

Neuroplasticity: Teaching An Old Brain New Tricks

Research shows that adults do, in fact, exhibit neuroplasticity. You can use this innate ability to treat a variety of visual system disorders.

By Dominick M. Maino, O.D., M.Ed.

Goal Statement: Because an adult brain can change, end organs, such as the eye, can be cortically altered, show improvement after insult and injury, and be remediated and enhanced. This paper provides an overview of neuroplasticity and demonstrates how optometrists can take advantage of this innate ability in adult patients.

A “sea change” is a transformation of such magnitude that it alters the very nature of the subject. Recently, we have experienced such a change in the study of neuroplasticity.

The current science of neuroplasticity shows us “a phenomenon where different stimuli lead to an increase or decrease in the number of brain cells and remodeling of synapses,” says Rudraprosad Chakraborty, M.D., D.P.M., senior resident at the Ranchi Institute of Neuropsychiatry and Allied Sciences.¹ “Neuroplasticity research has established, beyond doubt, that instead of being a static cell mass, our brain is actually a dynamic system of neural networks that has the capability of significant growth under favorable circumstances.”¹

Indeed, the brain is not simply a static, soft mass bathed in fluid and surrounded by a hard case. It is not finished in its development once we reach a certain age. The brain can grow. The brain can change—and with that change, end organs, such as the eye and its functional status, can be cortically altered, show improvement after insult and injury, and be remediated and enhanced.

Until very recently, many optometrists and ophthalmologists appeared unwilling to accept this conceptual sea change, when most other clinicians, scientists and lay individuals seemed to have already received the message.²⁻⁵

Critical and Sensitive Periods

In the past, optometrists and ophthalmologists who resist the concepts of neuroplasticity have frequently justified their beliefs by citing the work of Torsten N. Wiesel, M.D., and David H. Hubel, M.D.⁶ This justification rests on the misinterpretation of critical periods, periods of sensitivity and neuroplasticity. Further, this misinterpretation may have resulted in delayed treatments for many functional brain disorders, such as amblyopia.

• **Critical period.** The critical period occurs when an individual is more sensitive to outside environmental influences and stimulation than at most other periods during his or her lifetime.⁷ The concept of a critical period does not imply that neuroplasticity ends at a certain age. The critical period should have a beginning of strong plasticity in response to a sensory experience, a well-defined time period when initiation of plasticity is possible, and a time of reduced sensitivity when plasticity to the same stimulus no longer happens (at the same intensity level). The critical period includes three phases: ⁷

1. The **precritical phase**, which is the initial formation of neuronal circuits that is not dependent on a visual experience.
2. The **critical phase**, a distinct onset of robust plasticity in response to the visual experience, at which time the initially formed circuit can be modified by this experience.
3. **Closure of the critical phase** at which time the same visual experience no longer elicits the same degree of plasticity.

After closure of the critical period, the same degree of plasticity may not be available; however, varying degrees of neuroplasticity, under particular circumstances, may occur at some point in the individual's lifetime.⁷ This is an essential and fundamental concept that is the basis of the sea change in our perspective on neuroplasticity.

perspective on neuroplasticity.

All aspects of the critical period must occur in a precise, chronological manner to attain a maximum result. Nevertheless, animal studies show that both initiation and closure of the critical period may occur at various ages and can be changed or regulated by physiological and molecular manipulation, interference and enhancement.⁷

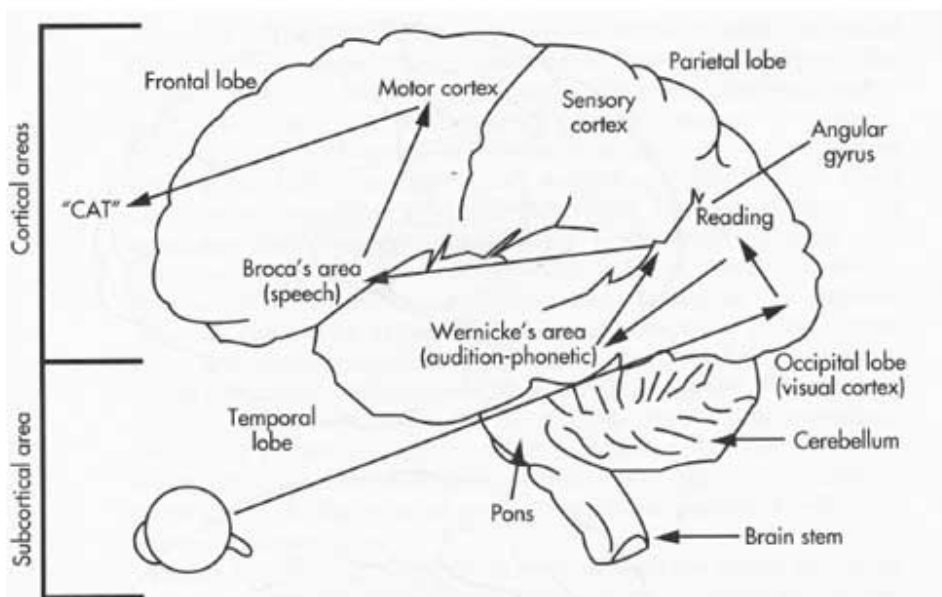
- *Sensitive period.* The sensitive period is somewhat different than the critical period—not only does it begin and end gradually, but also it provides a timeline for maximum sensitivity to stimuli. Sensitive periods may affect how subcortical regions of the visual system develop. For instance, recent studies have found that sensitive periods of visual development are similar to those of cortex development.⁷ This period of synaptic refinement spans the time of initial eye opening; but, it is spontaneous retinal activity, not vision, that drives the resultant changes to the visual system. The concept of a sensitive period also implies that neuroplasticity does not end at a specific age.⁷⁻⁹

