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Review

# The therapeutic benefits of perceptual learning

**Jenni Deveau[1], Gary Lovcik[2] and Aaron R. Seitz[1,*]**
[1]Department of Psychology, University of California – Riverside, Riverside, CA, USA,
[2]Anaheim Hills Optometric Center, Anaheim, CA, USA

## ABSTRACT

The modern field of perceptual learning addresses improvements of sensory and perceptual functioning in adult observers and provides powerful tools to ameliorate the effects of neurological conditions that involve a sensory or attentional deficit. While the sensory systems were once thought to be plastic only during early development, modern research demonstrates a great deal of plasticity in the adult brain. Here we discuss the value of perceptual learning as a method to improve sensory and attentional function, with a brief overview of the current approaches in the field, including how perceptual learning can be highly specific to the training set, and also how new training approaches can overcome this specificity and transfer learning effects to untrained tasks. We discuss these in the context of extant applications of perceptual learning as a treatment for neurological conditions and how new knowledge of mechanisms (including attention, exposure based learning, reinforcement learning and multisensory facilitation) that allow or restrict learning in the visual system can lead to enhanced treatment approaches. We suggest new approaches that integrate multiple mechanisms of perceptual learning that promise greater learning and more generalization to real world conditions.

**KEYWORDS:** perceptual learning, plasticity, vision therapy, mechanisms of learning

## INTRODUCTION

Our knowledge of the world is derived from our perceptions, and an individual's ability to navigate his/her surroundings or engage in activities of daily living such as walking, reading, watching TV, and driving, naturally relies on his/her ability to process sensory information. Thus deficits in visual abilities, due to disease, injury, stroke or aging, can have significant negative impacts on all aspects of an individual's life. Likewise, an enhancement of visual abilities can have substantial positive benefits to one's lifestyle. Notably, new approaches show that the brain can be trained to better process information that is received from the eye. These "brain-based" approaches to visual improvement, here referred to as perceptual learning, provide an important complement to standard medical approaches. For example, in cases of low-vision, where standard approaches are often insufficient to fully achieve patient goals and the lack of appropriate approaches to treat brain-based aspects of low-vision is a serious problem since in many cases a component of the individual's low-vision is related to sub-optimal brain processing [1]. Research on perceptual learning demonstrates that the adult visual system is sufficiently plastic to ameliorate effects of low vision, including amblyopia [2], presbyopia [1], macular degeneration [3], stroke [4, 5], and late-life recovery of visual function [6]. Likewise, normally seeing individuals have the potential to further improve their vision through perceptual learning. Here, we review the field of perceptual learning and its promise to achieve better outcomes in clinical practice. The significance of the development of effective, low-cost therapies to treat brain-based low vision can be life-altering for millions of people worldwide.

*Corresponding author: aseitz@ucr.edu

## Perceptual learning

Perceptual learning (PL) refers to a long lasting improvement in perceptual abilities as a result of experience and research on this topic has undergone tremendous development over the last 30 years. Plasticity in sensory systems was previously thought to occur only in early development. This view has been substantiated by studies of a "critical period". The concept of a critical period states that some processes develop early in life, and do not develop, or develop to a lesser degree, later in life. For example, classic experiments done in kittens demonstrate a critical period for ocular dominance where early patching enables inputs from the open eye to take over much of primary visual cortex. However, in adult cats patching has little impact on connectivity [7, 8]. This data was used to support the hypothesis that the low-level sensory stages need to consistently process primitive sensory features; such as in vision orientation, spatial frequency, and local motion. In contrast, high-level perceptual processing is more plastic; for example, people can quickly learn probabilistic sequences [9], use primes [10], or spatial contexts that predict target locations [11, 12] to improve their task performance. However, studies of perceptual learning show that even in adults, perceptual abilities, including elementary processes (e.g., contrast sensitivity [13] and visual acuity [1, 2]) can be strengthened through appropriate training approaches.

