



Effect of Cypermethrin Exposure during Gestation on the Learning and Memory Ability of Pups

Priyanka Shuklan¹, Khushboo Chauhan¹, Anshu Raj¹, Sujata Ahlawat¹, Sudesh Rani¹

10.18805/ag.D-6049

ABSTRACT

Background: The objective of the present study was to assess the impact of oral doses of cypermethrin (CYP) given to pregnant female Wistar rats, on the growing pups' cognitive ability and developmental processes.

Methods: Pregnant female rats were divided into four groups: group I was the control group and the remaining three groups were experimental groups that received CYP orally at a dose of 25 mg/kg (group II), 50 mg/kg (group III) and 75 mg/kg (group IV) body weight of rats from gestation day 6 (GD 6) till parturition. Pregnant female rats were closely monitored throughout the experiment to look for behavioural abnormalities, toxicity indicators and mortality.

Result: In 50 mg and 75 mg groups, pregnant females showed some signs of toxicity such as diarrhoea, respiratory distress, tilted neck and convulsion attacks. Less gain in body weight of exposed females was also noted. Additionally, the developmental study reported that the body weight and length of the treated females' pups were significantly reduced. The pups of all experimental group females exhibited a significant increase in their fur arrival and eye-opening times. The results of the Morris water maze (MWM) demonstrated that learning and memory were significantly compromised in pups exposed to CYP during pregnancy. The cognitive ability of pups was negatively impacted due to maternal CYP exposure. Therefore, the current study concluded that CYP exposure during gestation has a detrimental effect on the neurodevelopment of the pups as well as on the behaviour of the mothers.

Key words: Cognitive ability, Cypermethrin, Gestation period, Developmental landmarks, Morris water maze.

INTRODUCTION

Synthetic pyrethroids are more prominently used insecticides in agricultural areas due to their great effectiveness and minimal toxicity to mammals. Two forms of synthetic pyrethroids exist, distinguished by changes in their target location and chemical structure. Type I pyrethroids also known as non-cyano pyrethroids, alter sodium channels in neuronal membranes and cause them to open for comparatively brief amounts of time. The alpha-cyano group found in type II pyrethroids causes a greater delay in sodium channel inactivation, which prolongs the depolarization of the neuronal membrane (Hocine *et al.* 2016). Type I pyrethroids generally cause tremors, while Type II pyrethroids containing the α -cyano group cause salivation/choreoathetosis syndrome (Morgan *et al.* 2018). Cypermethrin is a member of type II Synthetic Pyrethroids. It is commonly used to kill agriculture and domestic pests (Carriquiriborde *et al.* 2007). It is neurotoxic and targets the central nervous system of mammals and insects (Ray, 2001). Cypermethrin has become one of the most used insecticides since its introduction in developing countries such as Egypt, Saudi Arabia, Nigeria, the Caribbean and India (Madu, 2015). Due to this, there is an increasing risk of contamination of food with insecticides and contaminated food may harm humans and domestic animals. Despite their low toxicity, persistent use of insecticides may be dangerous to mammals (Usmani and Knowles, 2001). Rats exposed to type II acute pyrethroid poisoning orally or intravenously exhibit salivation, increased jaw opening, rolling gait due to increased

¹Department of Zoology, Maharshi Dayanand University, Rohtak-124 001, Haryana, India.

Corresponding Author: Sudesh Rani, Department of Zoology, Maharshi Dayanand University, Rohtak-124 001, Haryana, India. Email: sudeshrani.zoo@mdurohtak.ac.in

How to cite this article: Shuklan, P., Chauhan, K., Raj, A., Ahlawat, S. and Rani, S. (2024). Effect of Cypermethrin Exposure during Gestation on the Learning and Memory Ability of Pups. *Agricultural Science Digest*. 1-8. doi: 10.18805/ag.D-6049.

Submitted: 07-05-2024 **Accepted:** 31-08-2024 **Online:** 13-12-2024

extensor tone in hind limbs, tremors and impaired coordination followed by tonic seizures and death. There is evidence that type II pyrethroid exposure causes memory impairments in rats (Nieradko-Iwanicka and Borzêcki, 2008). There is ample evidence of pyrethroid exposure in children, newborns and pregnant women (Berkowitz *et al.*, 2003). Pyrethroid exposure raises the risk of fetal toxicity and embryonic resorption (Joya and Sangha, 2016). The mother's cypermethrin exposure had an impact on the body and organ weight of the offspring (Huang and Li, 2014). Increments in pre and post-implantation losses, reduction in the implantation sites, corpus luteal and early mortality rate in pyrethroids-exposed rats were also noted (Ahmad, 2010). Research has demonstrated that mothers who were engaged in farming practices either before or during the first three months of gestation have a greater chance of having children with nervous system defects, mouth clefts, or numerous malformations (Ramon-Yusuf *et al.* 2017).

