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TESTOSTERONE INDUCES NEUROPROTECTION FROM OXIDATIVE STRESS. EFFECTS ON CATALASE ACTIVITY AND 3-NITRO-L-TYROSINE INCORPORATION INTO α-TUBULIN IN A MOUSE NEUROBLASTOMA CELL LINE

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INTRODUCTION

Neurons are highly polarized cells where microtubules are required for the formation and stability of axons and dendrites (4). Cyclic tyrosination/detyrosination of the C-terminus in α-tubulin subunit is one of the most studied posttranslational modifications of tubulin in dynamic microtubules (5). As is well known, tyrosinated α-tubulin is mainly expressed during neuronal plasticity events (12, 13). Tyrosine analogues can be incorporated into the C-terminus of α-tubulin with consequent possible alteration of the biochemical properties of tubulin, and formation of anomalous microtubules that affect normal cell functions (10). This is the case of 3-nitro-L-tyrosine (3NT), formed by nitration of tyrosine by nitric oxide-derived species following activation of glutamate NMDA receptors. Neural cells show a different sensitivity to nitrosative/oxidative stress agents with subsequent modification in many cellular compartments such as cytoplasmic membrane, nucleus and microtubular network. 3NT increases in many human diseases (7) and both nitrosative and oxidative insults may contribute to neuronal degeneration in various disorders (16). The severe effects of free radicals are kept under check by a delicate balance between the rate of their production and elimination by different antioxidant systems. Any shift in this critical balance could result in an increase in the peroxidative stress leading to cellular damage. Generation of several reactive oxygen species in neurons by glutamate action seems to play a relevant role in cell damage and death. In neurons, the deleterious effects of oxidant species can be controlled and prevented by enzymatic and non-enzymatic antioxidant defence systems. These include enzymes like catalase (2), which breaks down hydrogen peroxide, an oxidizing agent that gives rise to hydroxyl radicals, the most reactive oxygen intermediates.

Gonadal steroids are known to be of primary importance in the normal maintenance of brain functions. The brain seems to be an important target of sexual hormones, since these are able to cross the blood-brain barrier due to their high lipid solubility (25). There is a substantial evidence indicating that sexual hormones can modify cell proliferation, neuroplasticity and vulnerability to neural insults including oxidative stress (20). Sexual hormones exhibit neuroprotective and neurotherapeutic effects on many different populations of neurons in the peripheral and central nervous systems (11). Estrogens and their derivatives have shown

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