Perceptual Learning is exemplified by long-lasting improvement on simple but difficult perceptual tasks. The effects of perceptual learning have been shown to last months, even years [14-16]. The field of perceptual learning is one of growing interest largely due to the fact that training on visual perception can be highly specific to the trained visual features and can give clues into the stages of processing at which learning occurs. For example, a series of studies conducted by Schoups and colleagues [17, 18] showed that training subjects (human and monkey) on an orientation discrimination task around a particular reference orientation yielded learning effects that failed to transfer to other stimulus orientations at the trained location or at the same orientation at a different retinotopic location. They postulated that these learning effects were consistent with plasticity in neurons residing in primary visual cortex, which show a high degree of both retinotopic and orientation specificity. Follow-up physiological studies by this group confirmed these predictions with the demonstration of plasticity of orientation tuning across early visual cortex [17, 19]. Consistent with this, numerous behavioral studies show perceptual learning can be highly specific to a wide range of trained stimulus features including retinotopic location [20, 21], visual orientation [17, 22] and direction [14, 21], among others. Likewise, many studies designed with the goal of linking neural mechanisms to behavior give direct evidence of sensory plasticity in all stages of visual processing through single-unit recording in monkeys [17, 23-25] and fMRI signal changes in humans [26-28].

An important caveat is that physiological studies demonstrating low-level perceptual learning typically fail to explain the magnitude of the behavioral changes [29] and some models of perceptual learning demonstrate that channel reweighting in the readout of sensory areas can account for some aspects of perceptual learning specificity without requiring plasticity in primary sensory areas [30-33]. Other studies have found plasticity in higher-level visual areas that were originally hypothesized to be lower level features [16, 34-36]. For instance, Law and Gold [35] failed to find plasticity in the middle temporal cortex (MT) of monkeys, but found learning effects in a higher order processing area (lateral intraparietal cortex; LIP) that largely explained behavioral changes. Likewise, learning in visual area V4 has been found to be more robust than that in V1 [19, 24, 34, 37, 38]. Also, some aspects of learning could be taking place in other brain regions. An interesting case was recently found in which the superior colliculus [39, 40] and frontal brain areas [41] develop tuning to motion directions after extensive training. While the exact locus of visual plasticity in a given study is often an issue of significant controversy, as a whole these studies give indication that plasticity is likely occurring at all stages of visual processing; although with a distribution that varies across tasks and training paradigms.

## Applications of perceptual learning

In recent years, there has been significant progress in applying perceptual learning based treatments to improve outcomes in individuals suffering from impairments in vision. Here we outline a few areas in which progress has been most notable.

### Amblyopia

Amblyopia has been a particular focus of perceptual learning research and a variety of perceptual learning approaches show benefit in treating adult amblyopia [2, 42, 43]. In amblyopia, mismatched input from the two eyes during development leads the visual system to primarily respond to just one of the eyes. This results in a lack of stereovision and difficulty in seeing with the non-dominant eye (often called “lazy eye”). This problem persists even after the misalignment between the eyes is corrected. Amblyopia impacts 2-3% of the population and is typically considered untreatable in adults.

The gold standard for treating amblyopia is to restore stereovision. To accomplish this, cortical processing of the amblyopic eye needs to be improved, the amblyopic eye needs to be taught to successfully compete with the non-amblyopic eye, and binocular integration needs to occur. A variety of approaches based on perceptual learning show evidence of accomplishing these outcome goals. Patching one eye and training the amblyopic eye with perceptual learning based exercises [2, 42, 43], or more recently video games [44] demonstrate substantial improvements of vision in the amblyopic eye. Techniques that put the eyes in competition, by presenting different stimuli to each eye with brighter stimuli in the amblyopic eye, lessen suppression in the amblyopic eye. Another approach is using binocular integration training, which trains the two eyes to work better together [45] by using tasks where inputs from both eyes need to be processed in order to succeed. Together these approaches have led to numerous examples where stereoacuity is improved in individuals with amblyopia and have provided great promise for future perceptual learning based treatment approaches.

