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Visual Perceptual Remediation for Individuals with Schizophrenia: Rationale, Method, and Three Case Studies

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Abstract

Objective—Few studies have evaluated the effects of visual-remediation strategies in schizophrenia despite abundant evidence of visual-processing alterations in this condition. Here we report preliminary, case study-based evidence regarding the effects of visual remediation in this population.

Methods—We describe the implementation of a visual-perceptual training program called ULTIMEYES (UE) and initial results through three brief case studies of individuals with schizophrenia. UE targets broad-based visual function, including low-level processes (e.g., acuity, contrast sensitivity), as well as higher-level visual functions. Three inpatients, recruited from a research unit, participated in at least 38 sessions 3–4 times per week for approximately 25 minutes per session. Contrast sensitivity (a trained task), as well as acuity and perceptual organization (untrained tasks), were assessed before and after the intervention. Levels of progression through the task itself are also reported.

Results—UE was well-tolerated by the participants and led to improvements in contrast sensitivity, as well as more generalized gains in visual acuity in all three participants and perceptual organization in two participants. Symptom profiles were somewhat different for each participant, but all were actively symptomatic during the intervention. Despite this, they were able to focus on and benefit from the training. The adaptive nature of the training was well-suited to the slower progression of two participants.

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Conflict of Interest
This conflict of interest was reviewed and the research approved by the University of California - Riverside Conflict of Interest Committee and the Human Research Review Board. None of the other authors report grant support for this project or a conflict of interest.

Conclusions and Implications for Practice—These case studies set the stage for further research, such as larger, randomized controlled trials of the intervention that include additional assessments of perceptual function and measures of cognition, social cognition, and functional outcomes.

Keywords

Schizophrenia; cognitive remediation; visual perceptual training; perception

Introduction

It is now well established that schizophrenia is associated with cognitive dysfunction in domains such as processing speed, attention, working memory, and executive function (Green, 2006). With the growing awareness that such cognitive impairments are significantly related to poorer functional outcomes (Green, 2006; Green, Kern, & Heaton, 2004; McGurk & Mueser, 2004), along with the lack of clear positive results with regard to pharmacological treatments that target cognition (Barch, 2010), efforts to develop behavioral interventions to improve cognition in schizophrenia have increased dramatically over the last two decades. These interventions target cognitive impairments with the ultimate goal of improving real-world role functioning (Medalia & Choi, 2009). Numerous studies have demonstrated that cognitive remediation (CR) can improve cognitive and role functioning in individuals with schizophrenia (McGurk et al., 2013; McGurk, Twamley, Sitzer, McHugo, & Mueser, 2007; Twamley, Vella, Burton, Heaton, & Jeste, 2012; Wykes, Huddy, Cellard, McGurk, & Czobor, 2011), with recent meta-analyses of the CR literature indicating medium-sized effects of CR on cognition and small-to-medium effects on psychosocial functioning.

The majority of CR interventions that have been evaluated primarily target "higher level" cognitive processes, such as attention, working memory, and executive functioning (McGurk et al., 2007). However, given the well-documented impairments in perceptual processes associated with schizophrenia (Butler, Silverstein, & Dakin, 2008; Javitt & Freedman, 2015; Silverstein & Thompson, 2015), and the relation between these processes and higher-level cognition (Dias, Butler, Hoptman, & Javitt, 2011; Haenschel et al., 2007; Silverstein, Bakshi, Nuernberger, Carpinello, & Wilkniss, 2005), there is a growing interest in interventions that are specifically designed to improve perceptual processing in this condition. To date, most research using this "perceptual remediation" strategy has focused on auditory processing. In particular, there are now a number of studies reporting the effects of auditory training, implemented with the computerized auditory training module by Posit Science, among individuals with schizophrenia (Fisher, Holland, Merzenich, & Vinogradov, 2009; Fisher, Holland, Subramaniam, & Vinogradov, 2010; Fisher et al., 2015; Fisher, Mellon, Wolkowitz, & Vinogradov, 2016; Popov et al., 2011). Overall, results from this body of work have been promising, with reports of significant treatment-related improvements among individuals with schizophrenia in verbal working memory (Fisher et al., 2009; Popov et al., 2011), verbal learning and memory (Fisher et al., 2009; Fisher et al., 2010; Fisher et al., 2016), and global cognition (Fisher et al., 2009; Fisher et al., 2015; Fisher et al., 2016). In addition, significant gains in speed of auditory processing, a specific perceptual target of this intervention, were observed at the group level and were associated with improvements in global cognition (Fisher et al., 2015).

