

Glycation—a sweet tempter for neuronal death

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Accepted 14 November 2002

Abstract

Glycation, one of the post-translational modifications of proteins, is a nonenzymatic reaction initiated by the primary addition of a sugar aldehyde or ketone to the amino groups of proteins. In the early stage of glycation, the synthesis of intermediates leading to the formation of Amadori compounds occurs. In the late stage, advanced glycation end products (AGE) are irreversibly formed after a complex cascade of reactions. Several AGEs have been characterized chemically, while other new compounds remain to be identified. To date, studies of the contribution of glycation to diseases have been primarily focused on its relationship to diabetes and diabetes-related complications. However, glucose-induced damage is not limited to diabetic patients. Although it does not cause rapid or remarkable cell damage, glycation advances slowly and accompanies every fundamental process of cellular metabolism. It has recently become clear that glycation also affects physiological aging and neurodegenerative diseases such as Alzheimer's disease and amyotrophic lateral sclerosis. Glycation alters the biological activity of proteins and their degradation processes. Protein cross-linking by AGE results in the formation of detergent-insoluble and protease-resistant aggregates. Such aggregates may interfere with both axonal transport and intracellular protein traffic in neurons. In addition, glycation reactions lead to the production of reactive oxygen species. Conversely, glycation is promoted by oxidative stress. We speculate on the presence of synergism between glycation and oxidative stress. In this review, we provide an outline of glycation and propose some possible mechanisms of its cytotoxicity and defense systems against it.

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Theme: Development and regeneration

Topic: Neuronal death

Keywords: Advanced glycation end product (AGE); Alzheimer's disease; Amyotrophic lateral sclerosis; Glycation; Neuronal death