

Figure 4: Bar chart showing the number of neurons in CA1, CA3, and DG regions of the hippocampus for Sham, Sham + ALC, Kainate, and Kainate + ALC groups.

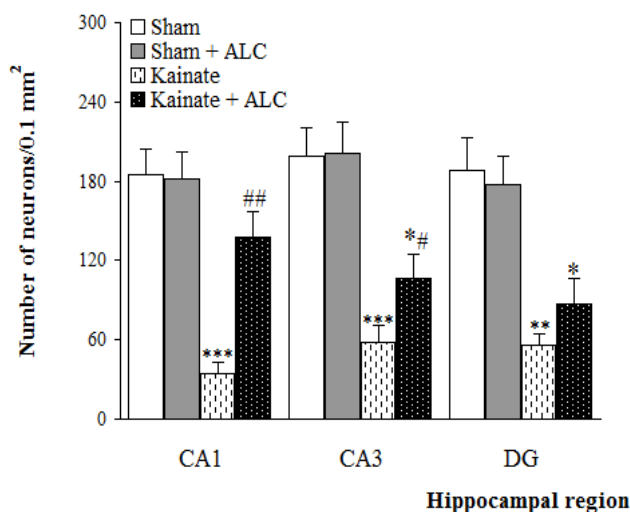


Figure 4: The number of neurons in CA1, CA3, and DG regions of the hippocampus. Sham: Sham group; Sham + ALC: Sham group with ALC; Kainate: Kainate group; Kainate + ALC: Kainate group with ALC. $p < 0.001$ (***) indicates significant difference from Sham; $p < 0.01$ (**) indicates significant difference from Sham + ALC; $p < 0.05$ (*) indicates significant difference from Kainate; $p < 0.05$ (#) indicates significant difference from Kainate + ALC.

The number of neurons in CA1, CA3, and DG regions of the hippocampus was significantly reduced in the Kainate group compared to the Sham group ($p < 0.001$). The number of neurons in CA1, CA3, and DG regions of the hippocampus was significantly reduced in the Kainate + ALC group compared to the Kainate group ($p < 0.05$). The number of neurons in CA1, CA3, and DG regions of the hippocampus was significantly reduced in the Kainate + ALC group compared to the Sham + ALC group ($p < 0.01$).

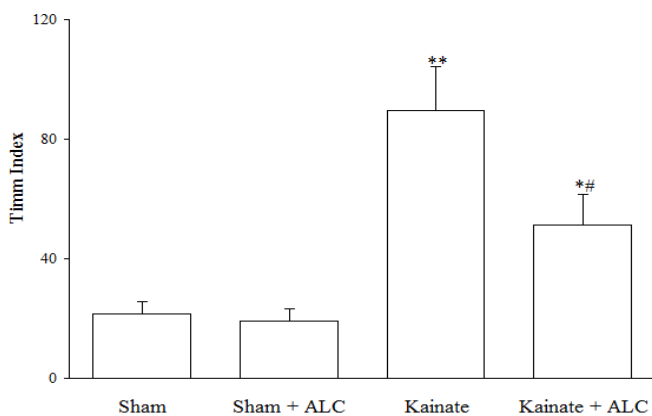


Figure 5: The Timm Index in CA1, CA3, and DG regions of the hippocampus. Sham: Sham group; Sham + ALC: Sham group with ALC; Kainate: Kainate group; Kainate + ALC: Kainate group with ALC. $p < 0.01$ (**) indicates significant difference from Sham; $p < 0.05$ (*) indicates significant difference from Kainate; $p < 0.05$ (#) indicates significant difference from Kainate + ALC.

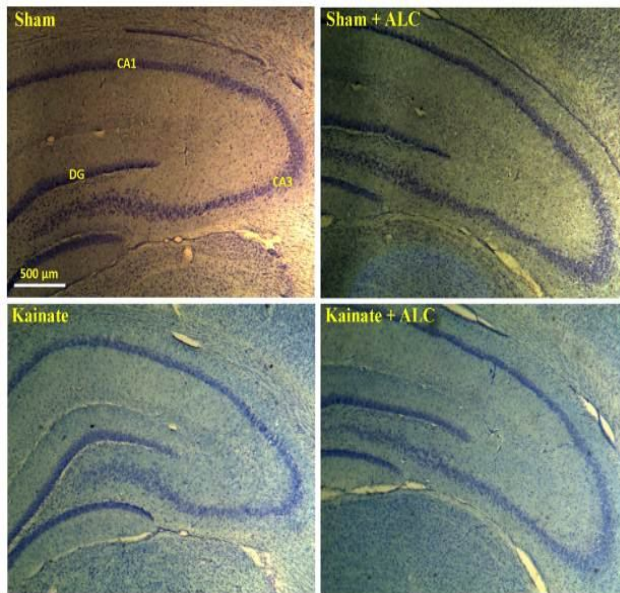


Figure 4 | Histology. The hippocampus was stained with cresyl violet to visualize the CA1, DG, and CA3 regions. Sham control shows normal hippocampal structure. Kainate-induced epilepsy shows significant damage and cell loss in the CA1, DG, and CA3 regions. ALC treatment shows partial recovery of hippocampal structure. Scale bar = 500 μm.

