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Cortical Visual Impairment: New Directions

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Abstract

Cortical visual impairment is the leading cause of bilateral low vision in children in the U.S., yet very little research is being done to find new diagnostic measures and treatments. Dr. Velma Dobson's pioneering work on visual assessments of developmentally delayed children stands out as highly significant in this field. Future research will assess new diagnostic measures, including advanced imaging techniques. In addition, research will evaluate methods to prevent, treat, and rehabilitate infants and children afflicted with this condition.

Keywords

cortical visual impairment

It is particularly apposite that this edition of *Optometry and Vision Science* should choose cortical visual impairment as a topic in an edition devoted to Velma Dobson's antaean efforts to study developmentally disabled and cortically-visually impaired children. Her work to adapt the Teller acuity card procedure to the study of children with special needs is arguably the apotheosis of her amazing career.[1-4] Millions of children have benefited directly or indirectly from her work. In this paper, I will describe future directions for the study of CVI, including changing terminologies, spectrum of injury, diagnostic findings, and treatments. The reader will note from various references that Dr. Dobson continues to play a major role in defining a brighter future for children with CVI.

That so much debate now centers on appropriate terminology for vision loss caused by neurological injury is testimony to improved understanding of the changing spectrum of injury in cortical visual impairment, and speaks to our improving understanding of impairments.[5] Whether neurologic vision loss is termed “cortical visual impairment,” “cerebral visual impairment,” or “retrogeniculate visual impairment” matters less than understanding its pathogenesis and many manifestations. I will use the term, “cortical visual impairment” throughout this text, recognizing that any form of neurological injury in young children, be it cortical or subcortical, ultimately affects the cerebral cortex. In adults with neurologic vision impairment, there is a compelling argument for the term “cerebral blindness,” because damage to optic radiations can lead to blindness and the brain is fully developed, exhibiting much less neuroplasticity. Not so for infants and children. A “cerebral” definition fails to take into account the developing cortical architecture and the influence of damage and pathologies that are downstream to the cortex. The most extreme example of this is amblyopia, wherein an ocular problem causes cortical change and reduced acuity during a critical phase of visual cortex development. But the same holds true for optic radiation damage in young children, where damage to subplate neurons adversely affects synaptogenesis in the visual cortex.[6]

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Quibbling over terminology aside, the study of CVI is advancing thanks to careful observations by people like Dr. Dobson. Long before CVI had become a mainstream diagnosis, she pioneered the use of the Teller acuity card procedure for evaluation of vision function in children with neurologic impairments.[1-4] Today, the diagnosis of CVI hinges in part on measures of grating acuity. A spectrum of acuity deficit exists in populations of children with CVI, so that the perspective that the condition is present, or not; i.e., binary, has been abandoned.[7-8] This will benefit children with CVI, because no 2 children are alike. Each has his or her special needs.

For example, vernier acuity may be selectively affected (compared with grating acuity) in children with CVI.[7] Many children with CVI have improved grating acuity under conditions of lower luminance, suggesting that other mechanisms affect grating acuity thresholds in this population of children.[9] In the future, it may be possible to assess a vision "profile" on individuals with CVI, addressing vision strengths and weaknesses and amassing an evidence-based, and individualized approach to rehabilitation. This assessment will include measures of grating acuity, accompanied by measures of other types of vision functions. Since motor and cognitive disturbances influence the use of vision, these, too, will be a part of the individualized approach to CVI.

In some children, stroke-like findings are present. Clinicians have become used to the child with global central nervous system disruption. Children with diffuse hypoxia and ischemia in infancy are multiply impaired, often with seizures, motor disabilities, and cognitive impairment. Yet there are other clinical patterns that can occur. Gordon Dutton and colleagues have, brought to our attention stroke-like syndromes and selective neurological deficits that occur as part of the CVI picture.[10,11] CVI now clearly occurs along a continuum of visual acuity loss, but also is associated with selective deficitis such as proposagnosia and simultanagnosia. In the future, we will be able to formally assess these deficits, again with an eye to rehabilitation.

