Diabetes, Depression and Oxidative Stress: The Detrimental Triangle

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Background: Diabetes Mellitus is a common metabolic disease. Diabetic peripheral neuropathy (DPN), a complication of the disease, has been shown to affect 50% of the patients. Depression is another complication of diabetes that occurs in some of the patients. The incidence of depression in the diabetic population is higher than that of the non-diabetic. The mechanisms underlying these two complications remain incompletely characterized. Reactive oxygen species (ROS) have been shown to cause myelin damage in the central and peripheral nervous systems in depression and DPN respectively.

Methods and Results: We investigated the role of ROS generated by nicotinamide adenine dinucleotide (NADPH) oxidase enzymes (Nox) in mediating biological responses in both the brains (prefrontal cortices and hippocampi) and sciatic nerves of mice. Our results show that diabetes, depression or diabetes-associated depression cause sensory and motor defects at the level of the peripheral nerves and were associated with altered central and peripheral myelin expression. Increase in both Nox1 and Nox4 levels and activity were recorded resulting in elevated ROS levels. Inhibiting Nox1/Nox4, managed to downregulate ROS production, reversal in myelin injury in the brain and sciatic nerves and more importantly restored the normal sensory-motor phenotype.

Conclusion: Our results indicate that diabetes associated depression cause myelin injury and sensory motor dysfunction through an NADPH-induced ROS mechanism. Our observations suggest a potential therapeutic role of the blockade of the NADPH oxidases system in diabetes and depression.