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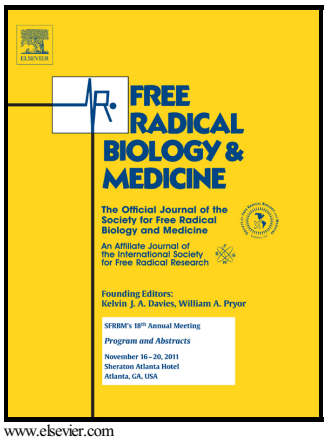

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Ageing-induced changes in the redox status of peripheral motor nerves imply an effect on redox signalling rather than oxidative damage.

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Abstract

Ageing is associated with loss of skeletal muscle fibers, atrophy of the remaining fibers and weakness. These changes in muscle are accompanied by disruption of motor neurons and neuromuscular junctions although the direct relationship between the nerve and muscle degeneration is not understood. Oxidative changes have been implicated in the mechanisms leading to age-related loss of muscle mass and in degeneration of the central nervous system, but little is known about age-related changes in oxidation in specific peripheral nerves that supply muscles that are affected by ageing. We have therefore examined the sciatic nerve of old mice at an age when loss of tibialis anterior muscle mass and function is apparent. Sciatic nerve from old mice did not show a gross increase in oxidative damage, but electron paramagnetic resonance (EPR) studies indicated an increase in the activity of superoxide and/or peroxynitrite in the nerves of old mice at rest that was further exacerbated by electrical stimulation of the nerve to activate muscle contractions. Proteomic analyses indicated that specific redox-sensitive proteins are increased in content in the nerves of old mice that may reflect an adaptation to regulate the increased superoxide/peroxynitrite and maintain redox homeostasis. Analysis of redox active cysteines showed some increase in reversible oxidation in specific proteins in nerves of old mice, but this was not universally seen across all redox-active cysteines. Detailed analysis of the redox-active cysteine in

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