

The Effects of Traffic Noise on Serum Levels of LDH in Male Rats

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Abstract—Noise pollution as stress may impose various effects on variety of body systems leading to changes in serum levels of biochemical enzymes. The main aim of this study was to determine the effects of noise pollution on serum levels of LDH in male rats. In our study male Wistar rats were randomly divided into control and groups exposed to traffic noise for 1, 3 or 6h/day of 5 rats in each group. After 8 weeks, blood samples were obtained using cardiac puncture method. Following serum preparation, level of LDH was measured using spectrophotometry method. Data were statistically analyzed and compared between groups using ANOVA. The results indicated that serum level of LDH was increased in rats exposed to noise pollution for 3 or 6h/day compared to control rats ($P<0.01$ and $P<0.05$, respectively). Our findings show that exposure to traffic noise pollution for long period of time enhances LDH which may indicate damage to liver, heart, lung, thyroid, blood system or other disorders.

Keywords—Traffic Noise, LDH, Male Rat.

I. INTRODUCTION

HUMAN beings can communicate to their environment better through their sense of hearing. For instance, human beings can detect danger by hearing warning sounds and can become calm by listening to rhythmic sounds. Vehicle noise comes from the engine and transmits to surroundings, exhaust noise, gear change, and use of heavy gear in patch surfaces roads, vehicle weak maintenance, which are the important agents in the road traffic noise production.[1] Also in high speeds the noise increases, because of friction between vehicle and air and road surface. Aerodynamic shape of cars decreases this effect and then noise pollution. Also drivers cause a high traffic noise by using of vehicle horn, playing loud music, unnecessary gear change and braking[2]. Nearly anyone who has been near a busy roadway, an airport, or industrial equipment can attest to the intensity of sounds produced by human activities. Many of these anthropogenic sounds can be physically harmful or distracting to humans or wildlife and are considered noise pollution (hereafter referred to as noise). Noise, characterized by high amplitudes and low spectral frequencies, is typical to habitats in and around human-altered landscapes[3]. Elevated noise level through anthropogenic activity is a global phenomenon and probably only

hearing-impaired people can say they have never experienced it. It is so common that most of us are habituated to unnaturally high noise levels[4]. Noise pollution, in the recent times, has been well recognized as one of the major trepidations that impact the quality of life in urban areas across the globe. Because of the rapid increase in industrialization, urbanization and other communication and transport systems, noise pollution has reached to a disturbing level over the years. Currently, residences far from the noisy sources and near silent secondary roads are becoming very popular and gaining immense importance[5]. There has been a considerable increase in noise from manmade sources during last 100 years, which is now doubling after every ten years[6]. Many surveys addressing the noise pollution problems has been conducted for several cities of the world and have clearly shown the scale of discomfort that noise causes in people's lives[7]. The effects of noise on human health and comfort are divided into four categories depending on its duration and volume. They are – (i) physical effects such as hearing defects; (ii) physiological effects, such as increased blood pressure, irregularity of heart rhythms and ulcers; (iii) psychological effects, such as disorders, sleeplessness and going to sleep late, irritability and stress; and (iv) effects on work performance, such as reduction of productivity and misunderstanding what is heard[8]. Environmental noise interferes with the social behavior and manifest in the form of psychological and physiological disorders through a variety of mechanisms. Exposure to a continuous noise of 85-90 dB could lead to progressive hearing loss and changes of the threshold sensitivities. These annoyance reactions are associated with the degree of magnitude, variety, and severity on the daily activities[9]. The health impacts of noise pollution and the potential implications of noise exposure are numerous, pervasive, persistent, cumulative and augmented synergistically and antagonistically, with corresponding real (economic) and intangible (well-being) losses[10]. An explicit link between environmental noise with the activation of sympathetic and endocrine systems has been witnessed, resulting in the changes of blood pressure, hypertension, peripheral vasoconstriction and cardiovascular disease[11]. Epidemiological studies have shown that irregular traffic noise of 45 dB has been interlinked to the interference of daily activities, sleeping, rest, study, communicating, and adverse health implications such as frustration, lower tolerance, and changes of blood compositions[12]. Specifically, road traffic annoyance is a major culprit with reported negative symptoms of hearing loss, gastric secretion, pituitary and adrenal gland stimulation, suppression of the immune response, and female reproduction

