

# Changes in Behavior and Learning Ability of Rats Intoxicated with Lead

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**Abstract**—Measuring the effect of perinatal lead exposure on learning ability of offspring is considered as a sensitive and selective index for providing an early marker for central nervous system damage produced by this toxic metal. A total of 35 Sprague-Dawley adult rats were used to investigate the effect of lead acetate toxicity on behavioral patterns of adult female rats and learning ability of offspring. Rats were allotted into 4 groups, group one received 1g/l lead acetate (n=10), group two received 1.5g/l lead acetate (n=10), group three received 2g/l lead acetate in drinking water (n=10) and control group did not receive lead acetate (n=5) from 8<sup>th</sup> day of pregnancy till weaning of pups.

The obtained results revealed a dose dependent increase in the feeding time, drinking frequency, licking frequency, scratching frequency, licking litters, nest building and retrieving frequencies, while standing time increased significantly in rats treated with 1.5g/l lead acetate than other treated groups and control, on contrary lying time decreased gradually in a dose dependent manner. Moreover, movement activities were higher in rats treated with 1g/l lead acetate than other treated groups and control. Furthermore, time spent in closed arms was significantly lower in rats given 2g/l lead acetate than other treated groups, while, they spent significantly much time spent in open arms than other treated groups which could be attributed to occurrence of adaptation. Furthermore, number of entries in open arms was dose dependent. However, the ratio between open/closed arms revealed a significant decrease in rats treated with 2g/l lead acetate than control group.

**Keywords**—Lead toxicity, rats, learning ability, behavior.

## I. INTRODUCTION

**S**IGNIFICANT successes in lowering blood lead levels have been achieved in countries that removed lead from paint and gasoline, even in such places many residual consequences of the prior uses of lead still remain. In the U.S., for example, such consequences include the lifetime elevated exposures experienced by the current elderly segment of the population, an exposure that has been posited to contribute to several diseases and disorders in this age group. Sustained contamination from the prolonged use of lead in paint and gasoline also underlies the current elevations of blood lead that now preferentially impact low socioeconomic, medically underserved inner city children residing in old housing stock, i.e., the same communities that also sustain low follow up rates after initial identification of elevated lead exposures. The impact of this problem has been significantly broadened by the

growing recognition of adverse cognitive effects at increasingly lower blood lead levels. Of course, elevated lead burden also remains a significant problem in countries where leaded gasoline remains in use and/or where environmental regulations remain secondary to industrial development [44].

Rats are sensitive to variations in environmental complexity. Impoverished living environments can lead to impaired brain development. Moreover, the behavioral responses can be quite varied depending on characteristics of both the stressor and the individual subjected to it; also behaviors that are labeled abnormal often can be considered normal responses to an abnormal environment. Although animals may initially display signs of acute stress they often adapt or learn to cope with many conditions [14].

Reference [2] found that the administration of lead acetate to rats orally caused a decrease in water intake when compared to control group. Moreover, [24] showed that a lead exposure during the pregnancy and lactation period causes reduction of feed intake. On the other hand, [34] showed that oral administration of 1000ppm of lead acetate to young rats for 30 days caused a reduction in sniffing, licking, biting and grooming behavior during a 20 minute testing period. Furthermore, early behavioral effects of lead perinatal exposure in rat pups was studied by [8] found that lead exposed 14 day old pups were significantly more active.

Prenatal stress can impair stress coping ability and is able to cause a disruption of behavior in aversive or conflict inducing situations in juvenile and adult offspring, prenatally stresses animals are reported to show retarded motor development, reduced exploratory and impairments of learning ability and maternal behavior also individual variation in the susceptibility to prenatal stress may exist. Behavioral inhibition and anxiety when exposed to novelty are typical results which may underline the effects of prenatal stress on learning and various behavioral responses this seems to be related to increased or prolonged activity in the hypothalamic-pituitary-adrenal axis produced by impaired negative feedback of glucocorticoids in the hippocampus although other neuroendocrine pathways may be involved. Since behavioral and neuroendocrine effects of prenatal stress in rodents are quite similar to those found in depressed humans and since increased fearfulness and frustration is implicated farm animals subjected to prenatal stress may be predicted to show a reduced ability to cope with a different environment and have increased propensity for developing behavioral disturbances and reduced welfare [4]. Moreover, it has been reported that numerous cognitive abilities are of importance

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for learning maze so poor performance is usually interpreted as an impairment of spatial memory formation [21].

The effect of different periods of lead exposure on deficits of learning and memory is still unclear. In this study, we investigate the effect of lead acetate toxicity on welfare of rats by measuring behavior of adult female rats and learning ability of their offspring.

## II. MATERIALS AND METHODS

### A. Animals

A total of 35 Sprague-Dawley pregnant female rats (3 months & 110-130g) were allotted into four groups, group one received 1g/l lead acetate in drinking water (n=10), group two received 1.5g/l lead acetate in drinking water (n=10), group three received 2g/l lead acetate in drinking water (n=10) [47] and group four received water without lead acetate (n=5) daily from day 8 pregnancy till weaning [9].