Neuroplasticity and the Brain

Can adult brain neurons actually exhibit neuroplasticity? The short answer: yes. Adult neural stem and/or progenitor cells are now known to continuously generate new neurons throughout life in various areas of the mammalian central nervous system.¹⁰ Neurogenesis is necessary for some forms of adult learning, memory and mood regulation to occur. The phrase “life-long learning” should now take on new significance for optometrists. Adults can learn throughout their entire lives. This means that we can make a considerable difference in the lives of all our patients, including adults.

One study suggested that adults taught how to juggle demonstrated a significant transient bilateral expansion of gray matter in the mid-temporal area and the left posterior intraparietal sulcus between baseline brain scan and follow-up.¹¹ The findings were specific to training stimulus; individuals who were not instructed how to juggle demonstrated no change in gray matter over the same period.¹¹ These findings oppose the conventional understanding that the anatomical structure of the adult brain does not change over time (except for alterations in form and structure caused by normal aging or disease).¹¹

In a similar study, the authors noted that long-term bimanual training also increases gray matter volume in experienced adult typists.¹² These results suggest that learning not only affects function, but also structure in adult brains.



With continued sensory processing in the adult brain, lateralization increases, as does the integration between subcortical areas.⁷⁷

Neuroplasticity and Rehabilitation

To improve a patient's brain function and take advantage of any neuroplasticity, Jeffrey A. Kleim, Ph.D., and Theresa A. Jones, Ph.D., suggest that we follow these 10 key principles:¹³

- *Use it or lose it.* If you do not drive specific brain functions, functional loss will occur.
- *Use it and improve it.* Therapy that drives cortical function enhances that particular function.
- *Specificity.* The therapy you choose determines the resultant plasticity and function.
- *Repetition matters.* Plasticity that results in functional change requires repetition.
- *Intensity matters.* Induction of plasticity requires the appropriate amount of intensity.
- *Time matters.* Different forms of plasticity take place at different times during therapy.
- *Salience matters.* It has to be important to the individual.
- *Age matters.* Plasticity is easier in a younger brain, but is also possible in an adult brain.
- *Transference.* Neuroplasticity, and the change in function that results from one therapy, can augment the attainment of similar behaviors.
- *Interference.* Plasticity in response to one experience can interfere with the acquisition of other behaviors.

These 10 principles can play a major role in how we treat our patients after the diagnosis has been made. Now that we know adults can exhibit neuroplasticity, which can result in not only anatomical and physiological changes in the cortex but also in functional changes of behavior, it is appropriate to review the current eye- and vision-care research that supports the concept of neuroplasticity as it applies to clinical optometry.

Neuroplasticity and Optometry

Though the definition of neuro-plasticity may change somewhat between professions and disciplines, Stanislav Trojan, M.D., D.Sc., and Jan Pokorny, Ph.D., have defined neuroplasticity and its various iterations in such a manner that it fits appropriately into the patient care schema of many O.D.s.¹⁴

iterations in such a manner that it fits appropriately into the patient care schema of many O.D.s.¹⁴ They note that mechanisms associated with neuroplasticity can be the result of natural or artificial stimuli, which may occur within an individual's internal or external environment. The end results of these stimuli on neuroplasticity can be positive or negative, and they can occur during development (evolutionary neuroplasticity), after short-term exposure (reactive plasticity), and after enduring or uninterrupted stimuli (adaptational plasticity).¹⁴ They also note that neuroplasticity can occur during functional or structural recovery from damaged neuronal circuits (reparation plasticity).