Cypermethrin can pass through the placenta and impact physiological processes linked to the development of the fetus's nervous system (Dewailly *et al.*, 2014) and fetal weight (Madu, 2015). Pesticide exposure is linked to diseases that manifest later in life (such as neurodegenerative disorders) as well as ailments that begin in childhood. In the previous study, it was reported that the herbicide atrazine toxicity also leads to memory impairment (Rastegar-Moghaddam *et al.*, 2018). Cyfluthrin exposure can cause nerve damage, leading to impairments in learning, memory, spatial exploration and autonomic motor function (Xie *et al.*, 2023). Acute and chronic exposure to chlorpyrifos causes cognitive impairment in animal models (Yan *et al.*, 2012). Learning and memory impairment in rats were studied by different scientists on different pesticide exposure using different behaviour tests but very few studies were conducted to find out the effect of synthetic pyrethroids exposure on the learning and memory of rats. Thus, the current study was created to evaluate the spatial learning and memory of pups whose mothers were treated with CYP during gestation. The cognitive ability of pups was studied using the MWM task.

MATERIALS AND METHODS

Name of the institute

The research was carried out at the Zoology Department, Maharshi Dayanand University, Rohtak.

Research period

1.5 to 2 years.

Chemicals

Cypermethrin (25 %EC), was acquired from the pesticide shop in Rohtak. Following the previously published studies (Sangha *et al.* 2013) with a few minor alterations, the doses for the current investigation were selected. As a result, the doses of 25 mg/kg, 50 mg/kg and 75 mg/kg body weight of rats were chosen as the low, medium and high doses, respectively.

Animals

From the disease-free small animal house at the Lala Lajpat Rai University of Veterinary and Animal Science in Hisar, Haryana, twenty-four fertile male and female Wistar albino rats (3 to 4 months old) were purchased. They were kept in plastic polypropylene cages under control conditions of temperature (25°C), humidity, proper ventilation and a 12-hour light/dark cycle. Animals were allowed to feed on standard laboratory food pellets and ad libitum to drinking water. The Institutional Animal Ethical Committee of M.D.U. Rohtak has approved the protocol used in this study. Animals were acclimatized for one week before the conduction of the experiment.

Mating

Oestrus female and fertile male rats were placed in one cage in the ratio of (2:1) for the mating. The vagina of the

female was checked daily for the vaginal plug. The presence of spermatozoa in the females' vaginal fluid confirmed that they had successfully mated. Vaginal plug presence is regarded as gestational day 0 (GD0) and daily gain in weight and belly size is further confirmation of pregnancy.

Experimental design

Pregnant female rats were randomly assigned to four different groups, each with 4 rats. Group I served as a control group, receiving no cypermethrin exposure. The experimental groups were designated as Groups II, III and IV. Pregnant females of the experimental groups received CYP orally at 25 mg/kg, 50 mg/kg and 75 mg/kg body weight (BW) from gestation day 6 till parturition. Doses were freshly prepared daily, dissolved in water and then given according to the body weight of the rats. Behavioural activity, food consumption, water intake and body weight were closely monitored throughout the prenatal stage. After parturition, the growth and development of pups were studied for one month. Parameters such as litter weight, litter size, opening of eyes and the arrival of fur in control and treated groups were recorded. The MWM was used to examine the cognitive ability of the pups after a month.

Behavioral test

Learning and memory of control and CYP-treated animals were studied through the Morris water maze (MWM) followed by Vorchees and Williams, (2006) with slight modifications. Five different tests were performed by the pups in MWM such as spatial acquisition test, reversal spatial acquisition test, discrimination learning test, latent learning test and trial-dependent working and memory test. All MWM test was performed by the pups of control and cypermethrin-treated female rats after one month of birth to check the effect of CYP on the learning and memory of pups.

Statistical analysis

The data was shown as mean $\pm$ SE. Tukey's post hoc comparisons test and one-way analysis of variance (ANOVA) were utilized to assess the statistical significance of variations in the mean values of the experimental and control groups. At $p \leq 0.05$, $p \leq 0.01$, $p \leq 0.001$ and $p \leq 0.0001$, the difference was statistically significant.

RESULTS AND DISCUSSION

Changes in body weight and behavior of pregnant females during the gestation period

Following CYP treatment during the gestation period, no evident adverse symptoms were observed in the lower dose (25 mg) group females. However, mild nausea, irritability and salivation were observed during the last days of gestation. In the 50 mg and 75 mg groups, pregnant females showed less intake of food and water, diarrhoea, respiratory distress and a tilted neck. The observed signs of toxicity in the current study show similarity with the results of previous study (Madu, 2015). Similar results were also noted in the study of Ramon-Yusuf *et al.* (2017) where

