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BEHAVIORAL AND ELECTROPHYSIOLOGICAL CHANGES INDUCED BY ACETYL-L-CARNITINE IN AGED FREELY-MOVING RATS

G. MARINI, M.CALVANI[1], P. CECCARELLI, AND M. MANCIA

Centro di Ricerca Sperimentale sul Sonno "Giuseppe Moruzzi", Università di Milano, Via Mangiagalli 32, 20133 Milano, Italy; [1] Sigma-Tau Laboratories, Pomezia, Italy

INTRODUCTION

Acetyl-L-carnitine (ALCAR) is the acetyl ester of carnitine (trimethylbetaine of γ-amino-β-hydroxybutyric acid) and is present in mitochondria in the central nervous system (see 3). The close structural similarity of this endogenous substance with acetylcholine (ACh) suggests cholinomimetic properties (28, 1, Brambilla et al., personal communication).

The brain is able to generate oscillations at a wide range of frequencies. Both normal and abnormal synchronized EEG activities depend on intrinsic properties and on synaptic interactions between neurons of the thalamocortical networks which are under the control of the brain stem cholinergic system (13, 27).

Cholinergic mechanisms have long been believed to be involved in electrocortical arousal (6, see for rev. 24). Acetyl-cholinesterase-rich afferents have been found to originate in the brain stem, particularly in the two neuronal groups at the mesopontine junction (pedunculo pontine tegmental nucleus, PPT, and laterodorsal tegmental nucleus, LDT). ACh has been identified as one of the main transmitters in such ascending pathways in different species (see 26). Activation of the ascending cholinergic system is responsible for EEG arousal and behavioral manifestations of attention in the rat too (29, 30).

Although attentive processes in the state of wakefulness are associated with fast (so called beta and gamma) rhythms, lower-frequency oscillations also develop when the animal expects targets that are not yet visible (2).

In some rat strains (e.g. Fischer, Wistar), in the awake but immobile animal generalized highly synchronized EEG patterns emerge. These neocortical rhythms, termed High Voltage Spindles (HVS), first described by Kingberg and Pickenhain (10), are characterized by large-amplitude rhythmic spike-and-wave discharges at 6-9.5 Hz. In view of these electrical characteristics associated with suppression of vigilance, attention, and exploratory activity, the HVSs have been considered an animal model of human "absence" (7).

Corresponding Author: Prof. Mauro Mancia, Via Mangiagalli 32, 20133 Milano, Italy - E-mail: mauro.mancia@unimi.it