- Evolutionary neuroplasticity is ideally suited for the developmental O.D. who specializes in vision function as it changes over time, either with or without intervention.
- Reactive plasticity can be thought of as the immediate effect that initial optometric treatment may have on a system. This can be reflected in an immediate, but often transient, change in the individual's accommodative system—i.e., when an uncorrected myope initially puts on his or her new spectacles.
- Adaptational plasticity could describe the long-term effects of in-office optometric vision therapy on disorders of the binocular vision system.
- Reparation plasticity, in contrast to adaptational plasticity, may occur during treatment by a low vision specialist or an O.D. working with those who have experienced a traumatic brain injury (TBI).

Neuroplasticity and Visual System Disorders

Which disorders of the visual system involve neuroplasticity? Almost any anomaly associated with visual development, visual perception or vision function is in this category.

- *Refractive error development.* Several recent studies have noted that neuroplasticity plays a significant role in refractive error development.¹⁵⁻²⁰ This research suggests that numerous external factors, such as retinal defocus, could affect the development of refractive error, and it details how optometric intervention may influence the onset and progression of a variety of refractive errors (i.e., myopia). Previous research on optometric intervention in the development of refractive error yielded mixed results.²¹ However, recent studies have been much more promising. Several clinical trials have suggested that, by altering an individual's vision through the use of progressive addition lenses or ophthalmic drugs, the practitioner can decrease myopia development.²²⁻²⁵

One study showed that progressive lenses significantly reduced the progression of myopia in Chinese children, while another clinical trial produced a similar conclusion for Japanese children.^{22,23} The results from the Correction of Myopia Evaluation Trial (COMET) also showed reduced myopic progression for those who used progressive addition lenses.²⁴ Additionally, one of the latest drug studies that used an M1-antagonist to slow myopia demonstrated nearly a 50% reduction in myopia progression over a two-year period.²⁵

As optometrists, we can and should alter refractive error development by using the tools readily available to us. In the not-too-distant future, additional lens applications, drugs and clinical approaches may be developed.

- *Amblyopia.* The Pediatric Eye Disease Investigator Group (PEDIG) is a research network funded by the National Eye Institute that consists of 80 distinct sites, 132 pediatric ophthalmologists, 52 pediatric optometrists and 11 colleges of optometry. This single entity has done more to dispel the myths and expand the science surrounding amblyopia and its treatment than any other single group in modern history.

One of PEDIG's most significant studies dispelled the myth that amblyopia cannot be treated in older children and young adults (individuals under 18 years).²⁶ The existence of neuroplasticity in older children and young adults allows an optometrist to treat amblyopia at any age. This study also noted that prescribing spectacles is an important first step in the treatment of amblyopia; 25% of the patients demonstrated improvement with glasses alone.

Another PEDIG study concluded that the treatment of bilateral refractive amblyopia with spectacle correction improves binocular visual acuity in children between three and 10 years of age; most improved to 20/25 or better within one year.²⁷ Further, a similar PEDIG paper concluded that strabismic amblyopia can be improved, or even resolved, with spectacle correction alone.²⁸ Once again, these results demonstrate that we can positively alter visual function in our patients by the appropriate use of spectacles.

Is optometric vision therapy an effective form of treatment for amblyopia? Though the necessary clinical trial has yet to be developed, a PEDIG pilot study suggested that performing near activities while patched may be beneficial in the treatment of amblyopia.²⁹ Other PEDIG studies have endorsed the use of atropine and reduced patching time.^{30,31}

use of atropine and reduced patching time.^{30,31}

We can diagnose and treat amblyopia in all our patients, no matter their age. Age may be a factor in how we choose to treat this disorder, but it should seldom dictate the range of available treatment options. Neuro- and cortical plasticity that occurs in the adult brain suggests that our treatment options are open and will continue to grow.

- *Strabismus and non-strabismic, non-amblyopic binocular vision disorders.* Much like PEDIG's work on amblyopia treatments, Mitchell Scheiman, O.D., and his Convergence Insufficiency Treatment Trial (CITT) colleagues have researched new treatments for binocular anomalies. The Randomized Clinical Trial of Treatments for Symptomatic Convergence Insufficiency in Children has clearly demonstrated the superiority of in-office optometric vision therapy (in conjunction with home therapy) vs. out-of-office therapy alone.³² The study concluded that optometric vision therapy/orthoptics was more effective than pencil push-ups or placebo vision therapy/orthoptics in reducing symptoms and improving clinical signs of convergence insufficiency.³² More clinical trials are needed to test how neuroplasticity may be applied to new treatment modalities for binocular vision disorders in patients of all ages.