### B. Management

Rats were fed ration containing 16.3% crude protein, 6.8% fat and 3.5% crude fibre, housed in 35 individual breeding plastic cages (37x30x14cm) with 1-2cm wood shaving bedding replaced two times per week. Rats were kept under natural light-dark cycle without any alteration in lighting program.

Vaginal smears were done to detect the time of positive oestrus according to [22] then mating took place by monogamous system where one female was regularly mated by one male introduced to females in breeding cages and then persists with pups till weaning. Pregnancy was detected by vaginal smears on the next morning and the day of finding sperms was called day zero of gestation.

### C. Behavioral Observations

Rats were observed three times weekly and four hours daily within periods of late morning and early afternoon. Focal sample observation, where the observed patterns were ingestive, bodycare, resting, locomotor, investigatory behavior, while, maternal behavior carried out according to [12] including licking (grooming), nursing, nest building and retrieving.

Learning ability was measured by using the elevated plus maze according to [36], where the elevated plus –maze apparatus was made of smooth brown opaque platforms with two open arms (50x10cm) and two closed arms of the same size, the wall of this chamber was 40cm high and the whole apparatus was elevated 50cm above floor. Each rat was placed in the central square (10x10cm) facing closed arm. At the end of each trial lasting 5min, the arms was cleaned and dried to remove excreta. The recorded parameters were time spent in open or closed arms, time of latency in seconds that rats took to enter open or closed arm, number of entries into open and closed arms and ratio spent in open and/or closed arms expressed as percentage.

### D. Statistical Analysis

All statistical analyses were performed using SAS (Statistical Analysis system, version 6, 4<sup>th</sup> Edition, SAS Institute, Cary, NC. USA.). The behavioral data was analyzed by two way analysis of variance ANOVA and learning ability was analyzed by one way analysis of variance proc GLM. Data are expressed as means±S.E.M. and P values<0.05 were considered significant in all tests, unless stated otherwise. Analyses of significant main effects of experimental treatment were performed using multiple range comparisons with Duncan multiple range test.

## III. RESULTS AND DISCUSSION

### A. Ingestive and Resting Behavior

The data presented in Table I showed revealed a dose dependent increase in the feeding time and drinking frequency, while standing time increased significantly in rats treated with 1.5g/l lead acetate than other treated groups and control ( $1.25 \pm 0.24$  vs.  $0.62 \pm 0.18$  min/hr), on contrary lying time decreased gradually in a dose dependent manner. These agreed with [1] who found that rats exposed to lead acetate in doses of 0.2 and 0.5mg/ml in drinking water for a period of 90 days showed mild to moderate changes in food consumption compared to control group.

TABLE I

LEAST SQUARE MEANS AND THEIR STANDARD ERROR OF THE EFFECT OF LEAD ACETATE AND PERIOD OF PREGNANCY AND LACTATION ON INGESTIVE AND RESTING BEHAVIOR OF RATS

Item	Ingestive behavior		Resting behavior	
	Feeding (Min/hr)	Drinking (Freq/hr)	Standing (Min/hr)	Lying (Min/hr)
<b>Treatment</b>				
Control	$5.65 \pm 0.59^c$	$0.66 \pm 0.08^b$	$0.62 \pm 0.18^b$	$36.78 \pm 2.05^a$
1 g/l lead acetate	$5.76 \pm 0.46^c$	$0.57 \pm 0.07^b$	$0.24 \pm 0.05^b$	$37.57 \pm 1.48^a$
1.5 g/l lead acetate	$8.34 \pm 0.62^b$	$0.63 \pm 0.06^b$	$1.25 \pm 0.24^a$	$30.66 \pm 1.98^b$
2 g/l lead acetate	$15.68 \pm 1.05^a$	$1.16 \pm 0.10^a$	$0.45 \pm 0.10^b$	$25.18 \pm 1.88^c$
<b>Period</b>				
2 <sup>nd</sup> Week pregnancy	$5.96 \pm 0.64^c$	$0.54 \pm 0.08^b$	$1.42 \pm 0.28^a$	$53.31 \pm 0.75^a$
3 <sup>rd</sup> Week pregnancy	$7.39 \pm 0.80^c$	$0.80 \pm 0.11^b$	$0.77 \pm 0.15^b$	$50.96 \pm 1.19^a$
1 <sup>st</sup> Week lactation	$7.24 \pm 0.69^c$	$0.65 \pm 0.06^b$	$0.50 \pm 0.16^{bc}$	$18.74 \pm 1.62^b$
2 <sup>nd</sup> Week lactation	$11.48 \pm 1.04^b$	$0.80 \pm 0.08^b$	$0.14 \pm 0.06^c$	$19.56 \pm 1.73^b$
3 <sup>rd</sup> Week lactation	$14.51 \pm 1.17^a$	$1.06 \pm 0.12^a$	$0.38 \pm 0.16^{bc}$	$17.13 \pm 1.54^b$

Means within the same column under the same category carry different superscripts are significantly different.

