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# ULTRASTRUCTURAL AND CYTOCHEMICAL STUDIES OF THE EFFECT OF SONIC AND ULTRASONIC WAVES ON THE MAMMALIAN NERVOUS SYSTEM

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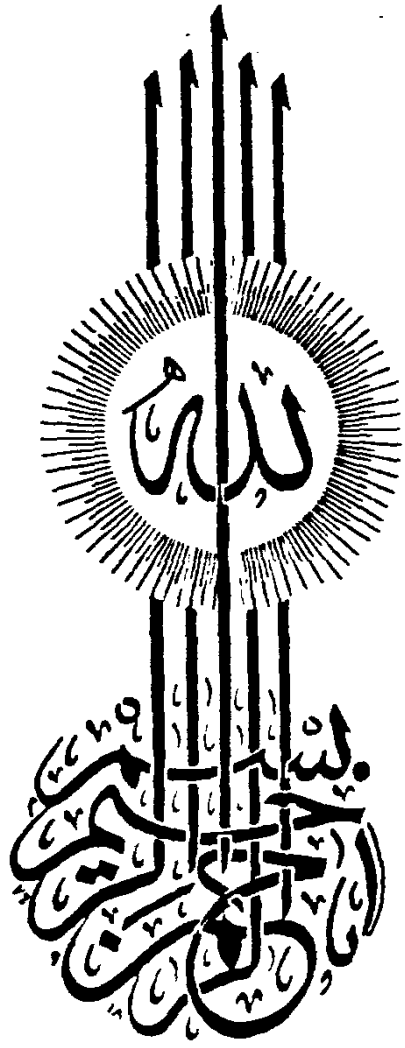