- *Learning-related vision problems and vision development or perception disorders.* Accepted therapy strategies for learning-related vision problems and vision development or perception disorders are widely supported by non-clinical trial research. This research includes an examination of the role vision plays in reading, the effect of vergence and accommodative therapy on reading eye movements and reading speed, the diagnosis and treatment of perceptual disorders, and the effect of therapy on various learning anomalies.³³⁻⁴³ Current research strongly favors a therapeutic approach that incorporates the principles of neuroplasticity.

- *Vision dysfunction associated with developmental disabilities.* Within both optometry and ophthalmology, there is a lack of documented research regarding proper treatment of special needs patients.⁴⁴ There are many barriers that restrain individuals with disabilities from being full participants in the health-care arena, such as poor training of health-care providers on how to address such patients and the inability of the patients to effectively communicate their symptoms.^{45,46}

Neuroplasticity and Visual System Disorders

Neuroplasticity can play a role in the current and future treatment of the following disorders:

- Refractive error development.
- Amblyopia.
- Strabismus.
- Non-strabismic, non-amblyopic, binocular vision disorders.
- Learning-related vision anomalies.
- Vision development or perception disorders.
- Vision dysfunction associated with developmental disabilities.
- Vision dysfunction associated with acquired brain injury.

The limited research that does exist on this topic notes that many problems might be overcome with the proper education of eye-care professionals.^{47,48} Practitioner education in this area is essential, considering that many patients who suffer from vision information processing dysfunction are special needs patients.⁴⁹⁻⁵⁸

Accommodative dysfunctions and esotropia in patients who have Down syndrome can be managed with multifocal lenses.^{59,60} Also, optometric vision therapy is an effective treatment for both accommodative and functional vision anomalies found in patients with cerebral palsy.⁶¹⁻⁶⁵

Neuroplasticity is present in patients with developmental disabilities and is usually noted in early intervention programs, such as Head Start.^{66,67} Research on neuroplasticity and Down syndrome is currently being examined in animal models, and similar research on cerebral palsy is now being conducted in clinical trials.^{68,69}

For patients with developmental disabilities, neuroplasticity will play a larger role in our treatment protocol; however, more research is needed to determine how we will apply the science of neuroplasticity to these special needs patients.

- *Vision dysfunction associated with acquired brain*

injury. Neuroplasticity should play a major role in your management of patients with acquired brain injury. TBI, cerebral vascular accident, and other forms of cortical insult could have a significant effect on the overall visual function of your patients. Patients with TBI often demonstrate accommodation anomalies, version eye movement dysfunction, vergence dysfunction (both strabismic and non-strabismic), photosensitivity, visual field loss and significant ocular health problems.⁷⁰

Research suggests that we can improve the oculomotor abilities of patients with TBI.⁷¹ But can we

Research suggests that we can improve the oculomotor abilities of patients with TBI.⁷¹ But can we sufficiently rehabilitate their oculomotor skills to perform demanding visual tasks, such as reading? One study showed that optometric vision therapy facilitated rehabilitation of reading-related oculomotor skills and produced significant subjective and objective gains in reading ability.⁷²

Also, neuroplasticity may play a role in the treatment of perceptual anomalies that are often caused by brain injury, such as agnosia, alexia, color dyschromatopsia and prosopagnosia.⁷³ Treatment of these perceptual disorders is often initiated by a psychologist, psychiatrist or physical therapist—not an optometrist. Nevertheless, following treatment, patients with prosopagnosia and alexia have demonstrated functional improvement.^{74,75}

Improving Brain Function and Neuroplasticity

Although the topic of improving brain function and neuroplasticity could be a book unto itself, it must be at least briefly discussed. The belief that there are specific “brain foods” dates back quite a long way—or at least as far back as the lifetimes of our grandmothers who fed us cod liver oil to “cure all ills and make us smart.” Today, we see an increasing abundance of research about the positive systemic and ocular effects of omega-3 fatty acids.⁷⁶⁻⁷⁹ Current research on the overall health benefits of increased omega-3 fatty acids is still somewhat mixed, but several experts believe that increased intake may improve brain functionality.⁷⁹

Interestingly, recent research has shown that certain medications may enhance neuroplasticity. The antidepressant Prozac (fluoxetine, Eli Lilly) has been used to restore plasticity in the adult visual cortex.⁸⁰ Tianeptine, another antidepressant, affects glutamate, which regulates neuroplasticity.⁸¹ Erythropoietin, a glycoprotein hormone, and L-arginine, a precursor of creatine synthesis, may also enhance plasticity.^{82,83} Still, there seems to be no “magic pill” that consistently promotes neuroplasticity.

