Archives Italiennes de Biologie, 142: 541-549, 2004.

UNCOUPLING PROTEINS AND SLEEP DEPRIVATION

C. CIRELLI[1] AND G. TONONI

Department of Psychiatry, University of Wisconsin-Madison, 6001 Research Park Blvd, Madison WI 53719

INTRODUCTION

Fifteen years ago Michel Jouvet showed that in pontile cats, who are poikilothermic, central temperature is the principal factor that regulates the quantity of paradoxical sleep (PS), its ultradian periodicity, as well as the duration of PS episodes (17). Ten years later, Jouvet and colleagues also showed that PS is exquisitely sensitive to conditions that impair oxidative metabolism, and linked the positive effect of hypothermia on PS to its ability to reduce metabolic rate, and to protect the brain against hypoxic alterations and oxidative stress (1). A few months ago, in occasion of the meeting held in Lyon in his honor, Michel Jouvet strongly maintained that the link between sleep regulation, energy metabolism, and thermoregulation should be further explored, because it may hold important clues relative to the functions of sleep. Below is the first study by our laboratory to address this issue, and we dedicate this work to Prof. Jouvet. The paper shows that sleep deprivation has profound effects on the expression of uncoupling proteins, which play a major role in thermoregulation, as well as in the response to oxidative stress.

Long-term sleep deprivation (SD) in rats causes an early increase in food intake and in energy expenditure (EE), followed by a complete loss of body fat, a decrease in body weight, and, ultimately, death (21, 22). In humans, EE is increased in insomniacs relative to normal sleepers (7), and in normal sleepers on nights of poor sleep relative to baseline nights (6). Also, humans affected by fatal familial insomnia, a prion disease characterized by an extreme and prolonged insomnia, show an early increase in EE followed by a decrease in body fat and body weight (20). Thus, SD appears to have significant and consistent metabolic effects in both humans and animals.

In long-term sleep deprived rats the rate of increase in EE correlates negatively with their survival time (21, 22). Most importantly, rats that show a similar increase in EE but are not sleep deprived do not die (21, 22). Thus, the increase in EE during SD is a core element of the syndrome developed when rats are prevented from sleeping, and clarifying its mechanisms may help understand the detrimental effects of prolonged sleep loss.

[1] Corresponding Author: Dr. Chiara Cirelli, University of Wisconsin/Madison, Department of Psychiatry, 6001 Research Park Blvd, Madison WI 53719 - Tel. 608 263 9236 - Fax 608 263 0265 - E-mail: ccirelli@wisc.edu