Identifying and Treating Visual Complications of Diabetes

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Research Abstract
Diabetic retinopathy (DR) with progressive vision loss affects more than 5% of American adults. DR has no effective treatment, likely because it is not diagnosed until after irreversible retinal damage has occurred, and because alleviating the symptoms of diabetes and DR, but not their underlying pathophysiology, is the goal of current therapy. We have overcome these obstacles in animal models of diabetes by showing that non-invasive measures of spatial visual behavior can detect progressive dysfunction, before overt symptoms of diabetes and DR arise, which is accompanied by ultrastructural pathology of retinal pigment epithelium (RPE) cells and their mitochondria. The visual decline and RPE pathology can be reversed with a water-soluble tetrapeptide (MTP-131) that targets the mitochondrial phospholipid cardiolipin and normalizes mitochondrial bioenergetics, without remediating hyperglycemia. Whereas mitochondrial oxidative stress has been postulated as the etiology of DR, ours is the first study to demonstrate a functional benefit from directly treating it. These results have enabled us to hypothesize that RPE mitochondrial dysfunction is an early, distinct and treatable complication of DR.

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