This could be explained by that several cerebral structures intervene in the regulation of feed intake processes and mostly neurotransmission is catecholaminergic and serotonergic, various works suggest that several neurotransmitters are involved in the regulation of feed intake as serotonin and dopamine that could play primordial role in the control of satisfaction [20]. Moreover, hormonal and neuronal substrates underlying the regulation of feed intake are extensive and complex; several neurotransmitter systems have been implicated in the regulation of feed intake including dopaminergic, serotonergic and cholecystokinin systems [17].

The majority (approximately 80%) of feed intake occurred during the dark phase which is consistent with the known nocturnal behavior of rats, this apparent specificity of lead on nocturnal feed intake may reflect actual differences in the physiological mechanisms mediating feed intake during the dark versus light period, for example, serotonergic mechanisms are known to influence both feed intake and diurnal patterns [18]. However, [29] stated that although exposure to lead initially resulted in decreased nocturnal meal size and duration towards the end of the study, the lead exposed rats had compensated in part by increasing these two parameters during the light phase.

With respect to effect of period of treatment (last two weeks of pregnancy and lactation period), feeding time and drinking frequency increased gradually during pregnancy and lactation period with high level during last week of lactation. Moreover, there was a significant gradual decrease throughout experimental period in standing and lying time. These are contrary to [2] found that the administration of lead acetate to rats orally caused a decrease in water intake when compared

to control group. Moreover, [24] showed that a lead exposure during the pregnancy and lactation period causes reduction of feed intake.

Lead may produce very fast actions in the central nervous system as [13] suggested that effect of lead on water intake may depend on impairment of central cholinergic and/or angiotensinergic functions. Moreover, it is well recognized that water intake can drive and vice versa, as if the primary effect of lead was to produce an aversion to the drinking water then the observed decrease in feed intake would be predicted and vice versa [19]. Furthermore, brain controls many aspects related to the homeostatic processes necessary to keep body fluid and electrolyte variables within the proper narrow limits as fluctuations in these variables make the brain trigger regulatory mechanisms that include renal water and electrolyte excretion and sodium appetite, the central regions localized in the vicinity of the third ventricle are especially involved in these homeostatic procedures and the most important are the hypothalamus, the subfornical organ, the organum vasculosum lamina terminalis and the anteroventral third ventricle region [23].

#### *B. Body Care, Movement and Investigatory Behavior*

Licking and scratching frequencies (Table II) revealed a dose dependent increase. Moreover, movement activities were higher in rats treated with 1g/l lead acetate than other treated groups and control ( $2.11 \pm 0.19$  vs.  $1.53 \pm 0.18$  freq/hr). However, treatment had non-significant effect on the investigatory behavior.

TABLE II  
LEAST SQUARE MEANS AND THEIR STANDARD ERROR OF THE EFFECT OF LEAD ACETATE AND PERIOD OF PREGNANCY AND LACTATION ON MOVEMENT ACTIVITIES, BODY CARE AND INVESTIGATORY BEHAVIOR OF RATS

Item	Body care behavior		Investigatory behavior		Movement (Freq/hr)
	Licking (Freq/hr)	Scratching (Freq/hr)	Cage (Freq/hr)	Trough (Freq/hr)	
Treatment					
Control	3.12±0.51 <sup>ab</sup>	3.08±0.54 <sup>ab</sup>	1.51±0.27 <sup>a</sup>	0.07±0.02 <sup>a</sup>	1.53±0.18 <sup>b</sup>
1 g/l lead acetate	2.74±0.22 <sup>b</sup>	2.04±0.18 <sup>c</sup>	1.20±0.13 <sup>a</sup>	0.07±0.01 <sup>a</sup>	2.11±0.19 <sup>a</sup>
1.5 g/l lead acetate	3.03±0.26 <sup>ab</sup>	2.89±0.27 <sup>bc</sup>	1.73±0.20 <sup>a</sup>	0.10±0.02 <sup>a</sup>	1.25±0.11 <sup>b</sup>
2 g/l lead acetate	3.59±0.24 <sup>a</sup>	3.88±0.42 <sup>a</sup>	1.62±0.13 <sup>a</sup>	0.13±0.03 <sup>a</sup>	2.01±0.16 <sup>a</sup>
Period					
2 <sup>nd</sup> Week pregnancy	4.31±0.48 <sup>a</sup>	4.96±0.62 <sup>a</sup>	2.15±0.29 <sup>a</sup>	0.12±0.02 <sup>b</sup>	1.30±0.17 <sup>c</sup>
3 <sup>rd</sup> Week pregnancy	3.03±0.29 <sup>b</sup>	2.42±0.32 <sup>b</sup>	1.39±0.17 <sup>b</sup>	0.20±0.05 <sup>a</sup>	1.17±0.14 <sup>c</sup>
1 <sup>st</sup> Week lactation	3.00±0.23 <sup>b</sup>	2.74±0.24 <sup>b</sup>	1.38±0.14 <sup>b</sup>	0.06±0.02 <sup>bc</sup>	1.95±0.17 <sup>b</sup>
2 <sup>nd</sup> Week lactation	2.70±0.24 <sup>b</sup>	2.66±0.35 <sup>b</sup>	1.21±0.15 <sup>b</sup>	0.04±0.01 <sup>c</sup>	1.83±0.15 <sup>b</sup>
3 <sup>rd</sup> Week lactation	2.57±0.23 <sup>b</sup>	2.02±0.16 <sup>b</sup>	1.46±0.18 <sup>b</sup>	0.05±0.01 <sup>c</sup>	2.51±0.23 <sup>a</sup>

Means within the same column under the same category carry different superscripts are significantly different.

