

## Nutritional regulation of glutathione in stroke.

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In contrast to cardiovascular disease, the impact of nutritional status on the prevention and outcome of stroke has received limited investigation. We present a mechanism based on animal studies, clinical data, and epidemiological data by which protein-energy status in the acute stroke and immediate postinjury periods may affect outcome by regulating reduced glutathione (GSH), a key component of antioxidant defense. As cysteine is the limiting amino acid for GSH synthesis, the GSH concentration of a number of nonneural tissues has been shown to be decreased by fasting, low-protein diets, or diets limiting in sulfur amino acids. The mechanism may also be relevant in brain since GSH in some brain regions is responsive to dietary sulfur amino acid supply and to the pro-cysteine drug, L-2-oxothiazolidine-4-carboxylate. The latter is an intracellular cysteine delivery system used to overcome the toxicity associated with cysteine supplementation. These findings may provide the mechanism to explain both the inverse correlation between dietary protein and stroke mortality and the documented association between suboptimal protein-energy status and diminished functional status following a stroke. Future investigations should examine the role of nutritional intervention in neuroprotective strategies aimed at improving stroke outcome. Pharmacological interventions such as L-2-oxothiazolidine-4-carboxylate should be investigated in animal models of stroke, as well as the impact of nutritional status on the response to these agents. Finally, micronutrient deficiencies that may accompany protein-energy malnutrition, such as selenium, should also be investigated for their role in antioxidant defense in cerebral ischemia.