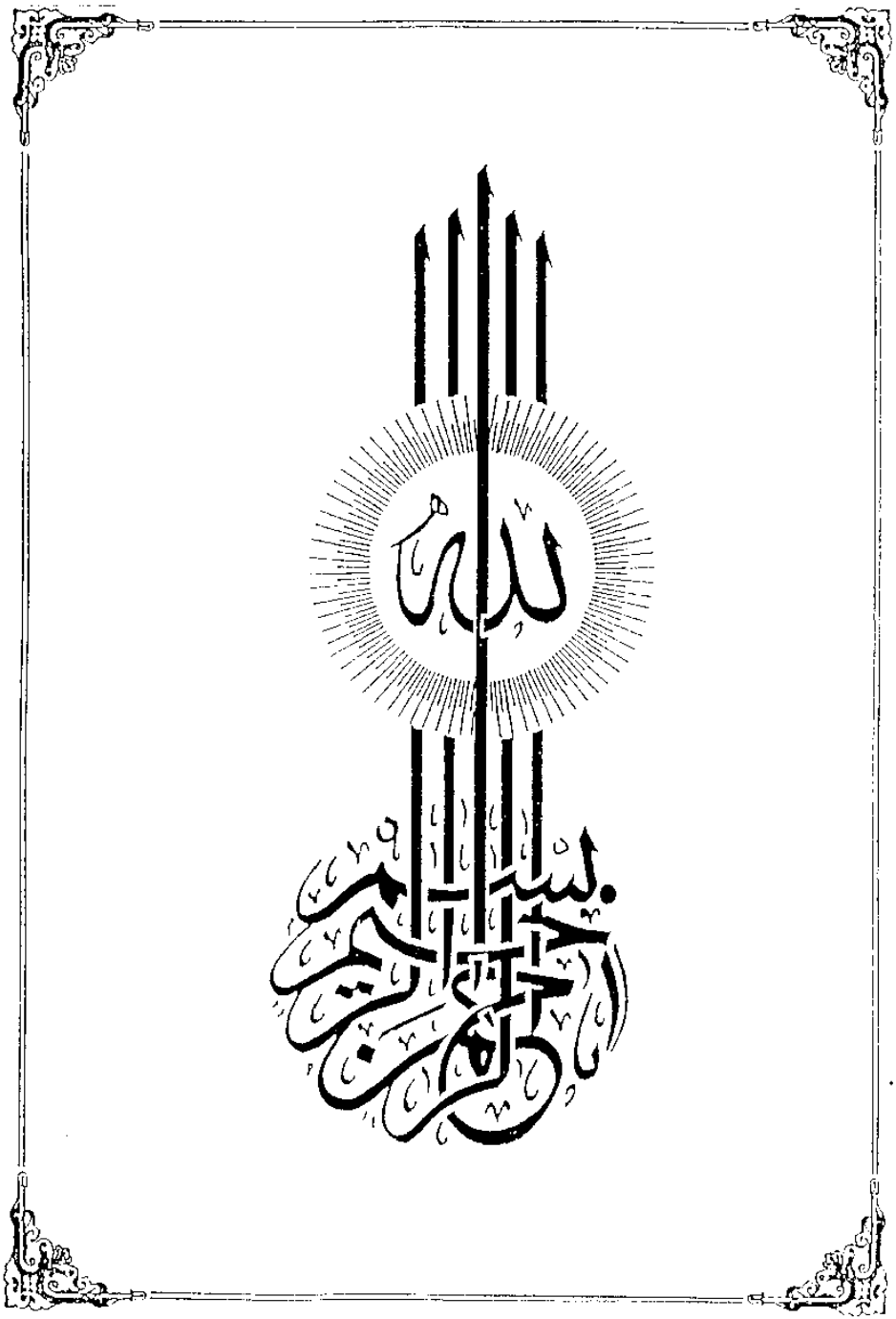

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# CONTENTS

# LIST OF ABBREVIATIONS

| | |
|---|---|
| AChE | = acetylcholinesterase. |
| ACP | = acid phosphatase. |
| an c | = anterior commissure. |
| bc | = bony cochlea. |
| bm | = basilar membrane. |
| BZR | = benzodiazepine receptor. |
| cc | = corpus callosum. |
| Cer | = cerebellum. |
| cer c | = cerebral cortex |
| cg | = cingulum. |
| cg c | = cingulate cortex. |
| Chr | = heterochromatin. |
| cl | = Claudius cell. |
| cn | = cochlear nerve. |
| Cor | = cortex. |
| cp | = cerebral peduncle. |
| cpu | = caudate putamen. |
| CT | = conditioning test interval. |
| DC | = Deiters' cell. |
| ec | = external cortex. |
| fr | = frontal cortex. |
| G | = Golgi cisternae. |
| GDH | = glutamate dehydrogenase. |
| GOT | = glutamate oxaloacetate transminase. |

| | |
|---|---|
| $GOT_m$ | = mitochondrial glutamate oxaloacetate transaminase. |
| $GOT_s$ | = soluble form of glutamate oxaloacetate transaminase. |
| G-6-PD | = glucose-6-phosphate dehydrogenase. |
| gp | = globus pallidus. |
| H | = helicotrema. |
| [$^3$H] Flu | = tritiated flunitrazepam. |
| Hip | = hippocampus. |
| hyp | = hypothalamus. |
| Hx & E | = haematoxylin and eosin. |
| IAS | = initial auditory stimulus (sensitized). |
| $IAS_{30}$ | = audiosensitized killed after 30 minutes. |
| $IAS_{=2days}$ | = audiosensitized killed after 2 days. |
| icp | = inferior cerebellar peduncle. |
| IDC | = interdental cells. |
| IHC | = inner hair cell. |
| IIS | = intermittent inhibitory stimulus (desensitized). |
| IPC | = inner pillar cell. |
| ISC | = inner sulcus cell. |
| K.d | = kilodalton. |
| LDH | = lactate dehydrogenase. |
| LSO | = lamina spiralis ossea. |
| lv | = lateral ventricles. |
| ly | = lysosomes. |
| m | = mitochondria. |

rm = Reissner's membrane.

rt l = reticular lamina.

sm = scala media.

sp g = spiral ganglion.

sp l = spiral ligament.

sp p = spiral prominence.

s t = scala tympani.

Stc = stereocilia.

St C = stellate cell.

St cy = stellate cell cytoplasm.

St n = stellate cell nucleus.

Str = sound stress.

sv = scala vascularis.

TC = tunnel of Corti.

th r = thalamic radiations.

tl = tympanic lip.

vl = vestibular lip.

mb = microbodies.

mc = membranous cochlea.

md = modiolus.

Med = medulla oblongata.

mg = medial geniculate body.

Mid = mid brain.

mol = molecular layer.

mvb = multivesicular bodies.

N = nucleus.

Nm = nuclear membrane.

Np = nuclear pores.

Nu = nucleolus.

oc = organ of Corti.

OHC = outer hair cell.

OPC = outer pillar cell.

PAGE = polyacrylamide gel electrophoresis.

par = parietal cortex.

PhC = phalangeal cell.

pol = polysomes.

pp = pars pictinata.

prh = perirhinal cortex.

pt = pars ticta.

pu = putamen.

pyr = pyriform cortex.

Re = rough endoplasmic reticulum.

Rdc = rod of Corti.

Rib = ribosomes.

# INTRODUCTION

In our modern life noise became the most ubiquitous pollutant specially in such countries having a large number of population like our country. Although much work has been done on different pollutants, noise is the least studied or understood. Even most of the work done on effects of noise was on its acute effect specially on the auditory system in adult subjects.