In contrast, very few studies have evaluated the effects of visual-remediation strategies in schizophrenia, despite abundant evidence of multiple visual-processing alterations in this condition. These include impairments in low-level vision, such as visual acuity (Smith, Pantelis, McGrath, Tangas, & Copolov, 1997; Viertio et al., 2007) and contrast sensitivity (Butler et al., 2005; Halasz, Levy-Gigi, Kelemen, Benedek, & Keri, 2013), and mid-level visual processes, such as those related to perceptual organization (e.g., figure-ground segmentation, coherent motion detection, contour integration, shape completion; Sehatpour et al., 2010; Silverstein & Keane, 2011; Uhlhaas & Silverstein, 2005; Chen, 2011; Tadin et al., 2006). There is also evidence for disturbances in higher-level visual perceptual processes, including alterations in the effects of prior knowledge on the processing of visual sensory information, as suggested by work using size constancy, depth inversion, and other visual illusion paradigms (Keane, Silverstein, Wang, & Papathomas, 2013; Silverstein et al., 2013). Research has indicated that among individuals with schizophrenia, specific visual-processing alterations are significantly related to poorer performance on higher-order cognitive tasks (e.g., pattern recognition, context processing; Dias et al., 2011; Silverstein et al., 2005); impaired social cognition, including facial and emotion recognition (Butler et al., 2009; Green, Hellemann, Horan, Lee, & Wynn, 2012; Soria Bauser et al., 2012); impaired reading ability (Revheim et al., 2014); poorer treatment response (Silverstein et al., 2013; Silverstein, Schenkel, Valone, & Nuernberger, 1998); and worse functional outcomes (Rassovsky, Horan, Lee, Sergi, & Green, 2011). Such findings suggest that therapeutic strategies that directly target the visual-processing impairments associated with schizophrenia could potentially drive gains in higher-level cognitive, social, and role functioning, in addition to improving visual functions.

It has been observed that, in many cases, perceptual learning is intact in schizophrenia (reviewed for the domain of perceptual organization in Silverstein & Keane, 2009). Such findings illustrate that with repeated exposure to a visual task over relatively short time periods (typically within one week), performance on the trained task can be significantly improved. These results support the application of a longer and more systematic course of visual training as a potential means to improve visual and other functions in this condition. Indeed, initial efforts to promote more generalized gains (i.e., to non-trained tasks) in visual processing in schizophrenia through visual perceptual training have shown promise. For example, Norton and colleagues (2011) observed improvements in visual motion perception among individuals with schizophrenia following 6 sessions of a perceptual-learning program that were significant for the trained task, and moderate, but non-significant, for an untrained motion perception task. Surti and Wexler (2012) employed a 10-session visual backward masking (VBM) intervention with 9 individuals with schizophrenia, and found significant improvements on the trained (VBM) tasks, as well as on measures of visual memory and global cognition. Although suggestive, both of these studies used small samples and training paradigms with a limited number of sessions, and neither used a control condition. Thus the potential benefits of visual remediation strategies for individuals with schizophrenia, including programs involving multiple visual tasks and longer courses of training, remain unclear.

