



# 4<sup>th</sup> International Congress of Turkish Neuroendocrinology Society | ISTANBUL

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## **Chronic high-fat diet affected plasma and hippocampal corticosterone and insulin levels as well as spatial memory in adult male rats: endoplasmic reticulum stress involvement**

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**AIM:** This study assessed the effect of a chronic high-fat diet (HFD) on plasma and hippocampal insulin and corticosterone levels, the hippocampus insulin receptor amount, and spatial learning and memory with or without receiving 4-phenyl butyric acid (4-PBA) in male rats.

**METHODS:** After weaning, the male wistar rats fed high fat or normal diet (ND) for 20 weeks, and based on diet (normal and high fat diet), drug (4-PBA), and its solvent (DMSO) they were divided in to 4 groups. Following 20 weeks of HFD or ND consumption, 4-PBA or DMSO were injected. Then, the spatial memory was investigated. The day after the last memory test, blood samples were collected, in fasting state, to measure plasma corticosterone and insulin concentrations. Eventually, the hippocampus was removed for determining the content of insulin and corticosterone.



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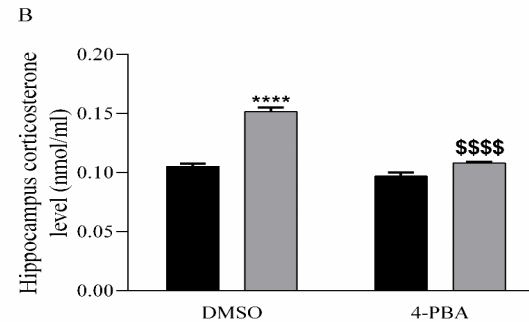
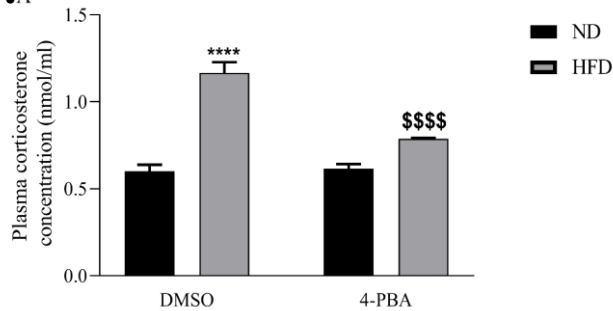
## RESULTS:

The effect of HFD/4-PBA on fasting plasma glucose, insulin and leptin levels, as well as abdominal fat weight

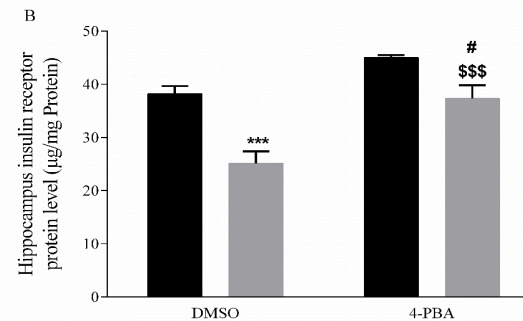
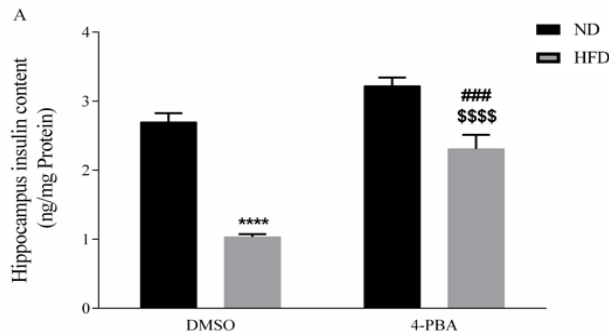
Group	ND+DMSO	HFD+DMSO	ND+4-PBA	HFD+4-PBA
Plasma glucose level (mg/dl)	105.70±3.71	180.50±2.75 <sup>a</sup>	115.70±2.85	110.50±4.26 <sup>b</sup>
Plasma insulin level (µg/l)	1.82±0.10	0.20±0.02 <sup>a</sup>	2.30±0.17	2.21±0.17 <sup>b</sup>
Plasma leptin level (ng/ml)	3.79±0.08	5.22±0.15 <sup>a</sup>	3.90±0.10	4.21±0.16 <sup>b</sup>
Abdominal fat weight (g)	3.17±0.25	10.67±0.29 <sup>a</sup>	3.19±0.19	10.73±0.34 <sup>a</sup>

Each value represents mean±SEM for six rats. <sup>a</sup>P<0.0001, significant difference with ND+DMSO group, <sup>b</sup>P<0.0001, significant difference with HFD+DMSO group. ND = normal diet, HFD= high fat diet, DMSO= Dimethyl Sulfoxide, 4-PBA= 4-Phenyl Butyric Acid.

