. Because not all areas were monitored for environmental noise levels, we used the Kriging spatial interpolation method to estimate noise levels at unmeasured locations based on GIS data from monitored areas. However, the monitored areas were randomly selected. Instead, the NNIS data were selected certain cities representative of the living conditions and the environmental noise level within a particular jurisdiction, specifically including 1) residential and commercial areas with a large resident population and many people passing through the area, (2) residential green areas close to the city centers, and (3) an industrial area that also had a lot of mixed residential functions. Thus, we may have overestimated the overall exposure to noise and therefore the risk. For example, the observed effect of exposure to road traffic noise on male infertility (approximately 10–30% risk increase per 10 dB) was relatively higher than the reported cardiovascular effect (approximately 5% risk increase per 5 dB) (Van Kempen and Babisch, 2012). Of course, our noise levels were measured over long periods, and the noise levels in our study tended to be higher than other studies on the health effects of noise in the general population (Eriksson et al., 2014; Franssen et al., 2004; Jarup et al., 2008). This may have influenced our finding of a high effect on risk for the observed outcome. However, bias from the overestimation of noise exposure may still exist. Furthermore, while we examined many covariates including socioeconomic characteristics, health behavior, and medical history, insufficient individual information was available on all risk factors that might affect infertility or noise exposure, including genetic factors and occupational exposures to noise or chemicals. We also cannot rule out the possibility of diagnostic misclassifications in the NHIS-NHS database.

In conclusion, our study provides evidence for an association between residential exposure to noise for four years and the subsequent incidence of male infertility. This finding supports previous reports on a potential link between noise exposure and male reproductive health and suggests that long-term residential exposure to noise may be a risk for male infertility.

5. Competing financial interests

Authors have no competing interests to declare.

Acknowledgments

This work was supported by Basic Science Research Program through the National Research Foundation of Korea funded by the Ministry of Education, Science and Technology (grant number, 2015R1A1A3A04000923, 2015R1D1A1A01059048).

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