On studying the effect of period of last two weeks of pregnancy and lactation period there was a significant gradual decrease throughout experimental period in licking frequency, while scratching frequency was higher during the 2<sup>nd</sup> week pregnancy and lower during last week of lactation. However, movement activities were high during 3<sup>rd</sup> week of lactation and low during the last week of pregnancy. Furthermore, dams exhibited high level of cage investigation especially during

2<sup>nd</sup> week pregnancy and low during 2<sup>nd</sup> week lactation, while trough investigation was high during last week of pregnancy and low during 2<sup>nd</sup> week of lactation.

TABLE III

LEAST SQUARE MEANS AND THEIR STANDARD ERROR OF THE EFFECT OF LEAD ACETATE AND PERIOD OF LACTATION ON MATERNAL BEHAVIOR OF RATS

Item	Licking (Freq/hr)	Nursing (Min/hr)	Nest building (Freq/hr)	Retrieving (Freq/hr)
<b>Treatment</b>				
Control	2.30±0.34 <sup>b</sup>	33.38±1.55 <sup>a</sup>	0.39±0.13 <sup>b</sup>	0.10±0.05 <sup>b</sup>
1 g/l lead acetate	2.66±0.30 <sup>b</sup>	30.53±1.41 <sup>a</sup>	0.47±0.09 <sup>b</sup>	0.12±0.03 <sup>b</sup>
1.5 g/l lead acetate	2.85±0.31 <sup>b</sup>	33.69±2.30 <sup>a</sup>	0.52±0.10 <sup>b</sup>	0.22±0.04 <sup>ab</sup>
2 g/l lead acetate	4.13±0.41 <sup>a</sup>	33.96±1.47 <sup>a</sup>	1.06±0.18 <sup>a</sup>	0.35±0.09 <sup>a</sup>
<b>Period</b>				
1 <sup>st</sup> Week lactation	4.50±0.42 <sup>a</sup>	4.50±1.51 <sup>a</sup>	0.80±0.13 <sup>a</sup>	0.29±0.07 <sup>a</sup>
2 <sup>nd</sup> Week lactation	2.83±0.22 <sup>b</sup>	2.83±1.61 <sup>ab</sup>	0.85±0.15 <sup>a</sup>	0.22±0.04 <sup>ab</sup>
3 <sup>rd</sup> Week lactation	1.92±0.19 <sup>c</sup>	1.92±1.54 <sup>b</sup>	0.27±0.04 <sup>b</sup>	0.12±0.03 <sup>b</sup>

Means within the same column under the same category carry different superscripts are significantly different.

Reference [31] suggested that chronic lead exposure may increase the number of D2 receptors in the striatum of rat offspring if the mothers had consumed lead chronically so it has been shown that lead is capable of affecting dopamine receptor subtypes. However, [6] found that lead produced functional dopaminergic super sensitivity which involves both the D1 and D2 receptor subtypes and alteration of synthesis of dopamine in the rat brain.

These results concerning body care behavior are in agreement with [33] found that lead increased grooming behavior in developmental offspring. Moreover, [43] studied lead toxicity in rat pups exposed from conception until weaning by submitting their dams to 750 ppm lead acetate in drinking water during pregnancy and lactation and found that grooming and rearing activity in the open field was increased. On contrary, [2] found that the administration of lead acetate to rats orally for a period of 12 weeks caused decrease in grooming behavior when compared to control group.

Moreover, [10] stated that the decrease in the neurotransmitter causes stress and depression which explains their stereotypical behavior such as sniffing and bite. While, [15] indicated that longer exposure to lead would cause increase in the blood-lead level which indicate a lead peak concentration necessary to the body care behaviors, furthermore, D1 and D2 dopaminergic mechanisms have been shown to be involved in body care behavior which suggested that this metal at least influences one of the dopamine receptors.

Effect of histochrome on the severity of delayed effects of prenatal exposure to lead nitrate in the rat brain was studied by [37] and found that motor activity of rat was stimulated in an elevated plus-maze. Moreover, [5] indicated that maximum ethanol induced locomotion increase was found in mice treated with lead acetate 7 days before ethanol administration while it did not affect locomotion induced by d-amphetamine and ter-butanol. Furthermore, [42] indicated that guinea pigs intoxicated with lead showed changes in motor activities which were characterized by periods of hyperactivity, with restless movements within the cages and in efforts to escape through the mesh holes of their individual cages which were decreased with the progress of experiment when compared to controls. On contrary, [34] showed that oral administration of 1000ppm of lead acetate to young rats for 30 days caused a reduction in locomotor activity during a 20 minute testing

period. Moreover, [25] they found that pups which parentally exposed to lead suffered from hypoactivity.