## RESULTS:A

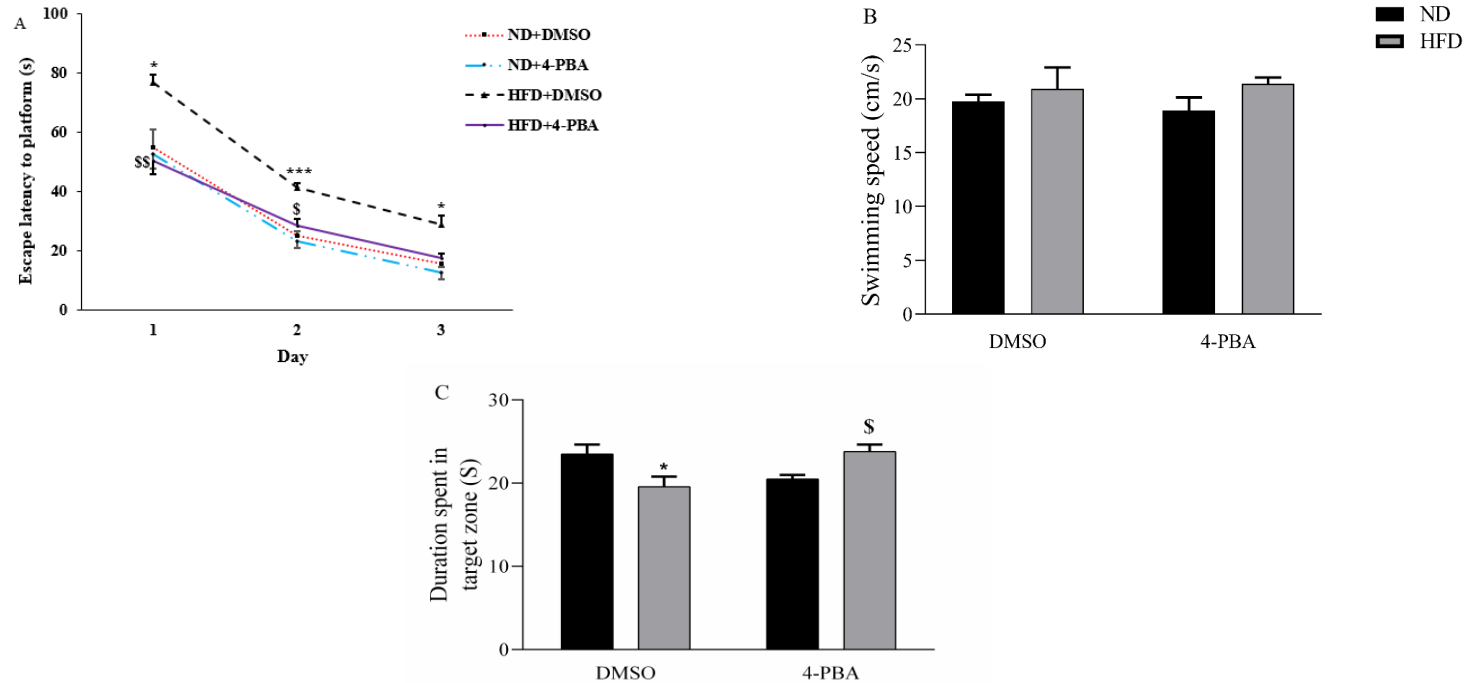


The effect of HFD/4-PBA on (A) plasma and (B) hippocampus corticosterone levels; each column represents mean±SEM for six rats. \*\*\*\*P<0.0001, significant difference with ND+DMSO group, \$\$\$\$P<0.0001, significant difference with HFD+DMSO group. ND = normal diet, HFD= high fat diet, DMSO= Dimethyl Sulfoxide, 4-PBA= 4-Phenyl Butyric Acid.



The effect of HFD/4-PBA on hippocampus insulin (A) content and (B) receptor protein level; each column represents mean±SEM for six rats. \*\*\*\*P<0.0001, \*\*\*P<0.001, significant difference with ND+DMSO group, \$\$\$\$P<0.0001, \$\$\$P<0.001, significant difference with HFD+DMSO group. ###P<0.001, #P<0.05 significant difference with ND+4PBA. ND = normal diet, HFD= high fat diet, DMSO= Dimethyl Sulfoxide, 4-PBA= 4-Phenyl Butyric Acid.

## RESULTS:



The effects of HFD/4-PBA on the (A) time required by the animal for reaching the hidden platform (Escape latency to platform) during three days of MWM test, (B) swimming speed of animals on the probe test day in MWM test and (C) time spent in the target quadrant following the probe test. Each point or column represents mean±SEM for eight rats. \*P<0.05 \*\*\*P<0.001 significant difference with ND+DMSO, \$P<0.05, \$\$P<0.01 significant difference with HFD+DMSO. ND = normal diet, HFD= high fat diet, DMSO= Dimethyl Sulfoxide, 4-PBA= 4-Phenyl Butyric Acid, MWM=Morris Water Maze.



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## CONCLUSION

This study showed that chronic HFD resulted in impaired spatial memory, possibly by reducing plasma insulin concentration and its hippocampal content, and/or elevated plasma and hippocampus corticosterone levels. Since 4-PBA improved these adverse changes, it may be concluded that HFD by inducing ER stress caused these impairments.