### Age-related macular degeneration (AMD)

Improvements in brain processing of visual inputs can also help compensate for reductions of vision originating from the eye. For example, perceptual learning has been shown to ameliorate the effects of AMD, a retinal disorder in which photoreceptors are damaged or displaced. It is the leading cause of low vision in adults, and is expected to affect nearly three million Americans by 2020 (*The Eye Diseases Prevalence Research Group, 2004*). Patients with AMD suffer from visual field loss, spatial distortions to the visual field, and impairments of acuity and contrast sensitivity. Despite a range of treatments to arrest the progress of AMD, damage to the retina cannot be reversed, resulting in a need for effective visual training therapies. There are a number of studies that show both functional learning in the development of preferred looking points [46-48] and cortical reorganization in foveal responses to peripheral stimuli [3, 49]. Difficulty in reading is a common complaint in AMD patients due to the central vision loss. Recently, Chung [50] demonstrated that perceptual learning can improve reading speed in these patients after training. Additionally, Liu *et al.* [51] trained individuals with profound visual impairment (including AMD, glaucoma, retinitis pigmentosa, and other conditions) on a visual search task. Search speed and accuracy improved after training, and the effects remained for at least one month.

While, there are limited perceptual learning studies in AMD and it is unclear the extent to which normally occurring reorganizations are driven through use-dependent mechanisms [52], there is significant potential benefit to applications of perceptual learning in AMD.

### Damage to visual cortex

Tumors, stroke, trauma, or infection, can result in cortical blindness [53, 54]. While there is some degree of spontaneous recovery within the first few months after the injury, significant visual field loss can persist [55]. For these individuals, the development of behavioral therapies is of key importance. Accordingly, a number of approaches have been shown to be effective in reducing the size of, and increasing the visual sensitivity within cortical blind-spots [56]. Training patients to detect light spots [57, 58], sinewave gratings [59], or motion stimuli [4] in and around the blind-field all lead to better patient outcomes. However, while these effects are slow to arise and can be very specific to the location of training [4], they enable a recovery from visual field loss that isn't available through other approaches.

In general, perceptual learning shows great promise for conditions for which there are no standard treatments. These include the conditions mentioned above as well as other low-vision conditions such as Glaucoma, Night Vision Deficits, Presbyopia, Retinitis Pigmentosa, Low Myopia, etc. In addition, medical technologies such as intraocular lens implantations and retinal implants improve the optics of the eye, however without altering the underlying cortical connections as well, patients are without the full potential benefits of the technologies. Perceptual learning can be a great compliment to these treatments, which focuses on cortical processing allowing maximum benefits to vision.

## Principles of perceptual learning

While existing perceptual learning approaches show significant promise, many do not take advantage of newer insights of the processes guiding perceptual learning. These newer insights from the field of perceptual learning provide a structure upon which new and better behavioral interventions can be devised. In the following sections, we review different mechanisms and approaches that help guide perceptual learning.

### Attention

Attention refers to a set of fundamental mental processes that selectively modulate the processing of relevant information over irrelevant information; attention influences decisions, guides memory processes and our executive functions – such as planning and working memory, to direct resources to act upon the world. A common belief is that perceptual learning cannot occur without persistent and intensive attention to the feature to be learned [60]. Profound learning effects are often present for task-relevant features but are typically absent or very limited for the task-irrelevant and unattended features. For example, Ahissar and Hochstein [60] found little to no transfer of learning effects between two tasks that involved judgments on different stimulus attributes (either orientation of local elements or global shape) of the same stimuli. It was also reported that the ability of subjects to discriminate the orientation of a line did not improve when the brightness rather than orientation of the line was attended [61]. Additionally, a single-unit recording study in monkeys found neuronal plasticity of V1 cells that corresponded to the spatial location of the training task, where more neurons in V1 became responsive to the trained orientation after training. No plasticity was found for cells with receptive fields overlapping the location of task-irrelevant stimuli presented at a location different from those relevant to the task [17]. In the next section we will discuss how attention to stimuli is not actually required for learning on those stimuli; nonetheless attention plays an important role in selecting what we do (and do not) learn.