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and fertility failures [13]. According to the World Health Organization (WHO), approximately 10 million of adults and 5.2 million of children in the United States are suffering from the irreversible noise-induced hearing impairment, and 250 million populations worldwide are exposed to the dangerous levels of environmental noise daily [14]. The most investigated non-auditory health endpoints for noise exposure are perceived disturbance and annoyance, cognitive impairment (mainly in children), sleep disturbance, and cardiovascular health[15]. Annoyance is the most prevalent community response in a population exposed to environmental noise. Noise annoyance can result from noise interfering with daily activities, feelings, thoughts, sleep, or rest, and might be accompanied by negative responses, such as anger, displeasure, exhaustion, and by stress-related symptoms [16]. Both short-term laboratory studies of human beings and long-term studies of animals have provided biological mechanisms and plausibility for the theory that long-term exposure to environmental noise affects the cardiovascular system and causes manifest diseases (including hypertension, ischemic heart diseases, and stroke). Investigators have repeatedly noted that noise exposure increases systolic and diastolic blood pressure, changes heart rate, and causes the release of stress hormones (including catecholamines and glucocorticoids)[17]. Chronic exposure can cause an imbalance in an organism's homeostasis, which affects metabolism and the cardiovascular system, with increases in established cardiovascular disease risk factors such as blood pressure, blood lipid concentrations, blood viscosity, and blood glucose concentrations. These changes increase the risk of hypertension, arteriosclerosis, and are related to severe events, such as myocardial infarction and stroke[15],[18]. Sleep disturbance is thought to be the most deleterious non-auditory effect of environmental noise exposure, because undisturbed sleep of a sufficient length is needed for daytime alertness and performance, quality of life, and health. Elderly people, children, shift-workers, and people with a pre-existing (sleep) disorder are thought of as at-risk groups for noise-induced sleep disturbance [19]. Repeated noise-induced arousals interfere with sleep quality through changes in sleep structure, which include delayed sleep onset and early awakenings, reduced deep (slow-wave) and rapid eye movement sleep, and an increase in time spent awake and in superficial sleep stages[15],[19].

Macro lactate dehydrogenase (LDH) complex is one of the macroenzymes. Macroenzymes are complexes of serum enzymes with a plasmatic protein. They have a higher molecular weight and more prolonged serum half life than those of unbound enzymes. Many enzymes in serum that are measured in clinical chemistry laboratories can occur in the form of a macroenzyme. Macroenzymes are important to the clinician because they frequently cause falsely increased total serum enzyme levels by interfering with common clinical laboratory testing methods, and as a result can cause diagnostic and therapeutic errors. LDH-immunoglobulin complex is known to often occur in certain diseases such as neoplasms, liver damage, and cardiovascular accidents [20]. Significant

kinetic differences exist between human heart (H) and human muscle (M) lactate dehydrogenase (LDH). At high pyruvate concentrations the heart enzyme is inhibited to a greater extent than the muscle enzyme. Similar differences have been found between the enzymes from human heart and human liver [21]. Functional lactate dehydrogenase are homo or hetero tetramers composed of M and H protein subunits encoded by the LDHA and LDHB genes, respectively:

LDH-1 (4H)—in the heart and in RBC (red blood cells)

LDH-2 (3H1M)—in the reticuloendothelial system

LDH-3 (2H2M)—in the lungs

LDH-4 (1H3M)—in the kidneys, placenta, and pancreas

LDH-5 (4M)—in the liver and striated muscle [22]