It should be noted that several research groups have now evaluated the efficacy of computer-based CR that includes both the auditory and visual training modules developed by Posit Science to improve cognition in schizophrenia. This reflects the growing awareness of the importance of targeting impaired visual, as well as auditory, perceptual processing in this condition. For example, Fisher et al. (2010) reported that individuals with schizophrenia who completed training with the auditory, visual, and cognitive-control modules improved to a significantly greater degree than those in the control condition on measures of processing speed, verbal learning and memory, cognitive control, and global cognition. Likewise, Subramaniam and colleagues combined auditory, visual, and emotion-identification modules, and observed significant treatment-related improvements in source memory (2012) and verbal working memory (2014), as well as within-group improvements in verbal memory and executive functioning (2012). It should be noted, however, that not all research groups that have employed these training modules have observed significant treatment-related effects (e.g., see Rass et al., 2012). At this time, it is difficult to directly compare the results obtained from such multi-modal approaches with those from studies of auditory training alone, as the "combined" training paradigms described in the papers cited above not only included training in multiple domains but also involved additional hours of training compared to studies of auditory training alone. However, Surti et al. (2011) found that among individuals with schizophrenia who completed auditory, visual, and cognitive-control training, gains on visual-training exercises were strongly and specifically associated with improvements in visual learning; such training gains did not relate to improvements in verbal learning, or verbal or spatial working memory. These results point to the need to specifically train visual functions to promote improvements in these and related processes.

Thus, we are currently conducting a pilot trial of a visual perceptual training program that we believe has promise for remediating visual processing and higher-level cognitive functions in schizophrenia. The intervention, ULTIMEYES (UE), developed by Seitz and colleagues at the University of California, Riverside (Deveau, Lovcik, & Seitz, 2014; Deveau, Ozer, & Seitz, 2014; Deveau & Seitz, 2014) focuses primarily on lower-level visual functions (e.g., contrast sensitivity, spatial frequency processing, central and peripheral acuity). Impairments in these functions can serve as a rate-limiting factor for mid-level vision (e.g., perceptual organization) and other higher-order functions such as face processing (Keane, Erlikhman, Kastner, Paterno, & Silverstein, 2014; Keri, Kiss, Kelemen, Benedek, & Janka, 2005; Turetsky et al., 2007). However, UE also targets higher-level visual functions, such as visual search and visual attention. Perceptual learning approaches have tended to emphasize individual mechanisms and to produce results that are specific to the trained stimulus features (Fahle, 2005; Li, Piech, & Gilbert, 2008), which has limited the development of training strategies that are designed to improve visual processing more broadly. UE addresses these issues by combining multiple approaches to perceptual learning (including engagement of attention, reinforcement, the use of multisensory stimuli such as tones to cue the location of stimuli, and manipulation of multiple stimulus dimensions) that individually contribute to increasing the speed, magnitude, and generalizability of learning, into an integrated perceptual training application.

Perceptual learning-based training with UE leads to improvements not only on the trained aspects of the task, including contrast sensitivity, but also to improvements in central and peripheral acuity, in normally-sighted young adults after approximately 30 training sessions (Deveau, Lovcik, et al., 2014; Deveau, Ozer, et al., 2014; Deveau & Seitz, 2014). It has been demonstrated that UE-related gains in visual processing can transfer to broader, real-world functioning, as evidenced by improved performance in college baseball players (e.g., fewer strikeouts, more runs batted in; Deveau, Ozer, et al., 2014), and improved reading acuity and speed (Deveau & Seitz, 2014) in young adults. UE-related improvements have also been observed in near visual acuity in adults with presbyopia, with many of these individuals reaching non-presbyopic acuity levels (0.0 logMAR, i.e., 20–20 vision, or better) after training (Deveau & Seitz, 2014). These findings provide evidence that perceptual learning-based visual training can improve real world skills used in daily life. Based on these results obtained with UE in non-psychiatric samples (Deveau, Lovcik, et al., 2014; Deveau, Ozer, et al., 2014; Deveau & Seitz, 2014), as well as the findings of intact perceptual learning ability in schizophrenia described above (e.g., Keane et al., 2014), we hypothesized that among individuals with schizophrenia, UE training would lead to improvements on the “trained task” of contrast sensitivity, as well as in central visual acuity and perceptual organization. In this preliminary report, we illustrate the implementation and effects of the UE visual perceptual training program with three individuals with schizophrenia.

Method

Participants

This pilot study was approved by the Institutional Review Board. All participants provided written informed consent after the procedures were fully explained to them. Participants were inpatients on a research unit. They were transferred from other settings, including other inpatient facilities, in order to participate in research protocols. Participants were between the ages of 18–55, were medically healthy, met diagnostic criteria for schizophrenia according to the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (APA, 1994), and were on stable doses of medication (i.e., no change in medication for at least two months prior to and during the study). Diagnostic status was confirmed with the Structured Clinical Interview for DSM-IV Axis-I Disorders (SCID-IV; First, Spitzer, Gibbon, & Williams, 1994).