Research aimed at preventing CVI is emerging around the world, and early identification of children at risk for CVI is on the near horizon. Already we know that certain interventions may reduce the spread of cortical damage in children with perinatal hypoxia and ischemia. Cerebral cooling, wherein the head or body of children with known hypoxic/ischemic injury is cooled, is under investigation.[12] This approach is based on the concept that inflammation plays an important role in spread of CNS injury after an initial insult to the brain. Inflammation can be reduced by lowering tissue temperatures.

Other interventions will be based on rapid identification of children particularly vulnerable to perinatal hypoxia ischemia. A sort of designer approach to diagnosis and treatment is emerging, wherein those infants likely to be affected by hypoxic injury are selected and treated. Other children not likely to experience damage are prioritized differently. If this seems a canard, consider that a growing body of basic science research suggests that boys, for example, respond quite differently to CNS injury than do girls.[13]

In our own labs, we have learned that in conditions that could cause CNS damage, boys are affected to a greater degree than girls, as measured with evoked potentials. While this data is very preliminary, it offers hope that a functional measure may be applied early in infancy to identify children who may be in particular need of developmental assessment and therapy. One factor that may influence early intervention in infants is sex of the child.

High throughput measures of serum proteins, and genome-wide sequencing, undoubtedly will aid in identification of at-risk children. In the former, proteins that are distributed in serum, for example, can be measured in the setting of CNS injury. Experiments that compare injured to non-injured infants can employ bioinformatics approaches to delineate those proteins that are

expressed during the acute phase of an injury. Then, working backwards, the protein can be sequenced and matched to the gene or genes that have expressed the protein. It barely takes a leap of faith to appreciate that those genes responsible for expressing proteins that affect the disease process can ultimately be silenced or altered in some fashion. The future researcher will have many possible approaches to alter the progression of brain damage based on this proteomic information.

In the genomic approach, genome-wide sequencing can be obtained to compare children who are injured by brain damage to those who are not injured. Polymorphisms and mutations can be evaluated, and eventually a genomic picture of the vulnerable child will emerge. Whereas proteomics requires serum or even tissue, genomic assessments can be run on cells from buccal mucosa at any time in the child's life.

Of course, matching children so that they can be studied and compared will require some quantifiable measure of brain injury. Already, progress is occurring in this realm.[14] Diffusion tensor imaging (DTI) measures water content in regions of interest in the CNS. Myelinated nerve fibers are designed to keep water out, and thus the formation of measurable amounts of water in the brain suggests injury. Water content is a quantifiable index of damage, and can be measured in appropriate regions, for example the optic radiations. Measures of vision function, such as grating acuity, will need to be applied to the continuum of change on DTI scans to learn whether diffusion scans indicate functional damage.

Prevention of diseases that lead to prematurity and hypoxia/ischemia at term is the ultimate goal. But with the incidence of premature infant on the rise and over 11% of all births in the US, we are miles from this goal. Still, it is worth reflecting on health care policies and approaches that could reduce conditions that damage infants. Premature birth can affect any socioeconomic group, but lower socioeconomic status confers significant risk. This is due to poor access to prenatal care. Health care policy that increases access to medical care could have a significant impact on the incidence of all diseases associated with prematurity, not simply CVI.

Today's clinical trials invoke visual acuity measures developed by Dr. Dobson. Her work also promises to take us into the future. The Teller acuity card procedure has been the primary outcome measure for many clinical trials such as the Early Treatment for Retinopathy of Prematurity Study and the Infant Aphakia Study.[15,16] Long after these trials have finished, results tabulated, and new trials begun, Dr. Dobson will continue to influence the world of pediatric low vision. She has influenced so many of us with her rigorous approach to methodology and clear thinking. Her interest in and compassion for those people most in need of help—infants with bilateral vision impairment-is legion. Her participation in our community's scientific process has been immeasurable. Future generations of children will be spared vision injury thanks to her tireless and dedicated work in the field.

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