### Reinforcement

Recent research demonstrates the fundamental importance of reinforcement processes (rewards, punishments, motivation, etc) in guiding perceptual learning. A useful paradigm to explore this has been that of task-irrelevant perceptual learning, which shows that sensory plasticity occurs without attention being directed to the learned stimuli, and even for those that participants are not aware [21, 62-72]. Seitz and Watanabe [67] found that a sensitivity enhancement occurred as the result of temporal-pairing between the presentation of a subliminal, task-irrelevant, motion stimulus and a task-target. In that experiment, four different directions of motion were presented an equal number of times during the exposure stage, but a single direction of interest was consistently paired (temporally preceded and then overlapped) with the task-targets. Learning was found only for the motion-direction that was temporally-paired with the task-targets and not for the other motion-directions. Similar results were obtained when the luminance contrast of the dots (100% coherence) was made so low that the subjects did not notice the presentation of the motion stimuli [62].

Seitz and Watanabe [63] suggested a model of perceptual learning where learning results from interactions between spatially diffusive task-driven signals and bottom-up stimulus signals. In this model, learning is gated by behaviorally relevant events (rewards, punishment, novelty, etc). At these times reinforcement signals are released to better learn the aspects of the environment (even those for which the organism is not consciously aware) that are predictive or co-vary with the event. Later research confirmed this idea by demonstrating that task-irrelevant perceptual learning can arise through pairing a stimulus with a liquid reward [64].

By now, task-irrelevant perceptual learning has been shown to be a robust learning phenomenon that generalizes to a wide range of stimulus features, for example, motion processing [21], orientation processing [72], critical flicker fusion thresholds [65, 73], contour integration [74], auditory formant processing [75], and phonetic processing [76]. While the phenomenon of task-irrelevant perceptual learning has been studied in most detail in the case of low-level perceptual learning, recent research has identified a high-level, fast form, of task-irrelevant perceptual learning (fast-task-irrelevant perceptual learning) [77-84]. In this fast-task-irrelevant perceptual learning paradigm, participants performed target detection tasks (looking for a target, letter, color, or word among a series of distractors), while also memorizing other stimuli (images, pictures) that were consistently paired with the stimuli of the target-detection task. Similar to task-irrelevant perceptual learning for low-level perceptual learning, visual memory was enhanced for stimuli that were paired with the targets of the target-detection task.

These results suggest that task-irrelevant perceptual learning is a basic mechanism of learning in the brain that spans multiple levels of processing and sensory modalities. Furthermore, task-irrelevant perceptual learning produces learning effects that are often as strong, and sometimes stronger, than learning effects produced through direct training [75, 76]. As such the use of task-irrelevant perceptual learning has significant promise as a therapeutic treatment, where, unlike in other approaches, patients can conduct tasks in which they are unimpaired and receive benefits that help ameliorate their impairments.

**Chemical system in attention and reinforcement**

Both attention and reinforcement are known to operate in part through the release of neuromodulatory signals in the brain. For example, the orienting of attention, in the direction of the target-arrow, has been linked with the acetylcholine neuromodulatory system [85]. Of interest, cholinergic enhancement through the use of donepezil improves both the attentional processing [86] as well as the magnitude [87] and longevity [88] of perceptual learning. Other neuromodulatory systems, such as dopamine and norepinephrine have also been linked to both attention [89, 90] and to learning [91, 92]. Indeed, these three neuromodulators (acetylcholine, norepinephrine, and dopamine) have been linked to the three attentional systems described by Posner and Petersen [89]: the alerting network that involves temporal cueing and the maintenance of an alert state (norepinephrine; [93-95]); the orienting network that spatially selects information from sensory input (acetylcholine; [85]); and the executive control network that resolves conflict among responses (dopamine; [96]). These studies indicate that attention and reinforcement are deeply interrelated and that a good training approach should aim to direct both attention and reinforcement in a manner to promote learning.

