

Public Abstract

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Title:Pupillary Light Reflex Deficits in a Canine Model of Neuronal Ceroid Lipofuscinosis and the Effects of Enzyme Replacement Therapy

The pupillary light reflex (PLR) is a change in pupil size that occurs in response to changes in the amount of light entering the eye. Changes in pupil size are controlled by nerve cells in the retina of the eye and in the brain. We studied the PLR in a dog model of a human neurological disorder called neuronal ceroid lipofuscinosis (NCL). NCL affects both the retina and the brain and causes behavioral and mental changes, seizures, and vision loss. Ultimately, the disease results in death, usually by the early teenage years. Our goal was to use the PLR as a non-invasive tool to monitor disease progression in the dog model and to assess whether experimental treatments are effective in slowing disease progression. By recording videos of the pupil as it responds to light, we found that dogs with this disease have reduced pupil constriction compared with normal dogs. Delivering missing enzyme to the central nervous system normalized the PLR in some of the treated dogs, indicating that this treatment can delay or prevent loss of brain functions. Tools such as the PLR allow us to study diseases and assess the efficacy and safety of treatment approaches in animal models before using them in people with the same disorder. Based on results from this study and concurrent studies that evaluated other measures of pathology in this disorder, enzyme replacement therapy for NCL will begin human clinical trials soon to treat children with this disease.