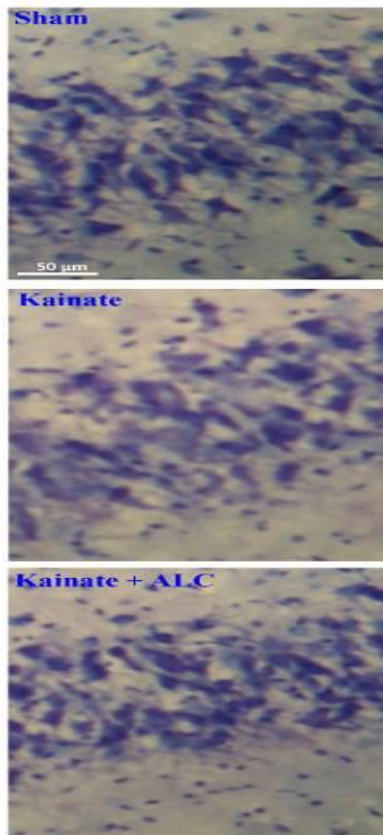


Figure 5 | High-magnification histology. Individual neurons in the CA3 region are shown. Sham control shows healthy neurons. Kainate-induced epilepsy shows neurons with pyknotic nuclei and condensed chromatin. ALC treatment shows neurons with more normal morphology. Scale bar = 50 μm.

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References:

1. Banerjee PN, Filippi D, Allen Hauser W. The descriptive epidemiology of epilepsy-a review. *Epilepsy Res* 2009; 85(1):31-45.
2. Riviello JJ .Classification of seizures and epilepsy. *Curr Neurol Neurosci Rep* 2003; 3(4):325-31.
3. McHugh JC, Delanty N. Epidemiology and classification of epilepsy: gender comparisons. *Int Rev Neurobiol* 2008; 83:11-26.
4. Jefferys JG. Advances in understanding basic mechanisms of epilepsy and seizures. *Seizure* 2010;19(10):638-46.

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5. Dichter MA. Emerging concepts in the pathogenesis of epilepsy and epileptogenesis. *Arch Neurol* 2009; 66(4):443-7.
6. Beghi E. Treating epilepsy across its different stages. *Ther Adv Neurol Disord* 2010; 3(2):85-92.
7. Kim HG, Oh MS. Natural products as potential anticonvulsants: caffeoylquinic acids. *Arch Pharm Res* 2012; 35(3): 389-92.
8. Abdul HM, Calabrese V, Calvani M, Butterfield DA. Acetyl-L-carnitine-induced up-regulation of heat shock proteins protects cortical neurons against amyloid-beta peptide 1-42-mediated oxidative stress and neurotoxicity: implications for Alzheimer's disease. *J Neurosci Res* 2006; 84(2):398-408.