**Applying rules of synaptic plasticity**

At the cellular level, it is widely accepted that the process of synaptic plasticity underlies learning and memory. Synaptic plasticity is the ability of the strength of the connections between synapses to change, strengthening or weakening the connections of existing neurons to modulate the effectiveness of their communication. Bliss and Lomo discovered a method to experimentally induce a persistent synaptic plasticity termed long-term potentiation (LTP) [97]. By inducing brief high frequency electrical stimulation in the perforant pathway of anaesthetized rabbits and recording in the dentate gyrus they discovered an increase of excitatory post-synaptic potentials (EPSPs) over baseline response that lasted up to 10 hours. Conversely, long-term depression (LTD) is induced by persistent low frequency electrical stimulation, resulting in weakened synaptic connections.

Recent research has established that non-invasive exposure-based stimulation protocols can be applied to the sensory systems and result in plasticity of the corresponding sensory cortices. Passive high frequency stimulation (HFS) (20 Hz) of the fingertip resulted in the behavioral improvement of a 2-point discrimination task, and low frequency stimulation (LFS) (1 Hz) decreased performance on this task [98]. Additionally, improvements on the behavioral task after HFS were correlated with cortical reorganization as assessed by mapping somatosensory evoked potentials. This effect was abolished by oral application of an N-methyl-D-asparate (NMDA) receptor antagonist, indicating this effect shares similar requirements to cellular LTP and long-term memory formation as identified in the animal model [99]. Using a visual stimulation protocol Beste *et al.* [100] demonstrated behavioral changes on a change-detection task. Here, two bars were presented where a change could occur in the luminance of one bar, the orientation of one bar, the luminance and orientation of the same bar, or the luminance of one bar and the orientation of the other bar. The participants had to report a change in luminance, and ignore a change in orientation. The orientation change in the last condition was highly distracting, and made the luminance detection more difficult. A visual stimulation protocol consisted of alternating black and white bars flashing at either a high (20 Hz) or low (1 Hz) frequency with the goal of increasing or decreasing luminance saliency. The authors found that a high frequency visual stimulation protocol improved the behavioral outcome on the detection task tested up to 10 days after induction. Conversely, a low frequency LTD-like protocol impaired performance. These studies of exposure-based learning provide a clear connection between the animal model and the human system, and suggest that approaches based on knowledge of synaptic plasticity can be applied to improved perception in humans.

**Multisensory facilitation**

The human brain has evolved to learn and operate optimally in natural environments in which behavior is guided by information integrated across multiple sensory modalities. Crossmodal interactions are ubiquitous in the nervous system and occur even at early stages of perceptual processing [101-105]. Until recently, however, all studies of perceptual learning focused on training with one sensory modality. This unisensory training fails to tap into natural learning mechanisms that have evolved to optimize behavior in a multisensory environment. Recent research shows that subjects trained with auditory-visual stimuli exhibit a faster rate of learning and a higher degree of improvement than found in subjects trained in silence [66, 106]. Critically, these benefits of multisensory training are even found for perceptual tests *without* auditory signals. In other words, *multisensory training facilitates unisensory learning*. While, to date, most vision training procedures either don’t include sounds as part of the task (other than as feedback) or include sounds that are not coordinated with visual stimuli, the advantage of multisensory training over visual-alone training is substantial; reducing the number of sessions required to reach asymptote by ~60%, while also raising the maximum performance [73]. We suggest that having complementary information about the target objects coming from different sensory modalities allows the senses to work together to facilitate learning.