This could be attributed to [40] have hypothesized that dual changes in the aminergic and cholinergic neurotransmitters systems with increase in aminergic and decrease in cholinergic activity are interrelated and result in lead induced hyperactivity.

Reference [27] suggested that lead could induce changes in motor skills and exploratory behavior that may be related to altered dopamine neurotransmission. Furthermore, these results agreed with [11] reported that pups born for pregnant mice administered lead acetate in drinking water by a dose of 0.25% had increased exploratory and social investigation at age of 3-4 weeks compared to controls. While it disagreed with [2] found that the administration of lead acetate to rats orally for a period of 12 weeks caused decrease in exploratory activity when compared to control group. Moreover, [39] showed that rats treated with 500mg/l Pb have less exploratory activity and high state of anxiety than control rats.

### C. Maternal Behavior

Reference [26] suggested that lactating mothers maintain responsiveness to specific and repeated psychological stressors in particular at the time of the diurnal peak in corticosterone secretion and depending on the stressor applied either neuroendocrine activation or changes in maternal behavior might be important determinants of the long term consequences in the offspring.

Maternal licking of pups is regulated in large part by maternal appetite for water in the dilute pup urine that is released when pups are licked but the stimuli generated by this behavior are used in a learned attraction to maternal odor and in the development of sexual behavior [32]. Moreover, mothers lick pups in response to their odor and to the urine and electrolytes they provide, young pups elicit maternal licking by adapting postures that facilitate it and male pups elicit more licking than female siblings by emitting testosterone dependent odor that mothers find particularly attractive [30].

Among the four types of treatments the maternal behavior of rats revealed a dose dependent increase in the licking litters, nest building and retrieving frequencies, however, treatment had non-significant effect on nursing time. On the other hand,

all maternal behaviors showed a gradual decreased during lactation period.

On the other hand, [28] showed that increased postnatal maternal care induced by an early adaption reverses the long-term effects on HPA reactivity induced by prenatal stress. Moreover, the nest has functional value in that young were

packed together in the nest thus helping to maintain body warmth and enhancing survival value of the species as these species require more protection since they are born relatively naked and mother sitting above the young to form heated roof for them [35].

TABLE IV  
LEAST SQUARE MEANS AND THEIR STANDARD ERROR OF THE EFFECT OF LEAD ACETATE ON LEARNING ABILITY OF RAT'S OFFSPRING

Item	Latency to closed arm (Sec)	Time spent in closed arm (Sec)	No of entries in closed arm	Latency to open arm (Sec)	Time spent in open arm (Sec)	No of entries in open arm	Ratio of open/closed arms
<b>Treatment</b>							
Control	1.79±0.93 <sup>b</sup>	170.75±22.23 <sup>b</sup>	3.36±0.49 <sup>a</sup>	1.07±0.49 <sup>a</sup>	127.39±22.48 <sup>a</sup>	2.07±0.26 <sup>b</sup>	99.38±0.50 <sup>a</sup>
1 g/l lead acetate	4.80±1.15 <sup>ab</sup>	239.41±9.73 <sup>a</sup>	4.06±0.40 <sup>a</sup>	1.57±0.81 <sup>a</sup>	54.61±9.22 <sup>b</sup>	2.10±0.30 <sup>b</sup>	98.01±1.14 <sup>ab</sup>
1.5 g/l lead acetate	7.41±2.55 <sup>a</sup>	245.52±10.94 <sup>a</sup>	4.10±0.49 <sup>a</sup>	1.38±0.82 <sup>a</sup>	45.69±9.74 <sup>b</sup>	2.41±0.47 <sup>b</sup>	97.07±0.91 <sup>ab</sup>
2 g/l lead acetate	6.67±1.25 <sup>a</sup>	187.70±11.86 <sup>b</sup>	4.59±0.34 <sup>a</sup>	3.49±0.84 <sup>a</sup>	102.14±11.79 <sup>a</sup>	3.84±0.39 <sup>a</sup>	96.61±0.51 <sup>b</sup>

Means within the same column under the same category carry different superscripts are significantly different.

It has been suggested that time spent in nest by dams is mainly regulated by heat production by the dams as she crouches over pups and the heat flow occurs only from dam to pups not vice versa [41]. Furthermore, pup retrieval is regulated by multisensory processes and can be considered as a chain of motor response elicited by a variety of stimuli emanating from female and/or pups which promotes orientation, attention and arousal, the initial stimuli induce proximity of dam and pups and perioral trigeminal stimulation elicits the retrieval and grouping of the pups in the nest and a variety of factors can affect pup retrieval behavior including pharmacological and environmental manipulation of mothers or pups [16].