The five isoenzymes that are usually described in the literature each contain four subunits. The major isoenzymes of skeletal muscle and liver, M4, has four muscle (M) subunits, while H4 is the main isoenzymes for heart muscle in most species, containing four heart (H) subunits. The other variants contain both types of subunits [21],[22]. Usually LDH-2 is the predominant form in the serum. A LDH-1 level higher than the LDH-2 level (a "flipped pattern") suggests myocardial infarction (damage to heart tissues releases heart LDH, which is rich in LDH-1, into the bloodstream). Concentrations of LDH and isoenzyme patterns are important in clinical diagnosis. Vessell and Bearn noted that the isoenzyme pattern of serum changes after myocardial infarction. Changes in the isoenzyme pattern are observed as early as 6- 12 hr after the initial attack of pain and have been shown to be a more sensitive indicator of myocardial necrosis than total serum activity. Changes in LDH isoenzyme patterns are a constant feature in diseases where liver-cell damage occurs. Malignancies, hemolytic anemias, and muscular dystrophy will also alter LDH concentrations and isoenzyme patterns of serum[22],[23]. The observation of variable LDH isoenzyme distributions in different tissues led to hypotheses regarding possible functions. The two most common isoforms, LDH-A and LDH-B, have overlapping tissue expression across mammals, with LDH-B predominantly expressed in the heart and LDH-A expressed in skeletal muscle. The expression profile of these two isoenzymes in the brain also shows marked variation across species and more pronounced differences in certain regions of the brain than in others[24]. The LDH subtype A is up-regulated in diverse tumor tissues including lung, pheochromocytoma, paraganglioma, esophageal squamous cell carcinoma, breast, endometrial adenocarcinoma, ovarian cystadenocarcinoma, hereditary leiomyomatosis renal carcinoma and colon carcinoma [22]. Unlike normal differentiated cells where lactate accumulation occurs anaerobically, cancer cells readily convert glucose into lactate aerobically, a phenomenon termed the Warburg effect. Elevated protein expression or enzyme function of LDH-A is a contributor to not only accumulated lactate, but also aggressive tumor growth, advanced progression, metastasis, acidity, and subsequent resistance to radiation and chemotherapy. LDH-A knockdown, or lowering the functional capacity of LDH-A can suppress tumor growth and metastasis, indicating that this

enzyme could serve as a novel targeted cancer therapy strategy [25].

LDH is a protein that normally appears throughout the body in small amounts. Many cancers can raise LDH levels, so LDH may be used as a tumor marker, but at the same time, it is not useful in identifying a specific kind of cancer. Measuring LDH levels can be helpful in monitoring treatment for cancer. Noncancerous conditions that can raise LDH levels include heart failure, hypothyroidism, anemia, and lung or liver disease [26]. Tissue breakdown releases LDH, and therefore LDH can be measured as a surrogate for tissue breakdown, e.g. hemolysis. Other disorders indicated by elevated LDH include cancer, meningitis, encephalitis, acute pancreatitis, and HIV. LDH is measured by the lactate dehydrogenase (LDH) test (also known as the LDH test or Lactic acid dehydrogenase test). Comparison of the measured LDH values with the normal range help guide diagnosis [25]. LDH is involved in tumor initiation and metabolism. Cancer cells rely on anaerobic respiration for the conversion of glucose to lactate even under oxygen-sufficient conditions. This state of fermentative glycolysis is catalyzed by the A form of LDH. This mechanism allows tumorous cells to convert the majority of their glucose stores into lactate regardless of oxygen availability, shifting use of glucose metabolites from simple energy production to the promotion of accelerated cell growth and replication. For this reason, LDH A and the possibility of inhibiting its activity has been identified as a promising target in cancer treatments focused on preventing carcinogenic cells from proliferating [25],[27]. Inhibition of LDHA activity enhances mitochondrial respiration and decreases mitochondrial membrane potential which both compromises the ability of the tumor cells to proliferate under hypoxia and lead to apoptosis [28]. LDH can also be used as a marker of myocardial infarction. Following a myocardial infarction, levels of LDH peak at 3–4 days and remain elevated for up to 10 days. In this way, elevated levels of LDH (where the level of LDH1 is higher than that of LDH2) can be useful for determining whether a patient has had a myocardial infarction if they come to doctors several days after an episode of chest pain [26]. High levels of lactate dehydrogenase in cerebrospinal fluid are often associated with bacterial meningitis. In the case of viral meningitis, high LDH, in general, indicates the presence of encephalitis and poor prognosis [29].

II. MATERIAL AND METHODS

A. Animals

Adult Wistar rats weighting 200 ± 30 g were purchased and raised in our colony from an original stock of Pasteur institute (Tehran, Iran). The temperature was at 23 ± 2 °C and animals kept under a schedule of 12h light:12h darkness (light on at: 08: 00 a.m.) with free access to water and standard laboratory chow. This study was performed according to ethical guidelines relating to working with laboratory animals [8].