**Promoting transfer of learning**

Classically, a translational barrier to perceptual learning has been its high degree of specificity to trained stimulus features [107], such as orientation [22], retinal location [108] or even the eye trained [64, 109]. For example training with a single visual stimulus at a single screen location can result in learning that is specific to that situation. While such studies have been informative regarding the mechanisms of learning, specificity limits therapeutic benefits.

Recent research suggests methods on how this “curse of specificity” can be overcome. Approaches that depart from the most simple training approaches, such as those using multi-stimulus training [110, 111] and video games [112, 113] show a greater generalization of learning. For example, the recently developed technique of ‘double training’ found that the specific learning effects found in their paradigms can show broad transfer when more than one stimulus attribute is trained at a time. Xiao *et al.*, [111] trained participants on a Vernier discrimination task at a specific orientation at a specific location in the visual field, which normally yields location and orientation specific learning effects [109]. However, when subjects subsequently were trained a second orientation at a different spatial location, the training induced changes for the second orientation transferred to the first location. Such findings of broad location transfer undermine the argument that this learning is due to plasticity in retinotopic visual areas.

There exists a growing number of studies that address how specificity, or its opposite, transfer, is controlled by different factors. In a discrimination task, Jeter, Dosher, Petrov and Lu [114] showed that transfer was observed in low-precision transfer tasks while specificity was observed in high-precision transfer tasks. Then, Jeter, Dosher, Liu and Lu [115] showed that specificity was the result of extensive training, confirming more classical results [22, 108, 116], while a substantial transfer was observed early in the training. Interestingly, another study, reported by Aberg, Tartaglia and Herzog [117] presented a series of experiments showing, on the one hand that the number of trials per session influenced the overall improvement of the participant's performance, and on the other hand, the transfer depended on the number of trials presented during each session, and not on the total number of trials. Zhang *et al.*, [118] showed that the peripheral orientation discrimination tasks transferred to new locations only after a pre-test was given to participants. These studies add to the double-training studies that show transfer after training multiple features or at multiple locations [110, 111]. Together these studies show that many factors (extent of training, blocking of trials, precision of training stimuli, diversity of training set, etc), influence the transfer of learning.

**Video-game training**

Another avenue of research is the adoption of commercial video games as a tool to induce perceptual learning. By testing habitual "action" video game players, Green and Bavelier [112] found this population has improved performance on a wide range of visual skills when compared to non-video game players. These skills included useful field of view, which is the area of visual space that useful information can be extracted; multiple object tracking, where the goal is to track many moving objects in visual space simultaneously; attentional blink, which is the phenomenon that occurs when multiple visual stimuli are presented in rapid succession and we fail to perceive the 2$^{nd}$ object; and performance in flanker compatibility tests, where responses to a target are slower when flanked by an incongruent stimuli, compared to a congruent stimuli. The authors also showed that 10 days of training with action video games improves these skills in participants that previously did not have video game experience [112]. Video game training also shows enhanced visual motion discrimination [119], and crowding [120]. Furthermore, recent research has found that even basic visual abilities such as contrast sensitivity [113] and acuity [44, 120] improve after video game use.

Computer software is now finding real world use in the visual world of binocular disorders, amblyopia, neuro-rehabilitation and visual enhancement. Researchers and software developers are encouraged by research showing that specific software use actualizes the potential of the visual system and translates into real life gains. For example, a number of commercial products such as GlassesOff™, RevitalVision™ and ULTIMEYES™ are designed to improve acuity and contrast sensitivity in individuals with visual impairments or for normal sighted individuals looking for an enhancement of vision. These approaches are becoming increasingly sophisticated, for example, ULTIMEYES™ combines many of the perceptual learning approaches described above (including engagement of attention, reinforcement, multisensory stimuli, synaptic plasticity protocols and multiple stimulus dimensions) into a simple video game framework. This game produces broad-spectrum improvements to central and peripheral vision (see Figure 1). A recent study found improved acuity and contrast sensitivity in normal sighted individuals after 2 months of ULTIMEYES training [121]. ULTIMEYES has also been used in the treatment of low vision conditions including presbyopia, amblyopia, post-LASIK rehabilitation, and post-cataract surgery rehabilitation (especially effective for multifocal patients), and also in athletes for improved sports performance [122]. As care-providers learn the potential benefits from these behavioral treatments, we expect them to become increasingly mainstream.