#### D. Learning Ability

It appears that there is a link with hippocampal serotonin and dopamine neurons and these systems are involved in the regulation of corticotrophin releasing factor that play an important role on the systems implicated in anxiety-like behavior, the serotonergic system plays a central role in modulation of anxiety and an increase in 5-HT levels in the hippocampus is associated with an anxiogenic effect [45]. Moreover, perinatal exposure to lead produced increased anxiety due to its capacity to cross the placenta and the blood-brain barrier and its harmful effects in the neonate brain. On the other hand, administration of this metal produced an inhibition of the activity of some enzyme which plays an important role in perinatal development and CNS maturation. Finally, perinatal lead exposure is extremely dangerous and its effects on various aspects of brain development, function and behavior it's considering like neurotoxin how potentially affect different processes of brain development [24].

From the obtained data it is clear that latency to closed arms increased in all treated groups than control group, moreover, time spent in closed arms was significantly lower in rats given 2g/l lead acetate than other treated groups, while other treated groups (rats given 1g/l and 1.5g/l lead acetate) exhibited significantly much time spent in closed arms than control group (239.41±9.73 and 245.52±10.94 vs. 170.75±22.23sec). On the other hand, rats given 2g/l lead acetate spent

significantly much time spent in open arms than other treated groups (102.14±11.79 vs. 54.61±9.22 and 45.69±9.74sec) which could be attributed to occurrence of adaptation. Furthermore, number of entries in open arms was dose dependent. However, the ratio between open/closed arms revealed a significant decrease in rats treated with 2g/l lead acetate than control group (96.61±0.51 vs. 99.38±0.50).

Our results agreed with [24] who found that lead administration reduced time spent exploring the open arms, the time spent in open arms and percentage of entries into the open arms which showed that the perinatal lead exposure of females in gestation and lactation reduced exploration faculty in weaned rats in addition there was an increase of the time of immobility of the lead exposed animals than control ones in forced swimming test which indicated the stress effect of lead. Moreover, [39] showed that by using open field test we demonstrated that rat treated with 500mg/l Pb spent more time in the periphery of the arena as compared to control rats while by using the elevated plus maze showed that treated rats with lead stayed less time in the open arms than control rats, moreover, they showed a decrease in immobility and an increase in swimming suggesting that lead exposure did not induce depressive-like behavior in rats.

Reference [7] showed that lead disrupts cognition through effects on the mesocorticolimbic dopamine pathway and altered HPA axis function may serve as a mechanism for the behavioral and catecholaminergic neurotoxicity associated with lead, as well as for the increased incidence of disease. Moreover, [3] deducted that developmental exposures to low levels of lead can produce gender-specific neurobehavioral deficits.

Lack of lead effects on foetal development and offspring learning when combined with alcohol in the Long-Evans rat was studied by [48] who found that Animals given lead only had longer first trial latencies in the passive avoidance test. On contrary, effects of exposure to low-level lead on spatial learning and memory and the expression of mGluR1, NMDA receptor in different developmental stages of rats was studied by [46] and suggest that exposure to lead in gestation and lactation periods could cause neurobehavioral deficits which

extend to adulthood, and lactation was a more sensitive period for lead exposure.

Developmental lead exposure has profound effects on cognition and behavior. Much is known about effects of lead on hippocampal-mediated behaviors and the influences of developmental timing of exposure and level of exposure as effect modifiers of lead exposure on the brain [38]. From these results it could be concluded that administration of lead acetate to rats in drinking water resulted in deviations in the normal behavior of adult female rats to adapt to their environment and this deviation extend to the offspring of the dam drink water containing lead acetate which was obvious in the form of increment in the time spent in open arms of elevated plus maze and number of entries in open arms of the maze which indicate adaptation.

#### IV. CONCLUSION

It could be concluded that there was behavioral changes due to lead exposure and learning disability in offspring's which decrease with adaptation to the contaminant environment.