B. Protocol of Study

Male Wistar rats were randomly divided into control and groups exposed to traffic noise for 1, 3 or 6h/day of 5 rats in each group. The traffic noise was recorded from environment from crowded areas of city and the animals were exposed to the traffic noise in situation very similar to what that people are exposed to such noise. After 8 weeks, blood samples were obtained using cardiac puncture method. Following serum preparation, level of LDH was measured using spectrophotometry method.

C. Statistical Analysis

All values are presented as mean \pm S.E.M. Statistical significance was evaluated by one-way analysis of variance (ANOVA) using SPSS 19. Differences with $P < 0.05$ were considered significant.

III. RESULTS

Table I and Figure I show the serum levels of LDH in male rats. The results indicated that serum level of LDH increased in rats exposed to noise pollution for 3 or 6h/day compared to control rats ($P < 0.01$ and $P < 0.05$, respectively); however, there was no significant difference in serum LDH level between rats exposed to traffic noise for 1h/day and control animals.

TABLE I
SERUM LEVEL OF LDH IN CONTROL ANIMALS AND RATS EXPOSED TO NOISE POLLUTION FOR 1, 3 AND 6H/DAY. P VALUES ARE VERSUS CONTROL GROUP. NS INDICATES NONSIGNIFICANT DIFFERENCE COMPARED TO CONTROL GROUP.

Group	LDH (IU/L)	P
Control	890.57 \pm 151.17	-
1h/day	618.43 \pm 109.02	NS
3h/day	1478.14 \pm 122.26	<0.01
6h/day	1293.71 \pm 197.15	<0.05

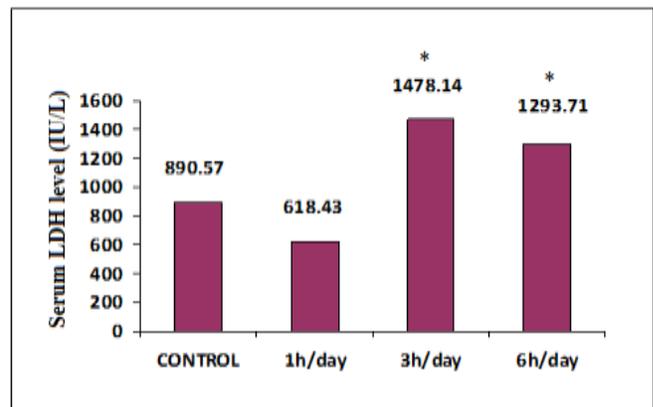


Fig. 1 Serum level of LDH in control animals and rats exposed to noise pollution for 1, 3 and 6h/day. * represents significant difference compared to control rats.

IV. DISCUSSION

Our study indicated that traffic noise pollution results in increased serum levels of LDH. In line with this finding there are reports indicating that a relationship between road traffic noise exposure and MI incidence, which cause elevation in levels of LDH [26]. Also noise pollution results in increased serum levels of other factors such as testosterone [30], which may impose changes in normal functions of various organs.

The effects of noise on human health include physiological effects, psychological effects and stress [8], which can bring about disturbances in body organs leading to changes in normal function of body organs resulting to elevating of enzymes such as LDH. An explicit link between environmental noise with the activation of sympathetic and endocrine systems has been also substantiated [11]. Studies have shown that traffic noise has been associated with adverse health implications [12] may lead to change in LDH level. Traffic noise has also negative effects on gastric secretion, pituitary and adrenal gland stimulation, suppression of the immune response [13], which can change serum LDH level. The most investigated non-auditory health endpoints for noise exposure is cardiovascular complaints [15], showing the effects of noise stress on cardiovascular system which may bring about a change in serum level of LDH. Investigations also have noted that noise exposure increases stress hormones (including catecholamines and glucocorticoids), which can affect on serum LDH level[17].

V. CONCLUSION

Our findings show that exposure to traffic noise pollution for long period of time enhances LDH which may indicate damage to liver, heart, lung, thyroid, blood system or other disorders. More studies in cellular and molecular level is required to clarify the mechanism of effects of noise pollution on body system resulting in enhanced serum LDH.

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