Conclusion

We have experienced a sea change in the understanding of neuroplasticity. Now, it is evident that we can take advantage of neuroplasticity to help correct many disorders of the visual system—we, as clinicians, simply have to begin utilizing these treatment options for the benefit of our patients.

In the meantime, if there is a magical switch for increasing neuroplasticity, research shows that it involves exercise, practice and exposure to new stimuli.⁸⁴

As for me, I just wanted a simple pill, an easy fix. Unfortunately, it now looks like I have to actually work for my neuroplasticity. See you in the gym or in the library.

Dr. Maino is a professor of pediatrics and binocular vision at Illinois College of Optometry in Chicago, an adjunct professor of pediatrics at the Centro de Optometria in Madrid, Spain, and is in private practice in Harwood Heights, IL. For more information, visit his blog at: www.mainosmemos.blogspot.com.

References

1. Chakraborty R, Chatterjee A, Choudhary S, Chakraborty PK. Neuroplasticity—a paradigm shift in neurosciences. *J Indian Med Assoc* 2007;105(9):513-4,516-8,520-1.
2. Sacks O. A neurologist's notebook. Stereo Sue. Why two eyes are better than one. *The New Yorker* 2006 Jun 19:64-73.
3. Krulwich R. National Public Radio. Going Binocular: Susan's First Snowfall. Available at: www.npr.org/templates/story/story.php?storyId=5507789 (Accessed December 8, 2008).
4. Press LJ. The story behind 'Stereo Sue' and a world-famous neurologist's discovery of vision therapy. *Optom Vis Dev* 2006;37(2): 55-7.
5. Levin HS. Neuroplasticity and brain imaging research: implications for rehabilitation. *Arch Phys Med Rehabil* 2006 Dec;87(12 Suppl 2):S1.
6. Wiesel TN, Hubel DH. Single-cell responses in striate cortex of kittens deprived of vision in one eye. *J Neurophysiol* 1963 Nov;26:1003-17.
7. Hook BM, Chen C. Critical periods in the visual system: Changing views for a model of experience-dependent plasticity. *Neuron* 2007 Oct;56(2):312-26
8. Ramey CT, Ramey SL. Prevention of intellectual disabilities: early interventions to improve cognitive development. *Prev Med* 1998 Mar-Apr;27(2):224-32.
9. Heuninckx S, Wenderoth N, Swinnen SP. Systems neuroplasticity in the aging brain: recruiting additional neural resources for successful motor performance in elderly persons. *J Neurosci* 2008 Jan 2;28(1):91-9.
10. Ge S, Yang CH, Hsu KS, et al. A critical period for enhanced synaptic plasticity in newly generated neurons of the adult brain. *Neuron* 2007 Mar;54(4):559-66.