Participants were approached for potential participation in the study by their clinicians or the study authors based on our aim to select a group that varied with regard to symptom presentation and level of disability. The cases described in this paper were chosen in order to illustrate the use of UE in individuals with schizophrenia with a range of symptoms and impairments (e.g., motoric slowness, negative symptoms, etc.).

The visual training sessions took place in a room on the inpatient unit. The three participants included in this report completed between 38–41 training sessions (Table 1) at a rate of 3–4 sessions a week over a period of 11–13 weeks; each session lasted approximately 25 min; thus these participants completed a total of 15.8–17.1 hours of training. Participants received payment ($10/hr) for completing the baseline and post-training assessments, but did not receive payment for the intervention, as it was considered part of clinical treatment.

Visual Remediation

The **ULTIMEYES (UE)** vision training program (Deveau, Lovcik, et al., 2014; Deveau, Ozer, et al., 2014) is implemented using video-game based custom software. The training stimuli consist of Gabor patches (game "targets," Figure 1) at 6 spatial frequencies (1, 2, 4, 8, 16 and 32 cycles/degree) and 8 orientations (22.5–337.5°). We describe the program as a "video-game" because numerous elements of the program are designed to promote task engagement and user enjoyment. For instance, points are given each time a target is selected (and taken away when distractors are selected), bonuses are given for rapid responses, and the difficulty level increases throughout training.

The dose of treatment (i.e. the number and length of the sessions) was determined based on results of previous studies with UE in which 30 sessions of ~25 min each produced changes in visual function, reading ability, and batting averages (Deveau, Lovcik, et al., 2014; Deveau, Ozer, et al., 2014; Deveau & Seitz, 2014). Thus all participants received at least 30 sessions. The number of trials per session depended, in part, on the participant's speed of responding on each trial.

Each session consisted of 8–12 training exercises that lasted approximately 2 min each, for a total of ~25 min. There was a screen with visual and written instructions before each exercise, including the calibration. At the beginning of each session, a calibration was run to determine the initial contrast values for each spatial frequency displayed during the training exercises for the given session. During the course of this research study, the UE program was updated, which resulted in a few minor changes in the program; however, the mechanisms and goal of the training exercises remained the same. We used the older version of the program with two of the participants presented here (Mr. A and Mr. B). In this version, calibration was determined by the method of limits, which consisted of a series of trials that each contained 3 Gabor stimuli at each of 7 contrast values ranging from supra-threshold to sub-threshold (these were adaptively determined across sessions based on previous performance levels), with all 21 stimuli on a given calibration trial at a single spatial frequency. Trials differed in the spatial frequency of the stimuli presented. The participant clicked on the targets that he saw. The initial contrast value, at each spatial frequency, in the first training exercise in each session was set at the lowest contrast level that the participant correctly detected all three times during the calibration procedure. With the third participant (Mr. C), the calibration was determined by a method of adjustment in which the participant moved a slider below the Gabor until he could just barely see the stimulus, which was done for each spatial frequency presented. Both the method of limits and of adjustment are standard procedures for perceptual assessment. Following the calibration, a 1-up, 3-down staircase procedure[a] was used in each exercise in order to maintain the difficulty level at threshold.

Exercises alternated between static and dynamic types. In the Static exercises, an array of targets of a single spatial frequency, at a randomly determined orientation and location, was

[a]The 1-up 3-down staircase procedure involved adjusting the contrast level of the Gabor stimuli to make the task more difficult when the participant correctly clicked on a Gabor stimulus, and adjusting the contrast to decrease the difficulty level if the participant made 3 errors in a row at a given contrast.

presented on the screen all at once. In the Dynamic exercises, targets of a randomly determined orientation/spatial frequency combination were presented one at a time, and faded in at pseudo-randomly determined locations on the screen. The goal of the exercises was to click on all of the Gabor targets as quickly as possible. Targets that were not selected during the time limit would start flickering at a 20-Hz frequency. Previous research (Beste, Wascher, Gunturkun, & Dinse, 2011) has shown that a visual stimulus flickering at 20 Hz can improve attention to targets, and thereby improve task performance. If targets were still not selected while they were flickering, contrast increased gradually until they were selected. This allowed participants to successfully select all targets.

