

Metabolismo, Sistemas Modelo y Terapias para la ELA. Tercer Encuentro Internacional de Investigación en ELA en España

Metabolism, Model Systems and Therapies for ALS

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ABSTRACT

Metabolic alteration in ALS

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It is now largely admitted that the successive failures of new therapeutics in ALS may be due to biases in clinical trials' methodology, such as the poor characterization of patients. Some clinical, imaging and biological data may be helpful to better specify some subgroups of patients. Metabolism alteration has been described as a key mechanism potentially linked to most of the known pathophysiological ways in ALS. These metabolic alterations may be observed by a variety of methods such as calorimetry, FDG PET, biochemistry parameters, thus representing an ideal tool to characterize patients. Some authors revealed that more than 50% of patients were hypermetabolic. This hypermetabolism may alter the body composition at diagnosis and is associated with a poor prognosis. Alterations of glucose and lipid metabolism have been reported in ALS patients and mice models and interestingly these modifications have been shown in blood but also in specific tissues such as muscle and brain, using omics strategies or targeted methods. Accordingly, to pursue this promising way, and to accurately highlight the metabolic nodes, several studies focused on metabolism by exploring cells models, thus revealing the brain alteration of lactate shuttle for example. To resume, some clinical and paraclinical parameters have clearly demonstrated metabolism alterations that have prognosis role in ALS patients. These findings have led to more fundamental experiments to deeply characterize the metabolic ways involved. However, therapeutics that target these ways, such as anaplerotic molecules, adapted diet (hypercaloric for example) have not provided convincing results on patients' evolution. This observation confirms that the aetiologies, the consequences and the inter-individual variability of metabolism alteration are not obvious. This promising avenue of metabolism alteration merits a careful attention to link clinical and fundamental data and finally to find the adequate therapeutic strategy.