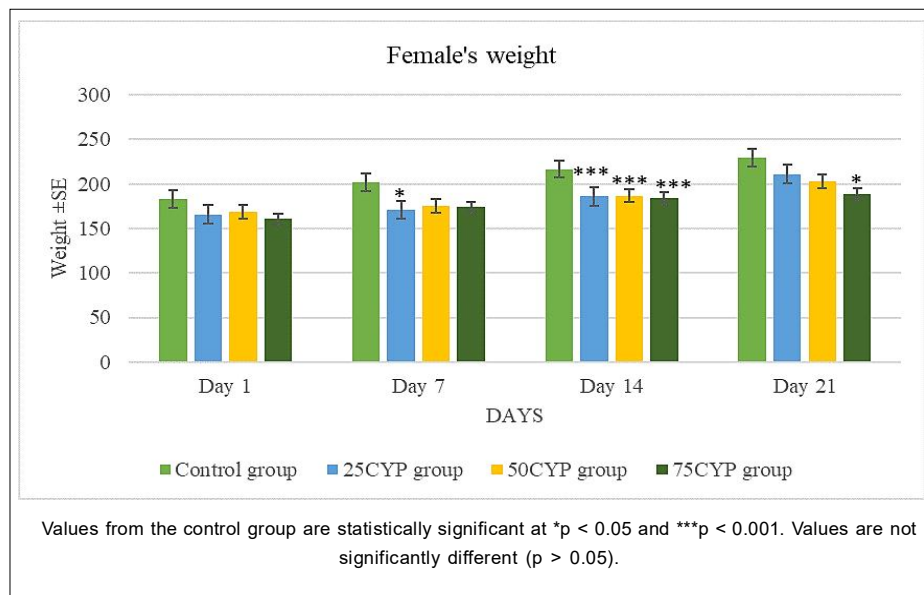


Fig 1: The data was expressed as the average weight of pregnant female rats $\pm$ SE of the control and CYP-treated experimental groups from day 1 to day 21.

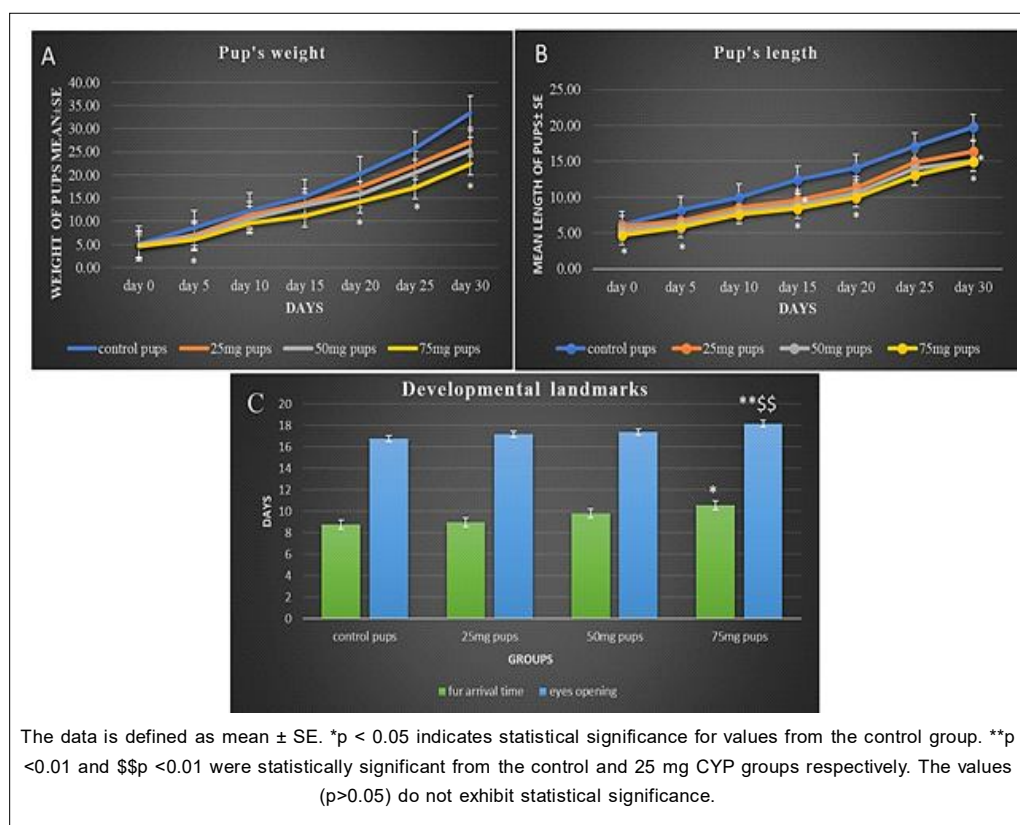


Fig 2: (A) Represented the weight of the pups in the control and CYP-treated groups. (B) Represented the length of the pups in the control and CYP-treated groups. (C) represented as the mean fur arrival and eye-opening time mean $\pm$ SE of CYP-exposed and control groups.

rats were treated in combination with cypermethrin and dimethoate.

Pregnant females of the control groups showed a significant increase in weight during the gestation period throughout the experiment. However, CYP-treated pregnant females of all experimental groups showed less gain in body weight during the gestation period than control group. 75 mg CYP treated group showed a lesser gain in weight as compared to the lower dose treated group (Fig 1). Mortality was also observed in the 75 mg dose group. Joya and Sangha (2016) also reported less gain in body weight in pregnant females treated with 0.1 mg/kg of deltamethrin. Similar results were noted in the study of Madu (2015).