The first few training exercises consisted only of targets (Gabors), but distractors were added as the training progressed. In the older version of UE (used by Mr. A and Mr. B), once distractors were added, all remaining levels used distractors. In the updated version of UE (used by Mr. C), distractors were added as the training progressed; however, each subsequent session included levels with and without distractors. The number of distractors varied for each participant based on both their within-session performance and the level they had reached in the program. As training progressed, distractors became more similar to the targets (starting off as blobs, then oriented patterns, then noise patches of the same spatial frequency as the targets). Many parameters of UE are adaptive (i.e., difficulty level is adjusted on an ongoing basis based on performance during the previous trials to maintain performance at a roughly equivalent level throughout the task), including contrast (using 1-up, 3-down staircases), number of stimuli on each trial (the number increases progressively as each stage is completed correctly), and rate of stimulus presentation (based upon average response time). Of note, in previous research with non-psychiatric samples, a typical user successfully progressed through 2–4 levels per session.

One of the authors was with the participant during each session. The progress of each participant was also monitored by reviewing the session logs. Participants were trained with the vision correction they normally used. Hence, if someone needed glasses but did not wear them (e.g., Mr. B), they were trained without glasses.

Visual-Processing Measures

For this pilot demonstration of UE in schizophrenia, we focused on outcome measures of contrast sensitivity, visual acuity, and perceptual organization. Each participant was assessed on the measures described below at baseline and following UE training.

Behavioral contrast sensitivity was assessed both before and after the UE training, and during the course of the training after every 5th session. A central “target” Gabor patch was surrounded by Gabor patches above, below, and to the right and left of the target. The task was to click on the surrounding striped patch that was oriented the same way as the middle Gabor patch. This was completed for spatial frequencies ranging from 1 (thicker stripes) to 30 (thinner stripes) cycles/degree. For each spatial frequency, the contrast of the middle Gabor patch was lowered using a 3-down, 1-up staircase that stops after 3 reversals (after the initial descent), resulting in a 79% threshold. The outcome measure was peak contrast sensitivity (quantified as the peak value of a truncated parabola fit of the contrast sensitivity function). Contrast sensitivity is the inverse of threshold. This was considered a trained task because contrast detection using the same type of Gabor stimuli was built into the UE training exercises.

Near visual acuity was measured with a near vision chart for testing at 16 inches. **Far visual acuity** was assessed with an ETDRS chart for testing at 13 feet. Note that a change in 0.1 logMAR (i.e., one line of the ETDRS chart) is considered a clinically significant change (Balcer et al., 2000; Beck et al., 2007).

Contour Integration, an aspect of perceptual organization, was assessed with 15 cards containing Gabor elements that combined to form a circular or nearly circular shape along with "noise" Gabor items (Silverstein et al., 2006; see Figure 2). The shape became more difficult to detect with each card due to an increase in the number/density of the noise elements relative to the number of contour elements (which remained constant on each trial). The dependent variable was the ratio (*D*) of the average distance between adjacent noise elements to the average distance between adjacent contour elements, on the last card on which the contour was successfully detected. The lower the *6* value, the more noisy the display was in which contours could be successfully detected. This variable (Kovacs, Polat, Pennefather, Chandna, & Norcia, 2000; Silverstein, Kovacs, Corry, & Valone, 2000) precisely represents the signal:noise ratio in each stimulus. Participants were asked to trace the contour on each card with their finger. There was a 30-second time limit for each card and the test was stopped after four consecutive failures.

