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Review article

Oxidative stress as an etiological factor and a potential treatment target of psychiatric disorders. Part 1. Chemical aspects and biological sources of oxidative stress in the brain

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ABSTRACT

Oxidative stress is a dysfunctional state of living cells, caused by the disturbance of the pro-/antioxidative equilibrium. This dynamic equilibrium, constitutive for all aerobic organisms, is an inevitable necessity of maintaining the level of oxidative factors on non-destructive value to the cell. Among these factors reactive oxygen species (ROS) and reactive nitrogen species (RNS) are the best known molecules. This review article shows the current state of knowledge on the chemical specificity, relative reactivity and main sources of ROS and RNS in biological systems. As a Part 1 to the report about the role of oxidative stress in psychiatric disorders (see Smaga et al., Pharmacological Reports, this issue), special emphasis is placed on biochemical determinants in nervous tissue, which predisposed it to oxidative damage. Oxidative stress can be identified based on the analysis of various biochemical indicators showing the status of antioxidant barrier or size of the damage. In our article, we have compiled the most commonly used biomarkers of oxidative stress described in the literature with special regard to potentially effective in the early diagnosis of neurodegenerative processes.

Contents

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Introduction

A characteristic feature of living cells in aerobic organisms under physiological conditions is existence of a dynamic pro-/antioxidative equilibrium. It is a balance derived from the presence of active oxidative agents and those preventing their action that constitutes the so-called antioxidative barrier. The presence of substances with oxidizing potential, which can be divided into direct oxidants, and indirect prooxidants, is an unavoidable consequence of the participation of oxidation and reduction processes in the most important life activity, that is, metabolism, especially respiration. Pro-/antioxidative imbalance resulting in a gradual increase in pro-oxidants over antioxidants is called oxidative stress [1–3]. There has been growing literature data showing its importance in the pathology of brain disorders.

Reactive species, cellular pro-/antioxidative balance

The most active oxidizing agents: reactive oxygen species (ROS) and reactive nitrogen species (RNS) are produced endogenously as byproducts in one-electron processes and in processes involved in defense against pathogens, and as intracellular and intercellular signaling molecules. Of course, when cells are exposed to a variety of exogenous xenobiotics, ROS and RNS may come directly from the oxidative metabolism of these compounds or their content increases due to the stimulation of the endogenous production in response to exposure.

Hypothetically, five borderline states can be distinguished based on the relationship between the total sum of ROS and RNS concentrations in the cell and the capacity of the antioxidant barrier, and the impact of these relationships on the resultant pro-/antioxidative equilibrium can be deduced. Fig. 1 shows schematically these five cases.

When cellular antioxidative barrier balances the supply of ROS and/or RNS, the equilibrium is maintained. This applies both to the physiological condition without any change in the level of both reactive forms and components of antioxidative barrier (Fig. 1. I), as well as the situation, in which the increase of ROS and/or RNS concentration is accompanied by mobilization of the barrier (Fig. 1. II). Three other cases concern the changes that shift the pro-/antioxidative balance toward more severe oxidative processes resulting either from an increase in the concentration of

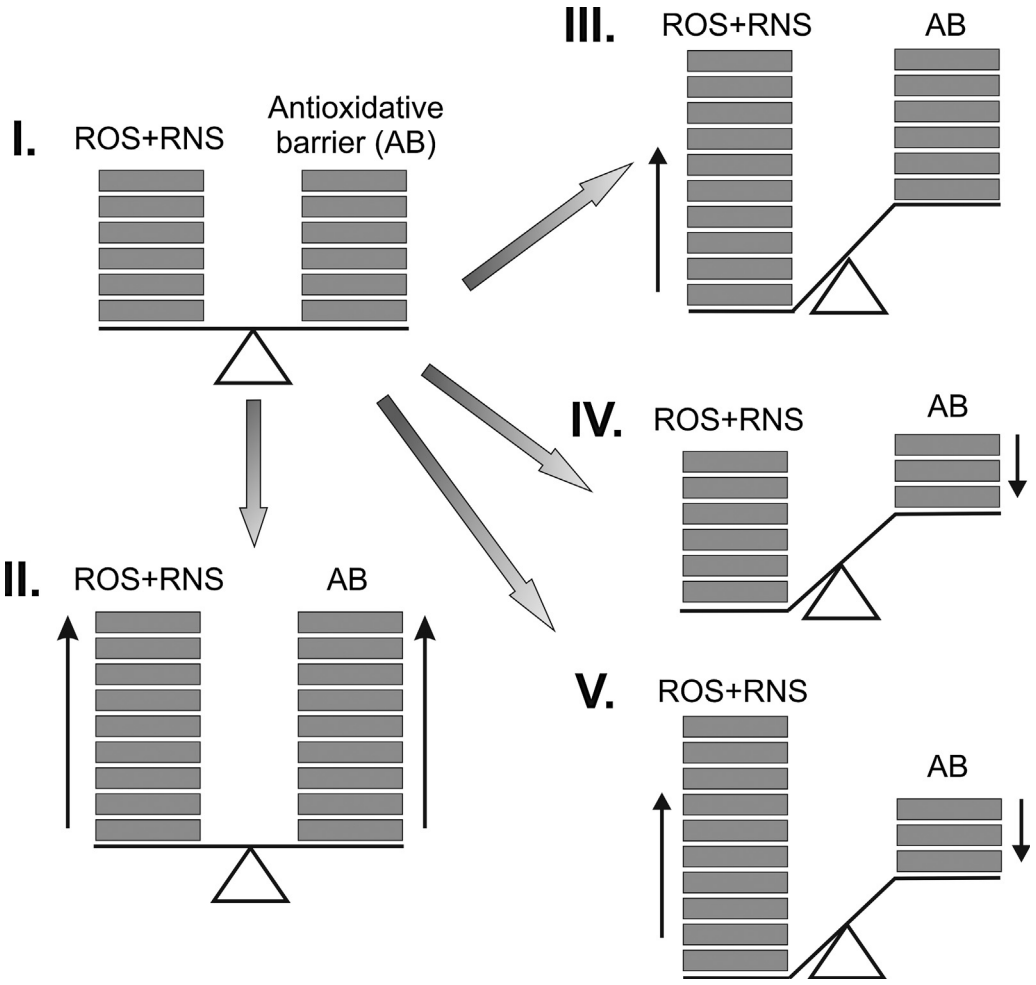

Fig. 1. Five hypothetical states of pro-/antioxidative balance resulting from the mutual relation between sum of ROS and RNS levels, and the capacity of the antioxidative barrier.