Intermittent Fasting Changes Energetic Metabolism by Induction of Hypothalamic and Redox Modifications

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Intermittent fasting (IF) is a dietary intervention often used in aging and metabolism studies. It comprises 24 hour cycles alternating ad libitum feeding and fasting. Despite overeating when food is available, IF animals displayed reduced body mass, indicating a lower efficiency of energy metabolism. In this sense, we assessed metabolic effects of IF to uncover the mechanisms involved in feeding control and energetic efficiency. As measured calorimetrically, IF animals presented high metabolic rates during feeding days and increased lipid oxidation on fasting days, which explains the lower body weight. To test if IF-induced effects on energetic metabolism were a consequence of alterations in hypothalamic function, we investigated the expression of neurotransmitters controlling food intake and energy expenditure in hypothalamus. IF animals presented an increased expression of orexigenic neurotransmitters even on feeding days that explains overeating. Levels of the neurotransmitter THR also were changed, and parallel with the feeding-dependent alterations in metabolic rates.

Since the consequences of dietary interventions such as CR on redox balance are well documented and the effects of IF on redox status are not, we also addressed the effects of IF on redox state in different tissues in order to uncover how changes in feeding frequency alter redox balance. Briefly, IF rat livers present increased mitochondrial respiratory capacity along with increased levels of protein carbonyls. Surprisingly, IF animals also presented an increase in oxidative damage in the brain. Conversely, IF promoted a substantial protection against oxidative damage in the heart. No difference in redox homeostasis was observed in skeletal muscle.

Overall, we find that intermittent fasting promotes functional hypothalamic alterations associated with differences in body weight and appetite. In addition, IF affects redox balance in a tissue-specific manner, leading from a redox imbalance in the liver and brain to a protection against oxidative damage in the heart.

Key words: Intermittent fasting, energetic metabolism, hypothalamus