Growth and developmental study of pups

Control group pups showed a significant increase in their body weight and length. At post-natal day (PND) 5, 20, 25 and 30, the higher dose (75 mg CYP) exposed group exhibited a significant ($p < 0.05$) reduction in their body weight from the control group (Fig 2A). 50 mg and 75 mg CYP exposed group denoted a significant ($p < 0.05$) decrease in their body length from the control group (Fig 2B). CYP treated group showed a lesser gain in their body weight and length. The growth and developmental findings of the current investigation were consistent with the results of previous studies (Joya and Sangha, 2016; Madu, 2015; Savithri *et al.*, 2014). The body fur arrival time and opening

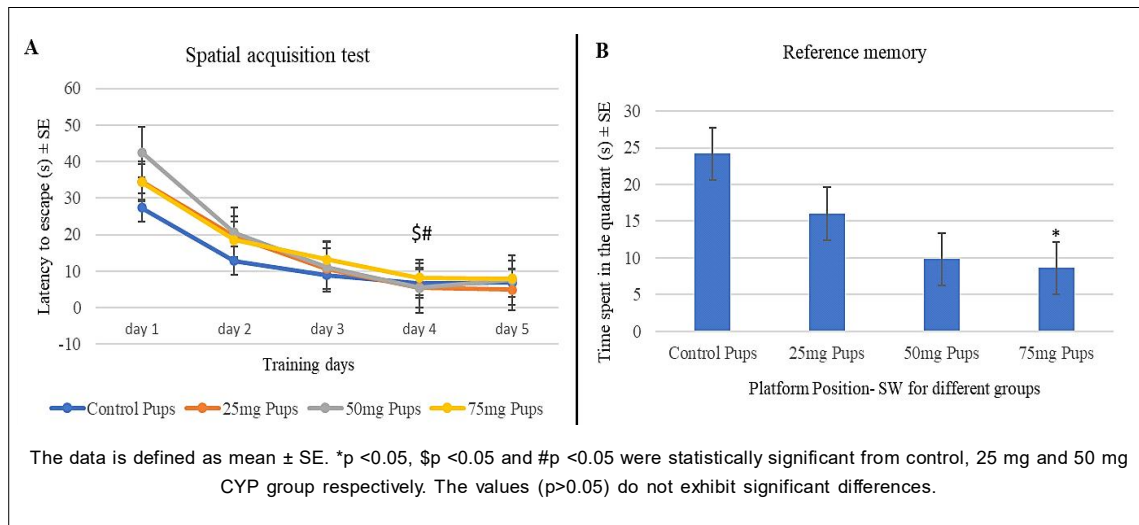


Fig 3: (A) represents the escape latency of pups in the spatial acquisition test from day 1 to day 5 between the control and CYP-treated groups. (B) represents how much time the pups spend in the platform area.

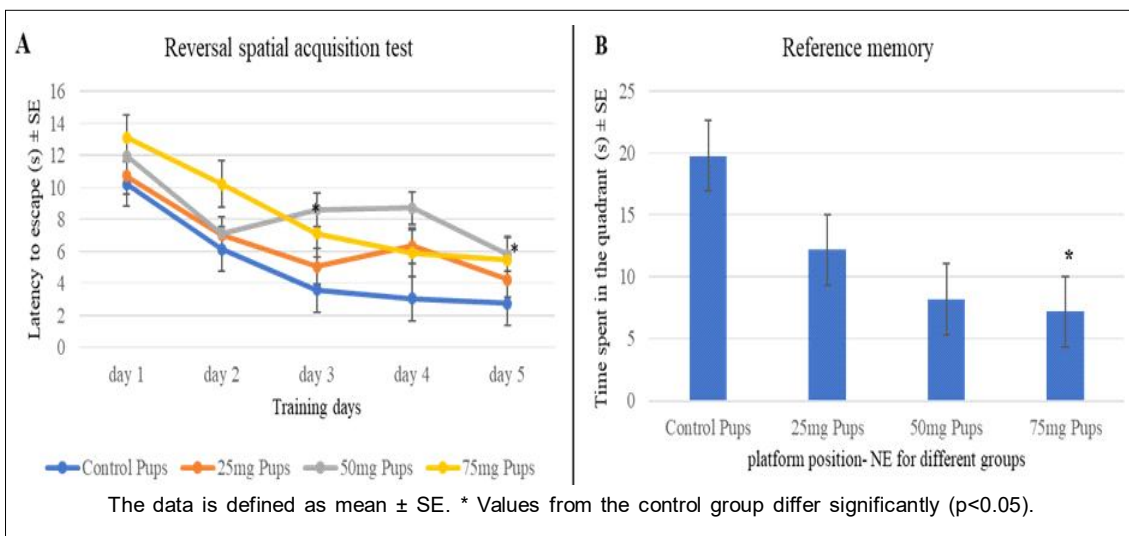


Fig 4: (A) represents the escape latency of pups in the reversal spatial acquisition test between the control and CYP-treated groups. (B) represents how much time the pups spend in the platform area.

of the eyes were found slightly delayed in the treated group as compared to the control group. 75 mg CYP treated group pups' eye-opening and fur arrival time was also found significantly different ($p < 0.01$) from the control and 25 mg CYP group (Fig 2C). A significant delay in developmental landmarks after deltamethrin exposure was also noted in previous studies (Joya and Sangha, 2016; Lazarini, 2001).