- adult brain. *Neuron* 2007 May;54(4):559-66.
11. Draganski B, Gaser C, Busch V, et al. Neuroplasticity: changes in grey matter induced by training. *Nature* 2004 Jan 22;427(6972): 311-2.
 12. Cannonieri GC, Bonilha L, Fernandes PT, et al. Practice and perfect: length of training and structural brain changes in experienced typists. *Neuroreport* 2007 Jul 2;18(10):1063-6.
 13. Kleim JA, Jones TA. Principles of experience-dependent neural plasticity: implications for rehabilitation after brain damage. *J Speech Lang Hear Res* 2008 Feb;51(1):S225-39.
 14. Trojan S, Porkorny J. Theoretical aspects of neuroplasticity. *Physiol Res* 1999;48(2):87-97.
 15. Ramamirtham R, Kee CS, Hung LF, et al. Wave aberrations in rhesus monkeys with vision-induced ametropias. *Vision Res* 2007 Sep;47(21):2751-66.
 16. Smith EL 3rd, Ramamirtham R, Qiao-Grider Y, et al. Effects of foveal ablation on emmetropization and form-deprivation myopia. *Invest Ophthalmol Vis Sci* 2007 Sep;48(9):3914-22.
 17. Smith EL 3rd, Kee CS, Ramamirtham R, et al. Peripheral vision can influence eye growth and refractive development in infant monkeys. *Invest Ophthalmol Vis Sci* 2005 Nov;46(11):3965-72.
 18. Ciuffreda KJ, Vasudevan B. Nearwork-induced transient myopia (NITM) and permanent myopia—is there a link? *Ophthalmic Physiol Opt* 2008 Mar;28(2):103-14.
 19. Hung GK, Ciuffreda KJ. Incremental retinal-defocus theory of myopia development--schematic analysis and computer simulation. *Comput Biol Med* 2007 Jul;37(7):930-46.
 20. Hung GK, Ciuffreda KJ. A unifying theory of refractive error development. *Bull Math Biol* 2000 Nov;62(6):1087-108.
 21. Pang Y, Maino D, Zhang G, Lu F. Myopia: Can its progress be controlled? *Optom Vis Dev* 2006;37(2):75-9.
 22. Leung JT, Brown B. Progression of myopia in Hong Kong Chinese schoolchildren is slowed by wearing progressive lenses. *Optom Vis Sci* 1999 Jun;76(6):346-54.
 23. Hasebe S, Ohtsuki H, Nonaka T, et al. Effect of progressive addition lenses on myopia progression in Japanese children: a prospective, randomized, double-masked, crossover trial. *Invest Ophthalmol Vis Sci* 2008 Jul;49(7):2781-9.
 24. Gwiazda J, Hyman L, Hussein M, et al. A randomized clinical trial of progressive addition lenses versus single vision lenses on the progression of myopia in children. *Invest Ophthalmol Vis Sci* 2003 Apr;44(4):1492-500.
 25. Siatkowski RM, Cotter SA, Crockett RS, et al. Two-year multi-center, randomized, double-masked, placebo-controlled, parallel safety and efficacy study of 2% pirenzepine ophthalmic gel in children with myopia. *J AAPOS* 2008 Aug;12(4):332-9.
 26. Scheiman MM, Hertle RW, Beck RW, et al. Randomized trial of treatment of amblyopia in children aged 7 to 17 years. *Arch Ophthalmol* 2005 Apr;123(4):437-47.
 27. Wallace DK, Chandler DL, Beck RW, et al. Treatment of bilateral refractive amblyopia in children three to less than 10 years of age. *Am J Ophthalmol* 2007 Oct;144(4):487-96.
 28. Cotter SA, Edwards AR, Arnold RW, et al. Treatment of strabismic amblyopia with refractive correction. *Am J Ophthalmol* 2007 Jun;143(6):1060-3.
 29. Holmes JM, Edwards AR, Beck RW, et al. A randomized pilot study of near activities versus non-near activities during patching therapy for amblyopia. *J AAPOS* 2005 Apr;9(2):129-36.
 30. Repka MX, Wallace DK, Beck RW, et al. Two-year follow-up of a 6-month randomized trial of atropine vs. patching for treatment of moderate amblyopia in children. *Arch Ophthalmol* 2005 Feb;123(2):149-57.
 31. Wallace DK, Edwards AR, Cotter SA, et al. A randomized trial to evaluate 2 hours of daily patching for strabismic and anisometropic amblyopia in children. *Ophthalmology* 2006 Jun;113(6):904-12.
 32. Convergence Insufficiency Treatment Trial Study Group. Randomized clinical trial of treatments for symptomatic convergence insufficiency in children. *Arch Ophthalmol* 2008 Oct;126(10):1336-49.
 33. Vidyasagar TR. Neural underpinnings of dyslexia as a disorder of visuo-spatial attention. *Clin Exp Optom* 2004 Jan;87(1):4-10.
 34. Solan HA, Shelley-Tremblay J, Hansen PC, et al. M-cell deficit and reading disability: a preliminary study of the effects of temporal vision-processing therapy. *Optometry* 2004 Oct;75(10):640-50.
 35. Solan HA, Larson S, Shelley-Tremblay J, et al. Role of visual attention in cognitive control of oculomotor readiness in students with reading disabilities. *J Learn Disabil* 2001 Mar-Apr;34(2):107-18.
 36. Gallaway M, Boas MB. The impact of vergence and accommodative therapy on reading eye movements and reading speed. *Optom Vis Dev* 2007;38(3):115-20.
 37. Goss DA, Downing DB, Lowther AH, et al. The effect of HTS vision therapy conducted in a school setting on reading skills in third and fourth grade students. *Optom Vis Dev* 2007;38(1):27-32.
 38. Crutch SJ, Warrington EK. Foveal crowding in posterior cortical atrophy: a specific early-visual-processing deficit affecting word reading. *Cogn Neuropsychol* 2007 Dec;24(8):843-66.
 39. Helms D, Sawtelle SM. A study of the effectiveness of cognitive therapy delivered in a video game format. *Optom Vis Dev* 2007;38(1):19-26.
 40. Vidyasagar TR. Neural underpinnings of dyslexia as a disorder of visuo-spatial attention. *Clin Exp Optom* 2004 Jan;87(1):4-10.
 41. Lawton T. Training direction-discrimination sensitivity remediates a wide spectrum of reading skills. *Optom Vis Dev* 2007;38(1): 33-47.
 42. Goldstand S, Koslowe KC, Parush S. Vision, visual-information processing, and academic performance among seventh-grade schoolchildren: a more significant relationship than we thought? *Am J Occup Ther* 2005 Jul-Aug;59(4):377-89.
 43. Fischer B, Königeter A, Hartnegg K. Effects of daily practice on subitizing, visual counting, and basic arithmetic skills. *Optom Vis Dev* 2008;39(1):30-4.
 44. Sands W, Taub M, Maino D. Limited research and education on special populations in optometry and ophthalmology. *Optom Vis Dev* 2008;39(2):60-1.
 45. Wesson M, Maino D. Oculo-visual findings in Down syndrome, cerebral palsy, and mental retardation with non-specific etiology. In Maino D (ed). *Diagnosis and Management of Special Populations*. Mosby-Yearbook, Inc. St. Louis: 1995:17-54. Reprinted *Optometric Education Program Foundation*. Santa Anna, Calif.. 2001.

