INTRODUCTION

Brain research is the science, which deals with the process underlying the most immediate aspects and most rapidly developing yet least established field in contemporary biology. The study of neurology is still indescribably remote from the mastery of the subject matter that now allows the molecular genetics to work with expectations. If scientific success in terms of solutions to fundamental problems and practical applications of knowledge are evident, the triumphs of neuroscience are as yet modest. Nevertheless perhaps the most compelling explanation for the current exuberance in brain research is the spirit of each of the ages within its diverse range.

The central tenet of modern neuroscience is that all behaviour is a reflection of brain function. The action of brain underlies not only relatively simple motor behaviours such as walking, breathing, and smiling but also elaborate affective and cognitive behaviours such as learning, thinking and composing a symphony. As a corollary, the disorders of affect (feelings) and cognition (thought) that characterize neurotic and psychotic illness can be seen as brain disturbances of brain function.

The task of neuroscience is to explain how the brain marshalls the nerve cells and vital cells to control behaviour and how, inturn the functioning of the constituent cells in an individual’s brain is influenced by that person’s environment. The
understanding of the adult nervous system and its control of behaviour have been enhanced by research into the development of the brain. Behaviour is dependent on individual classes of nerve cells with specialized functions and on the formation of specific interconnections between them.

Several studies on the development of the nervous system have thrown light on how neurons acquire specific identities and how the pattern of neuronal connections are established and maintained. The nervous system develops in a series of ordered steps, with a precise temporal sequence that is characteristic of each neural structure. While the architecture of anatomical and physiological nature of the brain is precisely net worked in the evolution to carry out the functions in a systematic procedure, the damage to such system might occur either spontaneously (accident, and idiopathic) or induced (brain damage by biological materials). Among the biological factors, the central nervous system is vulnerable to the toxic effects of various drugs and the developing brain is likely to undergo irreversible changes, if exposed to harmful drugs which can have demonstrable effects in motor functions and behavioural functions as the fetus grows.

Numerous research works have been carried out on the effects of drugs on the fetus, which are consumed by the pregnant female at different stages of pregnancy. The drugs that have a primary action on the nervous system of the organism are likely to have an effect on the developing fetal brain, provided the drug has access to the fetal brain by crossing the maternal placental barrier and the blood brain barrier of the fetus.
For many drugs, there is not sufficient evidence to ensure that such drugs are entirely harmless to the fetus, especially in first trimester of pregnancy. Special care is therefore required in prescribing medicines for the pregnant women in relation to the risk involved (Forfar et al., 1973). Hence, the ultimate effect upon the offspring depends on many factors, such as the timing of the insult in relation to the gestational age, the susceptibility of the fetus to damage and the inherent toxicity of the drug itself. An important point is that the fetus may be adversely affected by medications that are harmless to the mother.

All drugs consumed by the pregnant women are passively transferred across the placenta to the fetus. The rate of diffusion is determined by the molecular weight and lipid solubility. Peak levels are usually reached in fetal plasma within 0.5 – 2 hours. Metabolism of ingested medications occurs in the fetal liver, but fetal drug elimination is mediated mainly by the metabolic and excretory processes of the mother. This can present the neonates with problems.

Moreover, exposure to an embryopathic drug during pregnancy can alter the process of cellular differentiation to induce adverse developmental effects. Most commonly the use of CNS depressants during pregnancy exposes the neonate to the risk of serious depression of central nervous system.

Benzodiazepines are extensively used for anesthetic medications and they become even more useful since the development of agents with short duration of action have greater propensity to cause amnesia. These drugs are not analgesics and
they rarely cause nausea or vomiting. However Benzodiazepines can raise the threshold of CNS toxicity to local anesthetics. The drug of Benzodiazepines series characterized by the chemical structure.

Diazepam (DZP) is a minor tranquillizer, which acts as an antianxiety agent, and it is the most commonly used CNS depressant during pregnancy. It is used orally, poorly soluble in water and its absorption is irreversible after administration. It produces sedation, reduces aggressiveness and causes a calming effect. Although they are capable of memory impairment, the mechanism of antianxiety action is not known. They act at many levels of neuraxis and largely on brain reticular activating system (reducing sensory input) the limbic system, the median forebrain bundle and the hypothalamus. The drug has little effect on respiration at usual doses.

DZP, a lipophilic drug with a small molecular weight, crosses the placenta rapidly. Since the capacity of the fetus or newborn to dispose the drug is very small, the drug and its pharmacologically active metabolites accumulate in fetus. Studies with DZP have shown concentration in fetal plasma to be greater than those in maternal plasma (Cavanagh and Condo, 1964). The resultant large concentration of
DZP in fetal tissue has been noted to be comparable to those which have deleterious effects on human cells in tissue culture (Breen and Stenchever, 1970). Administration of DZP during gestation results in floppy infant syndrome (Speight, 1977) characterized by hypotonia, hypothermia, respiratory complications, hyperbilirubinemia and poor sucking response (Flowers et al., 1969; Joyce and Kenyon, 1972; McCarthy et al., 1973; Rowlatt, 1978; Woods and Malan, 1978; McAllister, 1980). Although more work has been studied on the changes on such organs, there is very less information regarding the changes in developing brain due to the actions of DZP.

Hence, to understand the pathobiology of DZP and its effect on developing brain, the present study is aimed to investigate such effect in developing albino rat brain by administering DZP during different trimesters.