Case Studies

Case 1

Mr. A was a 45-year-old man with a 26-year history of schizophrenia. At the time of visual remediation, he had been an inpatient in a state psychiatric facility for five years. He had been prescribed clozapine and various augmentation treatments for 10 years, and had adhered to his prescribed medication regimen. Over the course of his hospitalization, Mr. A's mood and level of interaction with others fluctuated. For periods of time he was generally pleasant, alert, in good spirits, helpful on the unit, displayed a sense of humor, and attended groups on the inpatient unit and on the grounds of the campus. The groups appeared to be beneficial for him, and he became more socially engaged on the unit. However, he also had periods of time when he was withdrawn and angry, isolated from others, and did not participate in groups. At the time the UE visual remediation began, he had stopped attending groups.

Even though he was in a somewhat withdrawn state, Mr. A was very enthusiastic about participating in the UE training. He did not normally wear glasses and thus did not wear glasses during the training. Mr. A eagerly went to the intervention room for each session. He easily learned the tasks, had no difficulty using the mouse, and was very engaged in the process. He did not require very much encouragement, although the investigators sometimes provided reminders about not clicking on distractors and searching the whole screen for the targets. At times he appeared to be responding to internal stimuli (e.g., he muttered and laughed to himself); however, these episodes did not appear to distract him from the task.

Mr. A completed 41 sessions of the UE intervention over a period of 11.5 weeks (3–4 sessions/week) for a total of 17.1 hours. He finished an average of 8.4 exercises per session, and, on average, advanced 1 level per session. When assessed following training, he demonstrated improvement on all three outcome measures of interest. Specifically, his peak contrast sensitivity (measured with a trained task) increased 23%. His performance on untrained tasks also improved. His near binocular vision improved from 20/32 to 20/20 (two lines on a vision chart), and his contour integration performance improved, specifically from a pre-treatment ability to identify contours at a signal:noise ratio of 0.65 (meaning that the adjacent background elements are 0.65x closer to each other than are contour elements to adjacent contour elements) to a post-treatment ability to identify contours at a more noisy 0.55 ratio (15.4% improvement). During debriefing after the intervention, Mr. A reported that the training seemed to help him focus. He commented that his “eye hand coordination, timing skills, and level of interest were improved...” and that “you do something you don’t do every day. It makes you want to try different things.”

Case 2

Mr. B was a 38-year-old man with an 18-year history of schizophrenia. At the time of the visual remediation, he had been an inpatient in a state psychiatric facility for over 2 years. He was adherent with his medication (olanzapine), was calm, and followed ward rules. Although he continued to have grandiose and paranoid delusions, these did not interfere with his daily routine. He attended groups and went on escorted passes with staff.

Mr. B was initially happy to participate in the intervention and was glad to receive $10/hr for the baseline assessments. However, once the remediation began (and he was no longer paid), he was initially somewhat reluctant and needed encouragement to participate. Prior to training, he had lost his glasses and had not worn them for a long time. Thus, he was trained without glasses even though his vision was poor. He had difficulty using the mouse and was very slow in his physical movements, including moving the cursor to the targets. The investigators provided a great deal of encouragement during the sessions, including prompting him to wait for the targets rather than key-pressing out of frustration when he did not immediately see the targets. However, once he started each session, he did not appear overly frustrated even though it was difficult for him.

Mr. B completed 40 sessions of the intervention over a period of 12 weeks (~3–4 sessions/week) for a total of 16.7 hours. He finished an average of 9.2 exercises per session, and advanced, on average, 0.5 levels per session (his slower rate of level advancement can be attributed to his slow response times and thus poorer scores on some of the exercises compared to Mr. A). The post-training assessment indicated that his peak contrast sensitivity increased 58% from baseline. His performance on the untrained tasks also improved. Specifically, his far binocular vision improved from 20/100 before training to 20/63 after training (two lines on a vision chart), and his contour integration improved from a signal:noise ratio of .70 to .65, reflecting an improved ability to detect contours in noise (7% improvement). By the end of the training, he became very interested in learning how to use the computer and seemed to have developed a sense of mastery regarding computer use. He also reported that he thought his vision had improved.

Case 3

Mr. C was a 36-year-old man with a 16-year history of schizophrenia. At the time the remediation was initiated, he had been on an inpatient unit at a state psychiatric hospital and taking antipsychotic medication (clozapine) for 8 months. He continued to experience delusions and hallucinations, and also exhibited negative symptoms, including blunted affect and emotional withdrawal. He generally kept to himself with minimal socializing on the unit, although he attended groups on the unit fairly regularly.