The growth of 75 mg CYP-treated female pups was comparatively less than the lower dose-treated groups. Body texture, size and behavioral activity were also different in the CYP-exposed group compared to the control group. Mortality was also reported in the experimental group's pups, this parameter was recorded as high in the 75 mg CYP-treated group and at some extent in the 50 mg group. The observed mortality of the offspring was found to be similar to the findings of (Savithri *et al.*, 2014).

Learning and memory study using MWM

From the results of the MWM task, it was observed that the performance of the control group pups was better than CYP-treated group pups.

In the spatial acquisition test, less time was taken by the control group pups to reach the platform as compared to CYP-treated group pups (Fig 3A). Reference memory data of the spatial test showed that the control group pups spent more time in the platform area than the CYP-treated group pups which means that the control group pups remember the position of the platform than the CYP-treated group pups (Fig 3B).

Similarly, in reversal spatial tasks better performance was noticed in the case of the control group than in CYP-treated groups (Fig 4A). In the case of experimental groups, 25 mg CYP group performs far better than the 50 and 75 mg group pups. Reference memory data also proved the same thing that controls and 25 mg group pups were able to memorize the position of the platform than the 50 and 75 mg CYP group pups (Fig 4B).

In the discrimination learning test, pups have to differentiate between true (static) and false (floating) goals. From the data, it was observed that the control group pups chose a static platform over a floating platform in most trials but CYP-treated pups chose more floating trials as compared to the control group pups (Fig 5C). On 1st day of the trial, all group pups take more time to reach the goal but on the last or 5th day of the trial control and 25 mg group pups take lesser time to reach the goal than 50 mg and 75 mg group pups (Fig 5A). Reference memory data also revealed that control group pups also spent more time in the static platform quadrant than experimental group pups (Fig 5B).

In the latent learning task, pups were placed on the platform for 5-10 seconds before each trial so that pups remember the location of the platform. However, it was observed that the 50 mg and 75 mg group pups performed poorly even after placing the pups on the platform before starting the trials. The performance of the control and 25 mg group was comparable in this task (Fig 6A). Reference memory data explained that the control group

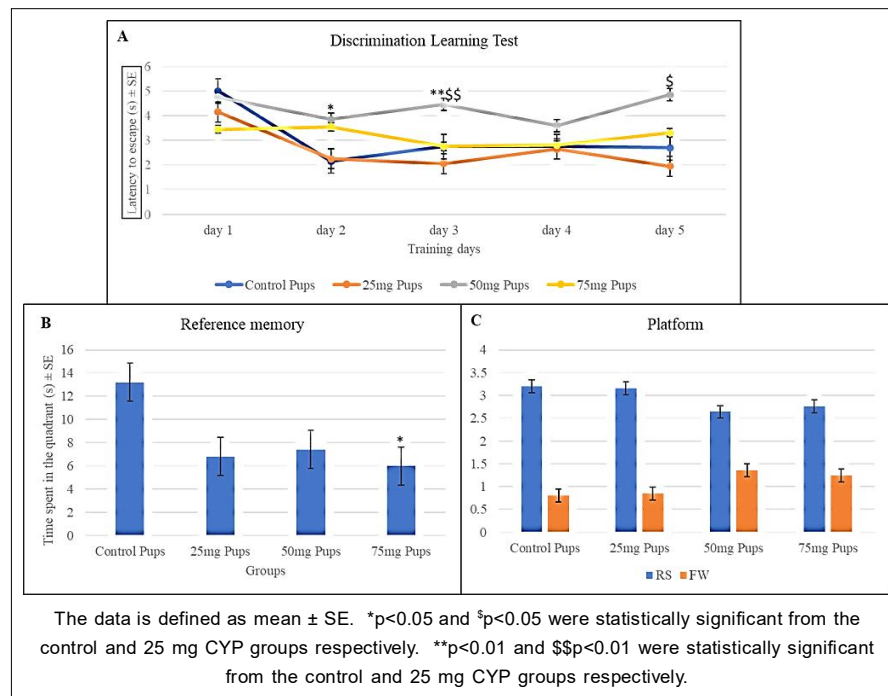


Fig 5: (A) represents the escape latency of pups in the discrimination learning test between the control and CYP groups. (B) represents how much time the pups spend in the platform area. (C) represents differentiation between static and floating platforms by pups.

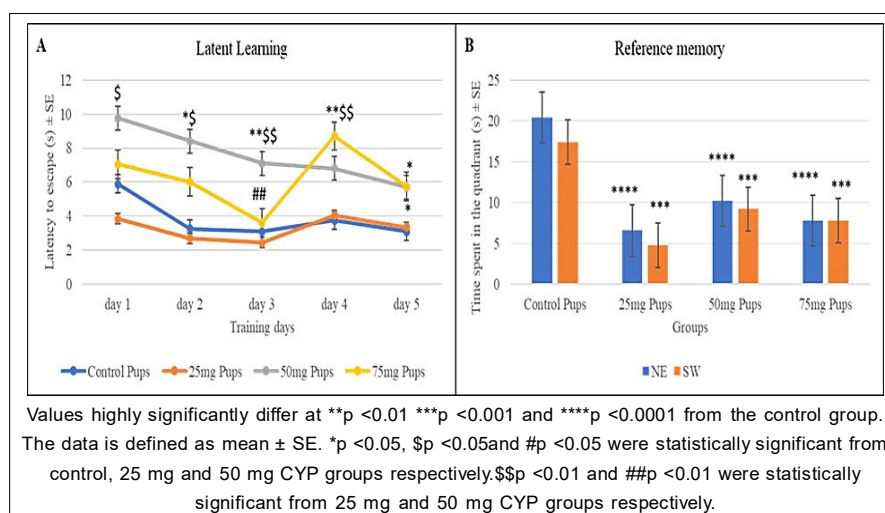


Fig 6: (A) The escape latency of pups in the latent learning test between the control and CYP-treated groups. (B) How much time the pups spend in the platform area.

