# Aging sensitizes toward ROS formation and lipid peroxidation in PS1M146L transgenic mice

**JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)**

**ID** 107178
**Author(s)** Schuessel, Katrin; Frey, Claudia; Jourdan, Claudia; Keil, Uta; Weber, Claudia C; Müller-Spahn, Franz; Müller, Walter E; Eckert, Anne
**Author(s) at UniBasel** Eckert, Anne ;
**Year** 2006
**Title** Aging sensitizes toward ROS formation and lipid peroxidation in PS1M146L transgenic mice
**Journal** Free radical biology & medicine
**Volume** 40
**Number** 5
**Pages** / **Article-Number** 850-62
**Keywords** aging, Alzheimer disease, amyloid beta, brain, antioxidant enzyme, lipid peroxidation, lymphocyte, mitochondria, hydroxynonenal, oxidative stress, presenilin, reactive oxygen species, transgenic mouse, transgenic, free radical
Mutations in the presenilins (PS) account for the majority of familial Alzheimer disease (FAD) cases. To test the hypothesis that oxidative stress can underlie the deleterious effects of presenilin mutations, we analyzed lipid peroxidation products (4-hydroxynonenal (HNE) and malondialdehyde) and antioxidant defenses in brain tissue and levels of reactive oxygen species (ROS) in splenic lymphocytes from transgenic mice bearing human PS1 with the M146L mutation (PS1M146L) compared to those from mice transgenic for wild-type human PS1 (PS1wt) and nontransgenic littermate control mice. In brain tissue, HNE levels were increased only in aged (19-22 months) PS1M146L transgenic animals compared to PS1wt mice and not in young (3-4 months) or middle-aged mice (13-15 months). Similarly, in splenic lymphocytes expressing the transgenic PS1 proteins, mitochondrial and cytosolic ROS levels were elevated to 142.1 and 120.5% relative to controls only in cells from aged PS1M146L animals. Additionally, brain tissue HNE levels were positively correlated with mitochondrial ROS levels in splenic lymphocytes, indicating that oxidative stress can be detected in different tissues of PS1 transgenic mice. Antioxidant defenses (activities of antioxidant enzymes Cu/Zn-SOD, GPx, or GR) or susceptibility to in vitro oxidative stimulation was unaltered. In summary, these results demonstrate that the PS1M146L mutation increases mitochondrial ROS formation and oxidative damage in aged mice. Hence, oxidative stress caused by the combined effects of aging and PS1 mutations may be causative for triggering neurodegenerative events in FAD patients.

**Publisher** Pergamon Press ;
**ISSN/ISBN** 0891-5849
**edoc-URL** http://edoc.unibas.ch/dok/A5253464
**Full Text on edoc** No;
**Digital Object Identifier DOI** 10.1016/j.freeradbiomed.2005.10.041
**PubMed ID** http://www.ncbi.nlm.nih.gov/pubmed/16520237
**ISI-Number** WOS:000236426300012
**Document type (ISI)** Journal Article