The more direct effect of noise is localized in the auditory pathways of the nervous system. These pathways consist of specific projections to the auditory cortex and non-specific projections to the reticular formation, which send impulses to the different parts of the brain thus influencing non auditory processes. So, it is reasonable to expect the effect of sound on cardiovascular system, endocrine system, reproductive system and behavior.

In mammals it was found that the developing central nervous system is more sensitive to sound stimuli than the well developed central nervous system in adult individuals and that environmental noise during early infantile development appears to have significant residual effects persisting into adult life (Iturrian and Johnson, 1975).

One of the most important phenomena observed in mammals due to the effect of sound is audiogenic seizure. The importance of its study came from its resemblance to human epilepsy. Audiogenic seizure has become a subject of interest for psychologists, pharmacologists and biochemists. Rodents proved to be the best models for epileptic studies. It was found that in these animals and specially in the developing youngs there is a period of maximum vulnerability at which they are more sensitive to audiogenic seizure. Some animal strains are normally sensitive or susceptible while others are normally resistant. The seizure susceptible animals can be made resistant to seizure by a behavioral process called desensitization and the resistant strains can be made susceptible by a process called sensitization (Henry, 1967).

It is interesting to note that these two processes persist for several days in treated animals, as they are long term processes. Audiosensitization and desensitization could be induced only at a specific age which differs in different strains. The underlying mechanisms and the biochemical implications of these two processes are still mysterious and under investigations.

Since neurological mechanisms of sensitization and desensitization are still obscure, the involvement of endogenous anticonvulsant system and benzodiazepine receptor system could be an attractive possibility that needs more investigations.

It is true that a reasonable amount of stimulation is necessary for normal development, and that in some instances the employment of sound in therapy has been proposed. It is also true that habituation occurs with exposure to sound, and that this provides some degree of short-lasting protection against subsequent exposure. Chronic overstimulation as in sound stress, however, has pathological consequences which might be irreversible as in hear loss, damage to the central nervous system structures or changing the metabolism of some enzymes (Artyukhina *et al.*, 1981 a, b; Artyukhina and Leveshina, 1984; Sakuma, 1984; Boadle-Biber *et al.*, 1989). While many studies had been done on the physiological effects of sound stress (Welch and Welch, 1970), there are only few studies on its effect on the central nervous system.

Modern advances in science and technology led to the increase of daily use of ultrasound in various purposes. One of the most interesting purposes is in medicine. Up

till now adverse effects have not been detected from exposure to diagnostic and therapeutic ultrasound. However it is of a particular concern that adequate epidemiological studies have not yet been performed, and that studies on the effect of ultrasound on human beings are rare, specially those on the nervous system. The work on the developing central nervous system in youngs is lacking, especially at the ages of maximum audiosensitivity which was reported in some rodent strains.

A great deal of experiments were achieved on the effect of ultrasound on cells in suspension or in culture which can not be extrapolated on intact animals or tissues of adult subjects. In addition,some studies were performed using exposure times longer than would normally be encountered in clinical purposes which made the evaluation of health risks from exposure to ultrasound extremely difficult.

So, it is urgent in this decade to investigate extensively the effects of ultrasound before we lose the real control especially in human beings.

# AIM OF WORK

The aim of this work, using a certain strain of mice (CF#1), is to investigate the two behavioral processes, audiosensitization and desensitization through which animals become susceptible or non susceptible to audiogenic seizure. The possibilities of changes in the brain proteins of the experimented animals due to the two induced processes have to be traced by the application of the SDS polyacrylamide gel electrophoresis. This method is a high resolution electrophoresis technique that reveals any minor changes in the brain protein pattern. Since the benzodiazepines are potent anticonvulsants used against various types of seizure the possibility of the involvement of the benzodiazepine receptor system in seizure susceptibility has to be investigated.

Studies on the regions of the nervous system which are responsible for the regulation of susceptibility to seizure are still conflicting. However, some authors suggest that damage to the inner ear might be responsible for the generation of this change in brain excitability. This has to be investigated by using scanning electron microscopy. Exposure of animals to sound stress (long time

exposure to sound) and to demonstrate how far it may affect the structure of the inner ear is one of the goals of this investigation. It should be noted that all kinds of populations are nowadays frequently exposed to such stresses. Changes of various metabolic activities in brains of sensitized, desensitized and sound stressed animals have to be studied through the investigation of some important isozyme systems. The present investigation deals with the ultrastructure of certain brain regions to throw light on the effects of sound and sound stress.

The daily use and the widespread applications of ultrasound and the shortage of the scientific literatures on its adverse effects on human beings or experimental animals made it necessary to study these problems. Also, it was necessary to investigate the effects of this type of non-ionizing radiation on the brain proteins, some important isozyme systems and the ultrastructure of some brain regions. This investigation might help for the assessment of health risks of ultrasound and also for further understanding of how ultrasound produces its adverse effects.