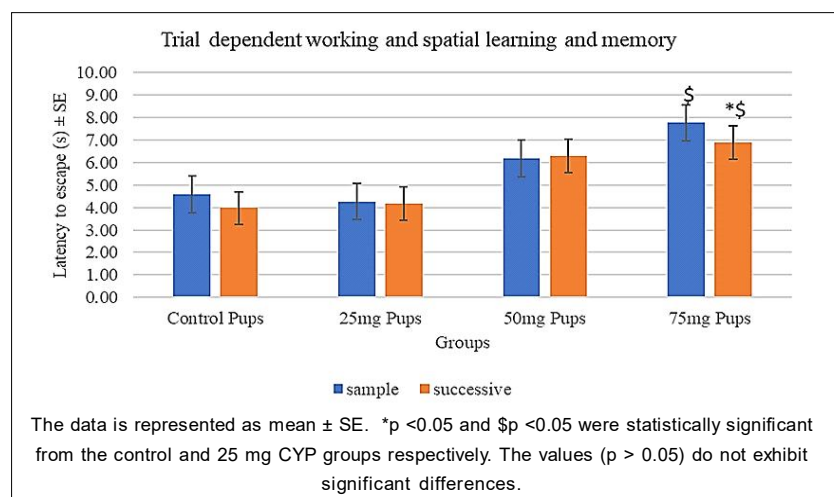


Fig 7: The escape latency of pups in the trial-dependent working and spatial learning and memory test between the control and CYP-treated groups

pups remember both the platform position (SW as well as NE) because control pups spent approximately equal time in both directions but CYP-treated pups significantly ($p < 0.001$) spent more time in the NE direction than SW as in the last 2 days of task platform was located in NE direction so CYP treated group pups able to build up only short memory than control group pups. Time spent by the treatment group in the SW quadrant showed a highly significant ($p < 0.0001$) difference from the control group pups (Fig 6B).

In trial-dependent working and spatial learning and memory tasks, the control group demonstrated superior performance. The 25 mg group's performance was likewise similar to that of control group but 50 mg and 75 mg treated groups performed poorly in this task. They take more time to reach the successive goal than the control

and 25 mg CYP group (Fig 7). From the data of Morris water maze task, it was observed that CYP treatment affects the learning and memory of pups. Terry *et al.* (2003) and Yan *et al.* (2012) also discovered that rats' performance on a spatial learning task was compromised following the treatment to Chlorpyrifos. A mixture of endosulfan and methyl parathion exposure leads to increased latency in searching the platform by the rats (Castillo *et al.*, 2002). In the previous studies, it is clearly stated that CYP exposure leads to nervous toxicity caused by oxidative stress and the generation of free radicals which harms the brain's cellular structure. So, the hippocampus is the crucial component of the brain that plays a vital role in learning and memory and injury to the hippocampus leads to the destruction of the memory. The impairment in learning and memory tasks of the treated group could be due to

impairment in the hippocampus region of the central nervous system (Lu *et al.*, 2021). Rastegar-Moghaddam *et al.* (2018) was also in agreement with our study by stating that atrazine-treated groups spent more time reaching the platform and also remained for less time in the target quadrant as compared to the control group. Similar results were also observed in the study of Zhang *et al.* (2019) where propamocarb fungicide-treated mice spent less time in the target zone and had poor memory. According to Nishiyori *et al.* (2014) a lady who attempted suicide after ingesting pesticides had anxiety and short-term memory problems, which is consistent with our findings.

Additionally, rats exposed to permethrin demonstrated a marked decline in their short-term memory and spatial orientation (Nasuti *et al.*, 2003). Beta-cyfluthrin was found to impair both motor coordination and spatial memory (Syed *et al.*, 2016). According to the current research, animals' ability to learn and remember things is adversely affected by CYP exposure, which is consistent with findings by Gargouri *et al.* (2018). Özdemir *et al.* (2014) found that offspring exposed to clothianidin exhibit low performance in the MWM task, which is in line with the current investigation. The prenatal exposure to melamine also damaged the cognitive abilities of rats. Similar results were also reported in the previous studies (Ghasemnejad-Berenji *et al.*, 2021; Maodaa *et al.*, 2024; Murshed *et al.*, 2023; Wasnik *et al.*, 2023). Xie *et al.* (2023) validated the current investigation by exposing the rats to three different doses (6.25 mg, 12.5 mg and 25 mg/kg) of cyfluthrin and observed a reduction in the spatial learning and memory abilities of rats. According to Imam *et al.* (2018), rats exposed to dichlorvos and chlorpyrifos for 14 days may have neurocognitive impairments and exhibit more anxiety-like behaviors.