Mr. C was enthusiastic about beginning the visual remediation. He appeared to understand the UE directions easily and had no difficulty using the mouse. In contrast to the other participants, at times he became very frustrated during the sessions. As stated above, Mr. C used the newer program in which the calibration was determined by the method of adjustment. Mr. C initially set the starting level of contrast to an easy level, but after encouragement over several sessions, he began to challenge himself by working at more difficult levels. Another participant, not described in this paper, also used the newer version of UE but did not have any difficulty moving the bar to a contrast level at which he could just notice the Gabors. Thus, while the method of adjustment is a standard psychophysical method, as with most methods, participants can respond to the task differently.

Mr. C completed 38 sessions over a period of 11 weeks (~3–4 sessions/week), finishing an average of 11 exercises per session for a total of 15.8 hours. On average, he advanced 2.9 levels per session. He probably progressed through more levels per session than the other participants included in this report because of his initial tendency to adjust the pre-task contrast calibration slider so that the stimuli were more easily detected, as noted above. However, like the other participants, he demonstrated improvement from the training. His peak contrast sensitivity improved 80.3%. On the untrained measures, his far binocular vision improved from 20/50 to 20/32 (two lines on a vision chart), whereas his contour integration performance remained constant (at a signal:noise ratio of 0.70) from pre- to post-treatment. During debriefing, Mr. C talked about his growing ability to tolerate not seeing the targets immediately. He also described an increased ability to tolerate stress. Thus, while Mr. C was sometimes reluctant to engage in the sessions and initially worked at less difficult contrast levels, he became much more comfortable with the training format as the sessions progressed, and was pleased with his increased ability to tolerate challenging situations.

Discussion

Given the large body of evidence indicating that schizophrenia is associated with multiple visual perceptual impairments, including low-level deficits (Butler et al., 2008; Butler et al., 2005; Javitt & Freedman, 2015), and the relation between these alterations and impairments in higher-level cognitive (Dias et al., 2011; Silverstein et al., 2005), social cognitive (Butler et al., 2009; Green et al., 2012), and role (Rassovsky et al., 2011) functioning, we sought to evaluate the efficacy of a visual perceptual training program to improve visual processing in this condition. The UE training program targets broad-based visual function, including low-level visual processes (e.g., contrast sensitivity) and higher-level visual processes (e.g., visual attention and search; Deveau, Lovcik, et al., 2014; Deveau, Ozer, et al., 2014; Deveau & Seitz, 2014). This training program has previously only been evaluated with non-psychiatric samples (Deveau, Ozer, et al., 2014; Deveau & Seitz, 2014). The three case studies we report here illustrate that the visual intervention, UE, is well tolerated by individuals with schizophrenia across a range of disability levels. Furthermore, results suggest that this intervention can lead to improvements in contrast sensitivity, as measured with a trained task, as well as more generalized gains in visual acuity and perceptual organization, in individuals with schizophrenia.

This is the first study with UE, or, to our knowledge, with any prolonged low-level visual training alone, in schizophrenia. As in previous work with non-psychiatric samples, including college students and older people with presbyopia (Deveau, Lovcik, et al., 2014; Deveau, Ozer, et al., 2014; Deveau & Seitz, 2014), the 3 participants with schizophrenia demonstrated improved performance on the trained task of contrast sensitivity, as well as more generalized improvement in visual acuity. For Mr. B and Mr. C, who had poorer far than near vision when assessed at baseline, binocular far vision improved. For Mr. A, who had similar near and far visual acuity at baseline, binocular near vision improved. Each participant, all of whom were actively symptomatic, showed an improvement of 0.2 logMAR, which is considered to be clinically significant (Balcer et al., 2000; Beck et al., 2007). The changes observed in this study are of similar magnitude to UE-related gains reported previously (i.e., improvements in peak contrast sensitivity of ~33–45% and in binocular acuity of ~0.1 logMAR) in non-psychiatric samples (Deveau, Lovcik, et al., 2014; Deveau, Ozer, et al., 2014) and in older people with presbyopia (Deveau & Seitz, 2014). With regard to trained tasks, in previous studies with non-psychiatric samples, Seitz and colleagues found that a typical user successfully progressed through 2–4 levels per session (personal communication). Mr. A and B progressed more slowly than this (1 and 0.5 levels per session on average, respectively), whereas Mr. C advanced at a rate that is typical of other samples (2.9 levels). Our observation here that the training was still effective in improving visual function even though two participants progressed at a relatively slow rate is encouraging for use of this type of training in a population characterized by slow speed of processing (Dickinson, Ramsey, & Gold, 2007).

