## Oxidative Stress and Neurodegeneration

• The brain has high susceptibility to oxidative stress due to high metabolic rate and relatively lower regenerative capacity.

• In cases of selective areas of neurodegeneration (seen in ALS, AD and PD), various ROS markers are upregulated - including products of lipid peroxidation, protein nitrosylation (associated with peroxynitrite and superoxide) and iron deposits.

• In AD, reduced activity is observed for SOD, catalase and glutathione antioxidant proteins in affected brain regions. In PD, glutathione levels are found to be reduced.

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• Although the role of ROS in initiating neurodegenerative diseases are unclear, it clearly contributes to events associated with neurodegeneration in a number of ways.

## ROS Production Associated with Amyloid Plaques

Neurodegenerative plaques are a result of misfolded proteins - transfecting plaque-forming proteins associated with AD, LD and ALS have led to increased ROS and/or indices of oxidative stress.

# ROS and Mitochondrial Dysfunction in Neurodegeneration

Effects of disease-associated mutant proteins on mitochondrial components

# Oxidative Stress and Glial Inflammation

• Glial cells are non-neuronal cells found in the brain that respond to cellular damage by releasing cytokines and often creating an inflammatory response.

• Nonspecific glial cell activation is a source of ROS and oxidative stress - mainly hydrogen peroxide and peroxynitrite.

• Increase in microglial activity-induced ROS has been implicated in beta-amyloid toxicity in cultured neurons.

• Sustained p38 MAPK activation in microglia has been associated with increase disease progression in ALS-SOD1 mice.

• May support a role for active immune response in development of neuropathologies.