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Editorial

About the many faces of autism spectrum disorder: from psychoanalysis to biological markers. Could the methionine sulfoxide reductase enzymes play a role?

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ABSTRACT

Autism spectrum disorder is a dramatic condition for the affected children, their families and the entire society. Genetic and environmental factors are involved in its pathogenesis and oxidative stress appears to be the main trigger. Methionine sulfoxide reductase enzymes are physiologically involved in the contrast to oxidative stress and disorders in their expression/activity could result in several diseases. In the fight against autism spectrum disorder, this neglected biochemical feature should be taken into account.

1. Introduction

Autism spectrum disorder is a complex, pervasive, and heterogeneous group of neurodevelopmental conditions. The knowledge about its etiology is limited, but genetic and environmental factors appear to be primarily involved. The human brain is especially vulnerable to oxidative stress because it accounts solely for 2% of body mass but consumes 20% of metabolic oxygen. Therefore, oxidative stress in brain could contribute to neuronal damage in genetically susceptible children, and this seems to be important in the pathophysiology of autism spectrum disorder.[1] Indeed, strong clinical evidence indicates that affected children display high levels of oxidative stress markers in blood cells and serum, and low levels of enzymatic/non-enzymatic antioxidants.[2] Therefore, redox imbalance and oxidative stress could contribute to the pathophysiology of autism spectrum disorder.

The oxidative damage targets many sensitive cellular components, including some proteinogenic amino acids. In particular, L-methionine residues in proteins can be easily converted to L-methionine sulfoxide by oxidation of the sulfur atom, often resulting in the loss of the functional properties of the affected protein. Reconversion of L-methionine sulfoxide to L-methionine is physiologically promoted by methionine sulfoxide reductase (Msr) enzymes.[3] In Homo sapiens, Msr enzymes are ubiquitously expressed in cells and tissues, particularly in the brain, highlighting the strategic role they play against oxidative stress**.** The uncontrolled oxidation of proteins and their accumulation in cells are involved in the etiology and/or progression of a certain number of inflammatory and degenerative human diseases, including Alzheimer's and Parkinson's.[4] Genetic or non-genetic disorders could contribute to this condition, by affecting one of the key factors that contribute to the maintenance of the intracellular redox balance. This hypothesis includes a decrease in the expression or in the activity of Msr enzymes, which would compromise one of the main components of the physiological tool for the contrast to oxidative stress.[5] A novel and effective approach to understanding the origin of autism spectrum disorder should contemplate the investigation of redox processes and their interaction with genetic and environmental factors in the onset and clinical course of this complex syndrome. An important asset in

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research protocols aiming at investigating its etiopathology would therefore be the careful study of Msr enzymes, still poorly characterized but which promise to offer a great impact in all medical knowledge.

2. Ethics Declarations

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