- Louis: 1995:17-54. Reprinted Optometric Education Program Foundation, Santa Anna, Calif., 2001.
46. Cui Y, Stapleton F, Suttle C. Developing an instrument to assess vision-related and subjective quality of life in children with intellectual disability: data collection and preliminary analysis in a Chinese population. *Ophthalmic Physiology Optics* 2008 May;28(3): 238-46.
 47. Maino D, Steele G, Tahir S, Sajja R. Attitudes of optometry students toward individuals with disabilities. *Optom Ed* 2002;27(2):45-50.
 48. Maino D. Special populations in the optometric curriculum. *Optom Ed* 2002;27(2):38-9.
 49. Maino D. Overview of special populations. In: Scheiman M, Rouse M. (eds) *Optometric Management of Learning-Related Vision Problems*. St. Louis: Mosby Inc., 2006;85-106.
 50. Maino D (ed). *Diagnosis and Management of Special Populations*. Mosby-Yearbook Inc.: St. Louis, 1995. Reprinted Optometric Education Program Foundation, Santa Anna, Calif., 2001.
 51. McCarthy P, Maino D. Alport syndrome: a review. *Clin Eye Vis Care* 2000 Dec;12(3-4):139-50.
 52. Block SS, Brusca-Vega R, Pizzi WJ, et al. Cognitive and visual processing skills and their relationship to mutation size in full and permutation female fragile X carriers. *Optom Vis Sci* 2000 Nov;77 (11):592-9.
 53. Maino D. The young child with developmental disabilities: An introduction to mental retardation and genetic syndromes. In: Moore BD (ed.) *Eye Care for Infants and Young Children*. Butterworth-Heinemann, Newton, MA:1997:285-300.
 54. Amin V, Maino D. The Fragile X female: Visual, visual perceptual, and ocular health anomalies. *J Am Optom Assoc* 1995 May;66 (5):290-95.
 55. Maino DM, Maino JH, Cibis GW, Hecht F. Ocular health anomalies in patients with developmental disabilities. In: Maino D (ed.) *Diagnosis and Management of Special Populations*. Mosby-Yearbook, Inc., St. Louis, MO. 1995:189-206. Reprinted Optometric Education Program Foundation, Santa Anna, Calif., 2001.
 56. Maino D, Wesson M, Schlange D, Cibis G, Maino J. Optometric findings in the fragile X syndrome. *Optom Vis Sci* 1991;68:634-40.
 57. Scheiman MM. Optometric findings in children with cerebral palsy. *Am J Optom Physiol Opt*. 1984 May;61(5):321-3.
 58. Maino D, Maino J, Maino S. Mental retardation syndromes with associated ocular defects. *J Am Optom Assoc* 1990;61:707-16.
 59. Stewart RE, Woodhouse JM, Clegg M, Pakeman VH. Association between accommodative accuracy, hypermetropia, and strabismus in children with Down's syndrome. *Optom Vis Sci* 2007 Feb;84(2):149-55.
 60. Clegg M, Woodhouse JM, Pakeman VH, et al. Accommodation and refractive error in children with Down syndrome: cross-sectional and longitudinal studies. *Invest Ophthalmol Vis Sci* 2001 Jan;42 (1):55-63.
 61. McClelland JF, Parkes J, Hill N, et al. Accommodative dysfunction in children with cerebral palsy: a population-based study. *Invest Ophthalmol Vis Sci* 2006 May;47(5):1824-30.
 62. Duckman RH. Vision therapy for the child with cerebral palsy. *J Am Optom Assoc* 1987;58(1):28-35.
 63. Duckman R. Accommodation in cerebral palsy: function and remediation. *J Am Optom Assoc* 1984;55(4):281-3.
 64. Scheiman M. *Understanding and managing vision deficits: a guide for occupational therapists*, 2nd ed. Slack: Thorofare, NJ, 2002.
 65. Maino D. Binasal occlusion for the child with Cerebral Palsy. *J Ill Optom Assoc* 1986;44(1):12,18.
 66. Battaglia F, Quartarone A, Rizzo V, et al. Early impairment of synaptic plasticity in patients with Down's syndrome. *Neurobiol Aging* 2008 Aug;29(8):1272-5.