#### REFERENCES

- [1] Amin, R. J.; Venkatakrishna-Bhatt, H. and Panchal, G. M. (1993): Effect of lead on anorexia and body weight in albino rats. *Indian. J. Physiol. Pharmacol.* 37:115-120.
- [2] Benlahcen, K.; Sansar, W.; Belhabri, L. and Slimani, M. (2009): Lead in water: Neurotoxicity and stressful effect on wistar rat. *Global Journal of Environmental Research.* 3:52-60.
- [3] Betharia, S. and Maher, T.J.(2012): Neurobehavioral effects of lead and manganese individually and in combination in developmentally exposed rats. *Neurotoxicology.* 33:1117-127.
- [4] Braastad, B. O. (1998): Effects of prenatal stress on behavior of offspring of laboratory and farmed mammals. (Review article). *Appl. Anim. Behav. Sci.* 61: 159-180.
- [5] Correa, M.; Miquel, M.; Sanchis-Segura, C. and Aragon, C.M.G. (1999): Acute lead acetate administration potentiates ethanol induced locomotor activity in mice: The role of brain catalase. *Alcoholism: Clinical and Experimental Research.* 23:799-805.
- [6] Cory-Slechta, D. A. and Widzowski, D. V. (1991): Low level lead exposure increases sensitivity to the stimulus properties of dopamine D1 and D2 agonists. *Brain. Res.* 553:65-74.
- [7] Cory-Slechta, D.A.; Virgolini, M. B.; Rossi-George, A.; Thiruchelvam, M.; Lisek, R. and Weston, D.(2008): Lifetime consequences of combined maternal lead and stress. *Basic. Clin. Pharmacol. Toxicol.* 102:218-227.
- [8] De Marco, M.; Halpern, R. and Barros, H. M.(2005): Early behavioral effects of lead perinatal exposure in rat pups. *Toxicology.* 211:49-58.
- [9] Delville, Y. (1999): Exposure to lead during development alters aggressive behavior in golden hamsters. *Neurotoxicol. Teratol.* 21:445-449.
- [10] Djebli, N.; Slimani, M. and Aoues, A. (2005): Effect of lead exposure on dopaminergic transmission in the rat brain. *J. Toxicology.* 207:363-368.
- [11] Donald, J. M.; Cutler, M. G. and Moore, M. R. (1987): Effects of lead in the laboratory mouse, development and social behavior after lifelong exposure to lead in drinking fluid. *Neuropharmacology.* 26:391-399.
- [12] Ferreira, A.; Pereira, M.; Agrati, D.; Uriarte, N. and Fernandez-Guasti, A.(2002): Role of maternal behavior on aggression, fear and anxiety. *Physiology and Behavior.* 77:197-204.
- [13] Fregoneze, J.B.; Cunha, M.; Bulcão, C.; Ferreira, H. and de Castro e Silva, E.(1994): Acute effect of intracerebroventricular administration of lead on the drinking behavior of rats induced by dehydration or central cholinergic and angiotensinergic stimulation. *Physiol. Behav.* 56: 129-133.
- [14] Friend, T.H. (1991): Symposium: Response of animals to stress. *J. Dairy. Sci.* 74:292-303.
- [15] Ghazi-Khansari, M.; Heidari, I. and Zarrindast, M.R. (1997): Effects of lead exposure on bromocriptine-induced penile erection in rats. *Pharmacol.Toxicol.* 81:81-84.
- [16] Giordano, A.L.; Johnson, A.E. and Rosenblatt, J.S. (1990): Halo-peridol induced disruption of retrieval behavior and reversal with apomorphine in lactating rats. *Physiology and Behavior.* 48:211-214.
- [17] Grignaschi, G.; Mantelli, B.; Fracasso, C.; Arelli, M.; Caccia, S. and Samanin, R. (1993): Reciprocal interaction of 5-hydroxytryptamine and cholecystokinin in the control of feeding patterns in rats. *Br. J. Pharmacol.* 109:491-494.
- [18] Grignaschi, G.; Neill, J.; Petrini, A.; Garattini, S. and Samanin, R. (1992): Feeding pattern studies suggest that d-fenfluramine and sertraline specifically enhance the state of satiety in rats. *Eur. J. Pharmacol.* 211:137-142.
- [19] Hammond, P. B.; Chernauek, S.D.; Succop, P.A.; Shukla, R. and Bornschein, R. L. (1989): Mechanisms by which lead depresses linear and ponderal growth in weanling rats. *Toxicol. Appl. Pharmacol.* 99:474-486.
- [20] Harris, R. B. S.; Zhou, J.; Youngblood, B. D.; Rybkin, I.; Smagin, G. N. and Ryan, D.H. (1998): Effect of repeated stress on body weight and body composition of rats fed low and high fat diets. *Am. J. Physiol.Regul.Integr.Comp.Physiol.* 275:1928-1938.
- [21] Hölscher C. (1999): Stress impairs performance in spatial water maze tasks. *Behav. Brain Res.* 100:225-235.
- [22] Jaramillo LM, Balcazar IB, and Duran C (2012): Using vaginal wall impedance to determine estrous cycle phase in Lewis rats. *Lab Anim (NY).* 41(5):122-128.
- [23] Johnson, A.K. and Thunhorst, R. L. (1997): The neuroendocrinology of thirst and salt appetite: Visceral sensory signals and mechanisms of central integration. *Frontiers in Neuroendocrinology.* 18:292-353.
- [24] Kahloulou, K.; Slimani, M. and Aoues, A. (2009): Behavioral and neurochemical studies of perinatal lead exposed in rat wistar. *European Journal of Scientific Research.* 35: 603-614.
- [25] Kaoud, H. A.; Kamel, M. M. and Abd ELRazek, A.H. (2008): Effect of neurotoxic metals on neurobehavioral and learning ability in rat pups. *J. Egypt. Vet. Med. Assoc.* 68: 1-14.
- [26] Leonhardt, M.; Mathews, S.G.; Meaney, M.J. and Walker, C.D. (2007): Psychological stressors as a model of maternal adversity: Diurnal modulation of corticosterone responses and changes in maternal behavior. *Hormones and Behavior.* 51:77-88.
- [27] Luthamn, J.; Lindquist, E.; Gerhardt, G.A.; Olson, L. and Hoffer, B.H. (1994): Alterations in central monoamine systems after postnatal lead acetate treatment in rats. *Environ. Res.* 65:100-118.
- [28] Maccari, S.; Piazza, P. V.; Kabbaji, M.; Barbazanges, A.; Simon, H. and Le Moal, M. (1995): Adoption reverses the long term impairment in glucocorticoid feedback induced by prenatal stress. *J.Neurosci.* 15:110-116.
- [29] Minneima, D. J. and Hammond, P. B. (1994): Effect of lead exposure on patterns of food intake in weanling rats. *Neurotoxicol. Teratol.* 16:623-629.
- [30] Moore, C. L. and White, R. H. (1996): Sex differences in sensory and motor branches of the pudendal nerve of the rat. *Hormones and Behavior.* 30:590-599.
- [31] Moresco, R. M.; Dallalio, R.; Gandolfi, O.; Govoni, S.; Di Giovine, S. and Trabucchi, M. (1988): Lead neurotoxicity: A role for dopamine receptors. *Toxicology.* 53:315-322.
- [32] Moriceau, S. and Sullivan, R. M. (2004): Unique neural circuitry for neonatal olfactory learning. *The Journal of Neuroscience.* 24:1182-1189.
- [33] Nagymajtenyi, L.; Desi, I.; Schutz, H. and Papp, A. (1998): Consequences of lead exposure of rats during pregnancy, lactation and post weaning. A combined behavioral and neurotoxicological study. *Int.J.Environ.Health.Res.* 8:121-135.
- [34] Nouredine, D.; Miloud, S. and Abdelkader, A. (2004): Effect of lead exposure on dopaminergic transmission in the rat brain. *Int.J.Ch.Neuropsychiatry.* 1:97-105.
- [35] Payne, A. (1976): Social behavior in vertebrates. Heinemann educational books.
- [36] Pellow, S.; Chopin, P.; File, S. E. and Briley, M. (1985): Validation of open-closed arm entries in an elevated plus-maze as a measure of anxiety in the rat. *J. Neurosci. Methods.* 14:149-167.
- [37] Ryzhavsky, B. Y.; Lebedko, O. A. and Belolubskaya, D. S. (2008): Effect of histochrome on the severity of delayed effects of prenatal exposure to lead nitrate in the rat brain. *Bull. Exp. Biol. Med.* 146:267-271.

