Oxidative Stress Mediates Sensory Decline

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Our senses dull as we age; we don't see as well, hear as well, or smell or taste as well. Insights from aging in the worm *Caenorhabditis elegans* connect oxidative damage of potassium channels to this process. The potassium channel KVS-1 is present in the worm's nervous system and in the ASE neurons that mediate the chemotactic response to food substances. Cai and Sesti found that, in a reconstituted system, KVS-1's electrophysiological properties were altered by oxidation (application of chloramine T or hydrogen peroxide). Oxidation increased KVS-1 conductance, which would decrease the excitability of the neuron, a change that was due to Cys^{113}, because a C113S mutant channel was resistant to oxidation-mediated changes in electrophysiological properties. By expressing either the wild-type KVS-1 channel or the C113S-KVS-1 channel in *kvs-1*-knockout worms, the authors showed that the loss of chemotactic response due to exposure to oxidants was much more pronounced in the worms expressing wild-type KVS-1 and that incubation with dithiothreitol (DTT) restored chemotaxis in these worms. In contrast, C113S-KVS-1–expressing worms showed a limited decrease in chemotaxis after exposure to oxidants and were largely unaffected by DTT. Electrophysiological analysis of the ASE neurons showed that the potassium currents were altered by application of oxidants in wild-type worms and worms reconstituted with the wild-type KVS-1 but not in those reconstituted with the C113S-KVS-1 channel. As the worms aged, more of the ASE neurons exhibited changes in their electrophysiological properties similar to those caused by exogenous application of oxidants. These changes were largely prevented by reconstitution with the C113S-KVS-1 channel or in worms overexpressing superoxide dismutase and catalase. Thus, accumulated oxidative damage of potassium channels contributes to reduced sensory perception associated with aging in worms.

S.-Q. Cai, F. Sesti, Oxidation of a potassium channel causes progressive sensory function loss during aging. *Nat. Neurosci.* **12**, 611–617 (2009). [PubMed]