9. Yasui F, Matsugo S, Ishibashi M, Kajita T, Ezashi Y, Oomura Y, et al. Effects of chronic acetyl-L-carnitine treatment on brain lipid hydroperoxide level and passive avoidance learning in senescence-accelerated mice. *Neurosci Lett* 2002; 334(3): 177-80.
10. Vivoli E, Di Cesare Mannelli L, Salvicchi A, Bartolini A, Koverech A, Nicolai R, et al. Acetyl-L-carnitine increases artemin level and prevents neurotrophic factor alterations during neuropathy. *Neuroscience* 2010; 167(4):1168-74.
11. Di Cesare Mannelli L, Ghelardini C, Toscano A, Pacini A, Bartolini A. The neuropathy-protective agent acetyl-L-carnitine activates protein kinase C-gamma and MAPKs in a rat model of neuropathic pain. *Neuroscience* 2010;165(4):1345-52.
12. Barhwal K, Hota SK, Jain V, Prasad D, Singh SB, Ilavazhagan G. Acetyl-L-carnitine (ALCAR) prevents hypobaric hypoxia-induced spatial memory impairment through extracellular related kinase-mediated nuclear factor erythroid 2-related factor 2 phosphorylation. *Neuroscience* 2009; 161(2):501-14.
13. Kobayashi S, Iwamoto M, Kon K, Waki H, Ando S, Tanaka Y. Acetyl-L-carnitine improves aged brain function. *Geriatr Gerontol Int.* 2010;10 Suppl 1: S99-106.
14. Miltiadous P, Stamatakis A, Koutsoudaki PN, Tiniakos DG, Stylianopoulou F. IGF-I ameliorates hippocampal neurodegeneration and protects against cognitive deficits in an animal model of temporal lobe epilepsy. *Exp Neurol* 2011; 231(2): 223-35.
15. Baluchnejadmojarad T, Roghani M. Coenzyme Q10 ameliorates neurodegeneration, mossy fiber sprouting, and oxidative stress in intrahippocampal kainate model of temporal lobe epilepsy in rat. *J Mol Neurosci* 2013; 49(1): 194-201.
16. Xie C, Sun J, Qiao W, Lu D, Wei L, Na M, et al. Administration of simvastatin after kainic acid-induced status epilepticus restrains chronic temporal lobe epilepsy. *PLoS One* 2011; 6(9): e24966.
17. Wu Z, Xu Q, Zhang L, Kong D, Ma R, Wang L. Protective effect of resveratrol against kainate-induced temporal lobe epilepsy in rats. *Neurochem Res.* 2009; 34(8): 1393-400.
18. Shi X, Yao BZ, Liu D. Lipoprotein lipase expression in the hippocampus and its effects on vitamin E levels in rats with epilepsy. *Zhongguo Dang Dai Er Ke Za Zhi* 2010; 12: 377-81.
19. Naziroglu M, Kutluhan S, Uuz AC, Celik O, Bal R, Butterworth PJ. Topiramate and vitamin e modulate the electroencephalographic records, brain microsomal and blood antioxidant redox system in pentylentetrazol-induced seizure of rats. *J Membr Biol* 2009;229:131-40.
20. Cao L, Xu J, Lin Y, Zhao X, Liu X, Chi Z. Autophagy is upregulated in rats with status epilepticus and partly inhibited by Vitamin E. *Biochem Biophys Res Commun* 2009; 379: 949-53.
21. Annadurai T, Vigneshwari S, Thirukumaran R, Thomas PA, Geraldine P. Acetyl-L -carnitine prevents carbon tetrachloride-induced oxidative stress in various tissues of Wistar rats. *J Physiol Biochem* 2011, 67(4):519-30.
22. Hota KB, Hota SK, Chaurasia OP, Singh SB. Acetyl-L-carnitine-mediated neuroprotection during hypoxia is attributed to ERK1/2-Nrf2-regulated mitochondrial biosynthesis. *Hippocampus* 2012, 22(4):723-36.
23. Navarro A, Bandez MJ, Lopez-Cepero JM, Gómez C, Boveris A. High doses of vitamin E improves mitochondrial dysfunction in rat hippocampus and frontal cortex upon aging. *Am J Physiol Regul Integr Comp Physiol* 2011;300(4):R827-34

THE EFFECT OF ACETYL L CARNITINE ON PREVENTION OF HIPPOCAMPAL NEURODEGENERATION AND MOSSY FIBER SPROUTING IN AN EXPERIMENTAL MODEL OF TEMPORAL LOBE EPILEPSY IN RAT

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Received: 9 Jul , 2014; Accepted: 21 Sep , 2014

Abstract

Background & Aims: Temporal lobe epilepsy is due to structural and metabolic changes in hippocampus including marked degeneration of neurons. Considering some evidences on antiepileptic and neuroprotective activity of acetyl L carnitine (ALC), this study was undertaken to evaluate the preventive effect of ALC on structural changes in hippocampus in an experimental model of temporal lobe epilepsy.

Materials & Methods: In this study, 32 rats were divided into sham, ALC-pretreated sham, epileptic, and ALC-pretreated epileptic group. Rat model of epilepsy was induced by unilateral intrahippocampal administration of 4 µg of kainic acid per rat. Rats received ALC (100 mg/kg, p.o) daily for 3 days before surgery. Finally, brain sections were stained with Nissl and Timm methods.

Results: The induction of epilepsy was followed by a prominent seizure and ALC pretreatment attenuated seizure intensity ($p < 0.01$). In addition, density of Nissl-stained neurons in CA1, CA3, and dentate regions of hippocampus was significantly lower in epileptic rats versus sham group ($P < 0.005-0.001$) and ALC pretreatment significantly increased it in CA1 and CA3 regions ($p < 0.05-0.01$). Regarding mossy fiber sprouting, epileptic rats showed a higher degree of sprouting as compared to sham group ($p < 0.005$) and ALC treatment significantly lowered it ($p < 0.05$).

Conclusion: ALC administration has an antiepileptic activity; it preserves neurons in CA1 and CA3 regions, and lowers mossy fiber sprouting in dentate gyrus of hippocampus in kainate-induced epileptic animals.

Keywords: Acetyl L carnitine, Epilepsy, Seizure, Hippocampus, Neurodegeneration, Mossy fiber sprouting

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SOURCE: URMIA MED J 2014; 25(8): 726 ISSN: 1027-3727

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