 67. Bonnier C. Evaluation of early stimulation programs for enhancing brain development. *Acta Paediatr* 2008 Jul;97(7):853-8.
 68. Morice E, Andrae LC, Cooke SF, et al. Preservation of long-term memory and synaptic plasticity despite short-term impairments in the Tc1 mouse model of Down syndrome. *Learn Mem* 2008 Jul 14;15(7):492-500.
 69. Gordon AM, Schneider JA, Chinnan A, Charles JR. Efficacy of a hand-arm bimanual intensive therapy (HABIT) in children with hemiplegic cerebral palsy: a randomized control trial. *Dev Med Child Neurol* 2007 Nov;49(11):830-8.
 70. Kapoor N, Ciuffreda KJ. Vision disturbances following traumatic brain injury. *Curr Treat Options Neurol* 2002 Jul;4(4):271-80.
 71. Ciuffreda KJ, Rutner D, Kapoor N, et al. Vision therapy for oculomotor dysfunctions in acquired brain injury: a retrospective analysis. *Optometry* 2008 Jan;79(1):18-22.
 72. Ciuffreda KJ, Han Y, Kapoor N, Ficara AP. Oculomotor rehabilitation for reading in acquired brain injury. *NeuroRehabilitation* 2006;21(1):9-21
 73. Zost M. Diagnosis and management of visual dysfunction in cerebral injury. In: Maino D (ed). *Diagnosis and Management of Special Populations*. Mosby-Yearbook, Inc., St. Louis: 1995:79. Reprinted Optometric Education Program Foundation, Santa Anna, Calif., 2001. [Figure used with permission of the editor.]
 74. DeGutis JM, Bentin S, Robertson LC, D'Esposito M. Functional plasticity in ventral temporal cortex following cognitive rehabilitation of a congenital prosopagnosic. *J Cogn Neurosci* 2007 Nov;19 (11):1790-802.
 75. Welbourne SR, Ralph MA. Exploring the impact of plasticity-related recovery after brain damage in a connectionist model of single-word reading. *Cogn Affect Behav Neurosci* 2005 Mar;5(1):77-92.
 76. Jia X, McNeill G, Avenell A. Does taking vitamin, mineral and fatty acid supplements prevent cognitive decline? A systematic review of randomized controlled trials. *J Hum Nutr Diet* 2008 Aug;21(4):317-36.
 77. Henriksen C, Haugholt K, Lindgren M. Improved cognitive development among preterm infants attributable to early supplementation of human milk with docosahexaenoic acid and arachidonic acid. *Pediatrics* 2008 Jun;121(6):1137-45.
 78. Kidd PM. Omega-3 DHA and EPA for cognition, behavior, and mood: clinical findings and structural-functional synergies with cell membrane phospholipids. *Altern Med Rev* 2007 Sep;12(3):207-27.
 79. Gomez-Pinilla F. Brain foods: the effect of nutrients on brain function. *Neuroscience* 2008;9(7):568-78.
 80. Maya Vetencourt JF, Sale A, Viegi A, et al. The antidepressant fluoxetine restores plasticity in the adult visual cortex. *Science* 2008 Apr 18;320 (5874):385-8.
 81. Kasper S, McEwen BS. Neurobiological and clinical effects of the antidepressant tianeptine. *CNS Drugs* 2008;22(1):15-26.

82. Adamcio B, Sargin D, Stradomska A, et al. Erythropoietin enhances hippocampal long-term potentiation and memory. *BMC Biol* 2008 Sep 9;6:37.
83. Chilosi A, Leuzzi V, Battini R, et al. Treatment with L-arginine improves neuropsychological disorders in a child with creatine transporter defect. *Neurocase* 2008;14(2): 151-61.
84. Forrester LW, Wheaton LA, Luft AR. Exercise-mediated locomotor recovery and lower-limb neuroplasticity after stroke. *J Rehabil Res Dev* 2008;45(2):205-20.

Copyright© 2000 - 2008 Jobson Publishing L.L.C. unless otherwise noted.
All rights reserved. Reproduction in whole or in part without permission is prohibited.