CONCLUSION

The current investigation concluded that prenatal exposure to CYP adversely affects the developmental parameters of the neonates. Body texture, weight, length, fur arrival, eye-opening time and behavioral activity of pups were also affected due to cypermethrin. CYP exposure impaired spatial learning and memory of pups. Exposure to CYP has a deleterious effect on the brain development of both adults and pups.

ACKNOWLEDGEMENT

The authors are highly thankful to the Department of Zoology, M.D.U. Rohtak and the Council for Scientific and Industrial Research (CSIR) for their support to carry out the research work.

Conflict of interest

The authors declare that they have no conflict of interest.

REFERENCES

Ahmad, L. (2010). Pathological Effects of Cypermethrin in Rabbits. Ph.D Diss, Dept Pathol, Univ Agric, Faisalabad, Pakistan.

- Berkowitz, G.S., Obel, J., Deych, E., Lapinski, R., Godbold, J., Liu, Z. and Wolff, M.S. (2003). Exposure to indoor pesticides during pregnancy in a multiethnic, Urban Cohort. *Environmental Health Perspectives*. 111(1): 79-84.
- Carriquiriborde, P., Díaz, J., Mugni, H., Bonetto, C. and Ronco, A.E. (2007). Impact of cypermethrin on stream fish populations under field-use in biotech-soybean production. *Chemosphere*. 68(4): 613-621.
- Castillo, C.G., Montante, M., Dufour, L., Martýnez, M. L. and Jiménez-Capdeville, M.E. (2002). Behavioral effects of exposure to endosulfan and methyl parathion in adult rats. *Neurotoxicology and Teratology*. 24(6): 797-804.
- Dewailly, E., Forde, M., Robertson, L., Kaddar, N., Sidi, E. A.L., Côté, S. and Ayotte, P. (2014). Evaluation of pyrethroid exposures in pregnant women from 10 Caribbean countries. *Environment International*. 63: 201-206.
- Gargouri, B., Yousif, N.M., Attaai, A., Bouchard, M., Chtourou, Y., Fiebich, B.L. and Fetoui, H. (2018). Pyrethroid bifenthrin induces oxidative stress, neuroinflammation and neuronal damage, associated with cognitive and memory impairment in murine hippocampus. *Neurochemistry International*. 120: 121-133.
- Ghasemnejad-Berenji, M., Nemati, M., Pourheydar, B., Gholizadeh, S., Karimipour, M., Mohebbi, I. and Jafari, A. (2021). Neurological effects of long-term exposure to low doses of pesticides mixtures in male rats: Biochemical, histological and neurobehavioral evaluations. *Chemosphere*. 264: 128464.
- Hocine, L., Merzouk, H., Merzouk, S. A., Ghorzi, H., Youbi, M. and Narce, M. (2016). The effects of alpha-cypermethrin exposure on biochemical and redox parameters in pregnant rats and their newborns. *Pesticide Biochemistry and Physiology*. 134: 49-54.
- Huang, C. and Li, X. (2014). Maternal cypermethrin exposure during the perinatal period impairs testicular development in C57BL male offspring. *PLoS One*. 9(5): e96781.
- Imam, A., Sulaiman, N.A., Oyewole, A.L., Chengetanai, S., Williams, V., Ajibola, M. I. and Ajao, M.S. (2018). Chlorpyrifos and dichlorvos-induced oxidative and neurogenic damage elicits neuro-cognitive deficits and increases anxiety-like behavior in wild-type rats. *Toxics*. 6(4): 71.
- Joya, J. and Sangha, G.K. (2016). Development and behavioural toxicity of deltamethrin on *Rattus norvegicus* following gestational exposure. *Journal of Applied and Natural Science*. 8(1): 40-45.
- Lazarini, C. A., Florio, J. C., Lemonica, I. P. and Bernardi, M. M. (2001). Effects of prenatal exposure to deltamethrin on forced swimming behavior, motor activity and striatal dopamine levels in male and female rats. *Neurotoxicology and Teratology*. 23(6): 665-673.
- Lu, D., Yu, L., Li, M., Zhai, Q., Tian, F. and Chen, W. (2021). Behavioral disorders caused by nonylphenol and strategies for protection. *Chemosphere*. 275: 129973.
- Madu, E.P. (2015). Teratogenic and embryotoxic effects of orally administered cypermethrin in pregnant albino rats. *Journal of Toxicology and Environmental Health Sciences*. 7(7): 60-67.
- Maodaa, S., Al-Quraishy, S., Abdel-Gaber, R. and Alatawi, A. (2024). Protective effects of *Teucrium polium* leaves ethanolic extract against eimeria papillata-induced behavioral changes in mice. *Indian Journal of Animal Research*. 58(10): 1722-1732. doi: 10.18805/IJAR.BF-1802.