- [38] Schneider, J. S.; Anderson, D. W.; Talsania, K.; Mettil, W. and Vadigepalli, R.(2012):Effects of developmental lead exposure on the hippocampal transcriptome: influences of sex, developmental period, and lead exposure level. *Toxicol. Sci.* 129:108-125.
- [39] Seddik, L.; Bah, T. M.; Aoues, M.; Benderdour, M. and Slimani, M. (2010): Dried leaf extract protects against lead induced neurotoxicity in wistar rats. *European Journal of scientific Research.* 42:139-151.
- [40] Silbergeld, E. K. and Goldberg, A. M. (1976): *Biology of cholinergic function.* New York: Raven press.
- [41] Stern, J. M. and Lonstein, J. S. (1996): Nursing behavior in rats is impaired in a small nest box and with hyperthermic pups. *Developmental Psychobiology.* 29:101-122.
- [42] Tawari-Fufeyin, P.; Ogie-Odia, E.A.; Asemota, O.C. and Balogun, A.F.(2008): Use of *Amaranthus hybridus* to reduce toxic effects of some heavy metals in guinea pig (*Cavia porcellus*) tissues. *Bioecience Reserch Communications.* 20:277-281.
- [43] Trombini, T. V.; Pedroso, C. G.; Ponce, D.; Almeida, A. A. and Godinho, A. F. (2001): Developmental lead exposure in rats: Is a behavioral sequel extended at F2 generation?. *Pharmacology. Bichemistry. Behavior.* 68:743-751.
- [44] Van Wijngaarden, E.; Campbell, J.R. and Cory-Slechta, D.A. (2009): Bone lead levels are associated with measures of memory impairment in older adults. *Neurotoxicol.* 30:572–580.
- [45] Voig, J. P.; Rex, A.; Shor, R. and Fink, H. (1998): Hippocampal 5-HT and NE release in the transgenic rat TGR (mREN2) related to behavior on the elevated plus maze. *Eur. Neuropsychopharmacol.* 9:279-285.
- [46] Wang, X. M.; Liu, W. J.; Zhang, R. and Zhou, Y. K. (2012): Effects of exposure to low-level lead on spatial learning and memory and the expression of mGluR1, NMDA receptor in different developmental stages of rats. *Toxicol. Ind. Health.*
- [47] Wilson, M. A.; Johnston, M. V.; Goldstein, C. W. and Mary, E. B. (2000): Neonatal lead exposure impairs development of rodent barrel field cortex. *Neurobiology.* 97: 5540-5545.
- [48] Zajac, C.S. and Abel, E.L.(1990):Lack of lead effects on foetal development and offspring learning when combined with alcohol in the Long-Evans rat. *Teratology.* 41:33-41.