Hsp60 Response in Experimental and Human Temporal Lobe Epilepsy due to hyppocampal sclerosis

<u>Antonella Marino Gammazza</u>^{1,2}, Gergely Orban^{1,2,3}, Massimo Pierucci^{1,3}, Giancarlo Di Gennaro⁴, Margherita Lo Bello², Roberto Colangeli³, Alfredo D'Aniello⁴, Fabio Bucchieri^{1,2}, Cristoforo Pomara^{5,6}, Arcangelo Benigno², Felicia Farina², Everly Conway de Macario⁷, Giuseppe Di Giovanni^{1,3}, Alberto JL Macario^{1,7}, Giovanni Zummo³, Francesco Cappello^{1,2}

¹Euro-Mediterranean Institute of Science and Technology, Palermo, Italy

² University of Palermo, Department BIONEC, Palermo, Italy

³ Department of Physiology and Biochemistry, University of Malta, Msida, Malta

⁴NEUROMED, IRCCS, Pozzilli, Italy

⁵ Department of Anatomy, University of Malta. Msida, Malta

⁶ Department of Forensic Pathology, University of Foggia, Foggia, Italy

⁷Department of Microbiology and Immunology, School of Medicine, University of Maryland at Baltimore; and

IMET, Columbus Center, Baltimore, MD, USA

Hsp60 is widely distributed in the brain, and its alteration has been involved in different neurological disorders. Epilepsy is considered one of the most common neurological disorders and typically involves the hippocampal formation. Compelling evidence describes a role of mitochondria, oxidative stress and both innate and adaptive immunity during epileptogenesis in temporal lobe epilepsy due to hyppocampal sclerosis (TLE-HS). Here, we investigate the Hsp60 involvement in experimental and human epilepsy. Firstly, expression and distribution of Hsp60 in epileptic hippocampi of a rat model of temporal lobe epilepsy (TLE), based on the phenomenon of maximal dentate gyrus activation (MDA), using western blotting and immunohistochemistry was evaluated. Moreover, the circulating levels of Hsp60 in the plasma derived from the blood of TLE-HS patients before and after epileptic seizure and agematched controls, using ELISA were investigated. Protein level and immunostaining of Hsp60 were increased in both the ipsilateral and contralateral hippocampi of the epileptic rats. The Hsp60 up-regulation was observed on neurons somata and neuropil of the dentate gyrus (DG) and in hippocampus proper (CA3, CA1). Moreover, Hsp60 plasmatic levels in patients after epilepitic seizure, compared to levels of the same subjects before seizure was significantly higher. These results demonstrate that Hsp60 synthesis is increased in response to epileptic seizures and could be used as a biomarker for hippocampal stress response in TLE-HS. In conclusion, our findings suggest that Hsp60 could play an importanty role in TLE-HS and support the possible involvement of immunological factors in epileptogenesis.

Keywords

Temporal lobe epilepsy, Hsp60, stress response, hippocampus.