- Morgan, M.K., MacMillan, D.K., Zehr, D. and Sobus, J.R. (2018). Pyrethroid insecticides and their environmental degradates in repeated duplicate-diet solid food samples of 50 adults. *Journal of Exposure Science and Environmental Epidemiology*. 28(1): 40-45.
- Murshed, M., Aljawdah, H.M., Mares, M. M. and Al-Quraishy, S. (2023). *In vivo* anticoccidial efficacy of calotropis procera leaf extract as an alternative treatment against *Eimeria papillate* infection in mice. *Indian Journal of Animal Research*. pp 1-8. doi: 10.18805/IJAR.BF-1607.
- Nasuti, C., Cantalamessa, F., Falcioni, G. and Gabbianelli, R. (2003). Different effects of Type I and Type II pyrethroids on erythrocyte plasma membrane properties and enzymatic activity in rats. *Toxicology*. 191(2-3): 233-244.
- Nieradko-Iwanicka, B. and Borzęcki, A. (2008). Effect of cypermethrin on memory, movement activity and co-ordination in mice after transient incomplete cerebral ischemia. *Pharmacological Reports*. 60(5): 699.
- Nishiyori, Y., Nishida, M., Shioda, K., Suda, S. and Kato, S. (2014). Unilateral hippocampal infarction associated with an attempted suicide: A case report. *Journal of Medical Case Reports*. 8: 1-4.
- Özdemir, H.H., Kara, M., Yumrutas, O., Uckardes, F., Eraslan, E., Demir, C.F. and Bal, R. (2014). Determination of the effects on learning and memory performance and related gene expressions of clothianidin in rat models. *Cognitive Neurodynamics*. 8: 411-416.
- Ramon-Yusuf, S.B., Aliu, Y.O., Salawu, O.A., Chahoud, I. and Ambali, S.F. (2017). Maternal and foetal toxicity induced by exposure to mixture of dimethoate and cypermethrin in albino rats. *Journal of Toxicology and Environmental Health Sciences*. 9(6): 59-65.
- Rastegar-Moghaddam, S.H., Mohammadipour, A., Hosseini, M., Bargi, R. and Ebrahimzadeh-Bideskan, A. (2018). Maternal exposure to atrazine induces the hippocampal cell apoptosis in mice offspring and impairs their learning and spatial memory. *Toxin Reviews*. 38(4): 298-306. <https://doi.org/10.1080/15569543.2018.1466804>.
- Ray, D.E. (2001). Pyrethroid Insecticides: Mechanisms of Toxicity, Systemic Poisoning Syndromes, Paresthesia and Therapy. In: *Handbook of Pesticide Toxicology*. Academic Press. pp. 1289-1303.
- Sangha, G.K., Kaur, K. and Khera, K.S. (2013). Cypermethrin induced pathological and biochemical changes in reproductive organs of female rats. *Journal of Environmental Biology*. 34(1): 99.
- Savithri, Y., Sekhar, P.R., Sravanthi, P.P. and Rao, J.K. (2014). Teratogenic effects of sodium fluoride and cypermethrin synergism in albino mice. *International Journal of Chemical and Pharmaceutical Sciences*. 5: 61-7.
- Syed, F., Chandravanshi, L.P., Khanna, V.K. and Soni, I. (2016). Beta-cyfluthrin induced neurobehavioral impairments in adult rats. *Chemico-Biological Interactions*. 243: 19-28.
- Terry, A.V., Stone, J.D., Buccafusco, J.J., Sickles, D.W., Sood, A. and Prendergast, M.A. (2003). Repeated exposures to subthreshold doses of chlorpyrifos in rats: Hippocampal damage, impaired axonal transport and deficits in spatial learning. *Journal of Pharmacology and Experimental Therapeutics*. 305(1): 375-384.
- Usmani, K.A. and Knowles, C.O. (2001). Toxicity of pyrethroids and effect of synergists to larval and adult *Helicoverpa zea*, *Spodoptera frugiperda* and *Agrotis ipsilon* (Lepidoptera: Noctuidae). *Journal of Economic Entomology*. 94(4): 868-873.
- Vorhees, C.V. and Williams, M.T. (2006). Morris water maze: Procedures for assessing spatial and related forms of learning and memory. *Nature Protocols*. 1(2): 848-858.
- Wasnik, S., Gautam, V., Mishra, P., Sharma, R., Jain, S. and Gond, V.K. (2023). Alterations in biochemical markers of liver and kidney function and oxidative stress indices on sub-acute exposure Meloxicam in Albino rats. *Indian Journal of Animal Research*. pp 1-7. doi: 10.18805/IJAR.B-4981.
- Xie, Y., Zhao, J., Li, X., Sun, J. and Yang, H. (2023). Effects of Cyfluthrin Exposure on Neurobehaviour, Hippocampal Tissue and Synaptic Plasticity in Wistar Rats. *Toxics*. 11(12): 999.
- Yan, C., Jiao, L., Zhao, J., Yang, H. and Peng, S. (2012). Repeated exposures to chlorpyrifos lead to spatial memory retrieval impairment and motor activity alteration. *Neurotoxicology and Teratology*. 34(4): 442-449.
- Zhang, Y., Jin, C., Wang, X., Shen, M., Zhou, J., Wu, S. and Jin, Y. (2019). Propamocarb exposure decreases the secretion of neurotransmitters and causes behavioral impairments in mice. *Environmental Toxicology*. 34(1): 22-29. <https://doi.org/10.1002/tox.22653>.