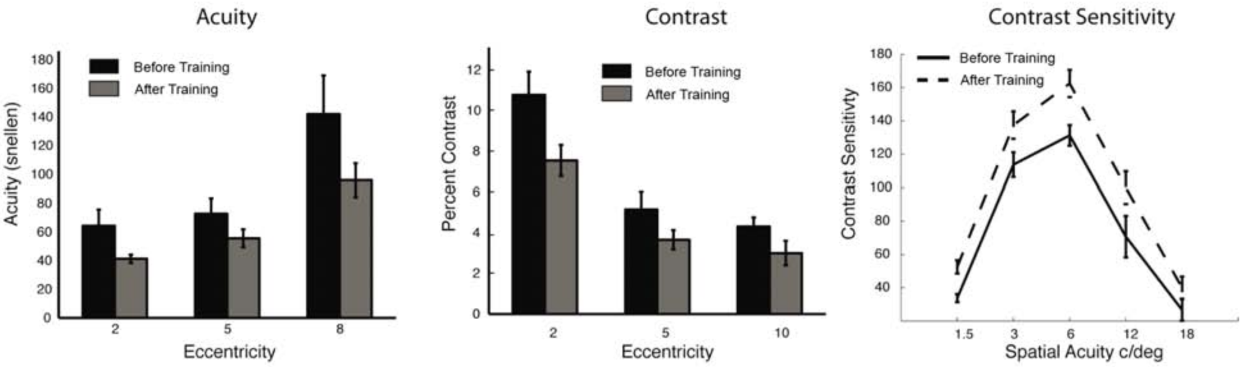


**Figure 1.** Data from 14 subjects (ages 18-55) completing 24 sessions of ULTIMEYES$^{TM}$. **Left,** for acuity, Landolt C size thresholds were measured at different locations in the visual field (with an eye-tracker to enforce fixation). **Middle,** contrast sensitivity thresholds were measured by varying the contrast of an "O" presented at visual field locations. **Right,** an Optec Visual Analyzer (Stereo Optical Company, Chicago, IL, USA) measured foveal visual acuity and contrast sensitivity. Data from pre-training tests (black) is shown against data of post-training tests (grey). In the left two graphs, lower values represent better performance. Acuity values (left) are based on standard 20/20 scores in the fovea (peripheral scores values are poorer). Weber Contrast (center). Contrast Sensitivity (right) shows contrast as a function of spatial frequency in central vision (higher values are better). Training-induced benefits are all significant at least to the $p < 0.05$ levels. Error bars represent standard error of the mean.

## CONCLUSION

With time we expect that perceptual learning based approaches will be increasingly utilized, together with drug, device, and surgical treatments, in order to provide a more complete treatment to improve vision.

While extant applications of perceptual learning to neurology show great promise, a limitation of modern perceptual learning research is that learning is studied in very specific ways, focusing on one particular stimulus or factor. This narrow focus has limited the understanding of the multiple learning factors that are present in natural settings and how these factors interact to determine the speed and nature of learning. We suggest a new paradigm of integrating perceptual learning methodologies into a coordinated approach that achieves a more comprehensive form of perceptual learning than typically studied in the lab. An ideal approach is one that combines many factors that are known to promote neural plasticity and generalization of learning. Additionally, principles derived from video games should be combined with those from the field of perceptual learning to create enriching user experiences that encourage compliance with treatment while effectively optimizing how the brain process its ocular inputs.

## CONFLICT OF INTEREST STATEMENT

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