Aging- and Oxygen-induced Modifications in Brain Biochemistry and Behavior[a]

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INTRODUCTION

Reactive oxygen species (ROS) have been causally associated with a number of

TABLE 1. ROS Generating Systems that May Catalyze Oxidation of Protein

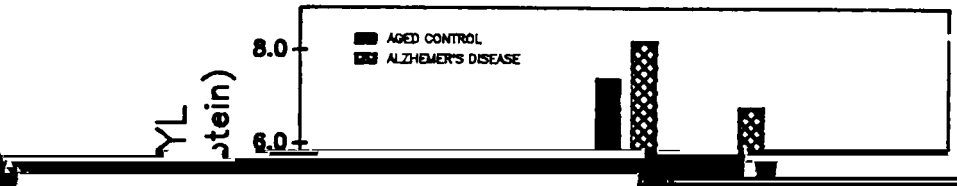
$Fe^{+2} + O_2$
$Fe^{+2} + H_2O_2$
Fe^{+3} + Ascorbate O_2
$NO + O_2^-$
Xanthine Oxidase/hypoxanthine/Fe^{+3}/O_2
NAD(P) H oxidase/WAD(P)H/Fe^{+3}/O_2
Cytochrome P_{450} reductor/cytochrome P_{450}/NADPH/ Fe^{+3}/O_2
SOD/O_2^-

Modified from Stadtman.[26]

certain pathologic conditions (e.g., Alzheimer's disease), and in normal aging, this level of cellular protein oxidation is increased.[13] Furthermore, changes in the level of ROS production may occur in conditions of either insufficient (hypoxia, ischemia) or excess (hyperoxia, hyperbaric oxygen) oxygen.

These findings are highly significant under the supposition that increased ROS

activity by comparison of activity in the presence and absence of adenosinediphos-


AGED CONTROL
ALZHEIMER'S DISEASE
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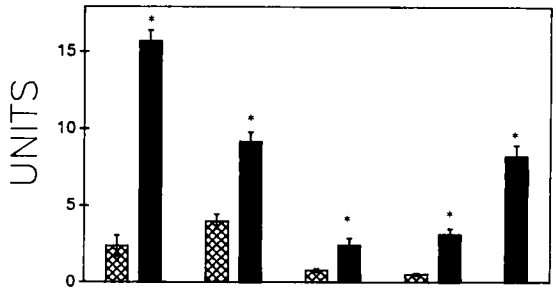
number of commonly observed aging phenomena. An increasingly secure candidate for such a process is the oxidation of normal cellular constituents mediated by ROS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both neocortical DHBA/SA and soluble protein fraction carbonyl content. Paralleling the increased level of oxidized soluble protein, there is a significant loss of MAL-6 binding sites on cytoskeletal protein. Similar changes in MAL-6 binding have been observed in aged red cells and are interpreted to indicate a loss of or damage to the weak binding sites on the surface of cytoskeletal proteins. These changes in ROS production and protein oxidation were paralleled by changes in the level of locomotor activity and radial maze errors.

We have previously reported that aged gerbils are differentially sensitive to IRI with respect to locomotor activity, early gene expression, and metabolic recovery from ischemia.[25] FIGURE 5 demonstrates the consistent, age-related enhanced vulnerability to ROS following IRI. Aged gerbils demonstrated significantly greater