This is also the first study to report on the effects of training on perceptual organization in schizophrenia, beyond short-term perceptual learning. For two of the three participants, results suggest that visual training that emphasizes low-level visual processes meaningfully improved the mid-level function of perceptual organization. The degree of improvement in contour integration we observed in two of the three participants is similar to the degree to which controls demonstrated superior perceptual organization compared to participants with schizophrenia in our prior non-treatment studies using a single session with no training provided. For example, in Silverstein et al. (2000), controls performed 13.5% better than individuals with schizophrenia overall on the same task we used in the present project. Similar results were found in other past studies (e.g., schizophrenia-control differences of between 9% and 19% were found in Silverstein et al., 2009) across conditions of contour element orientation jitter (the manipulation used in that study instead of signal:noise ratio). Therefore, we believe that the gains we report here are clinically significant in that they improved performance to a point that closed the gap typically observed between performance of participants with schizophrenia and controls. Of course, the durability and generalizability of these gains are not known and this is an important issue for future studies.

Because many of the parameters of the UE program are adaptive (e.g., contrast, number of stimuli, and rate of stimulus presentation), individuals with attentional and motoric challenges and little experience with computers, such as Mr. B, were able to benefit. In addition, points were provided to improve motivation. There is a rich literature showing that reinforcement and motivation are key to promoting perceptual learning (Seitz & Watanabe, 2009), and that error-based feedback yields little benefit compared to block-wise (Herzog & Fahle, 1997) or motivational (Shibata, Yamagishi, Ishii, & Kawato, 2009) feedback (i.e., positive reinforcement for correct responses). While this approach to training may superficially resemble the errorless learning (EL) method that has been used in compensatory approaches to cognitive and vocational training (e.g., Leshner, Tom, & Kern, 2013), it differs significantly in that EL provides tangible, extrinsic reinforcers and is based on principles of instrumental conditioning and shaping, whereas perceptual learning, including UE-related improvements, are not driven by external reinforcers (other than non-systematic social reinforcement; see below) and are thought to promote neuroplasticity in sensory systems and attention-mediated strengthening of sensory signals.

It should also be noted that participants were generally able to read and understand the instructions on the computer screen provided at the beginning of each exercise quite well and to generally work independently. Encouragement was routinely provided by the investigator several times throughout the session (e.g., “you earned a lot of points that time,” or “good, you got the ones that were hard to see”). In addition, encouragement was provided when participants appeared frustrated, and the investigators re-stated instructions (e.g., “don’t press the mouse button until you see a target”; “don’t click on the distractors”; “try to set the bar to where you can just barely see the stimulus”) as needed. Of note, when participants disregarded the instructions, it appeared to be primarily out of frustration or impulsivity rather than confusion. This happened most frequently with Mr. B, although he was also frequently able to work on his own.

There are several limitations to this study, which in general also serve as future directions for this area of research. First, given that this study describes several case studies, a clear limitation is the small sample size and lack of control group. However, our goal with this initial project was simply to determine if people with a range of schizophrenia-related impairments would tolerate and benefit from the intervention. Our intent is to use the results of these case studies to complete an initial efficacy study that will then inform the design of a larger-scale randomized controlled trial (RCT) that would use an a priori analytical approach to more precisely characterize the effects of the intervention. A larger study could also control for potential moderating variables, such as baseline visual acuity, motivation, practice effects, symptom severity, and researcher feedback. Second, while the visual outcome measures were theory-driven and chosen to reflect both trained and untrained visual processes, a larger study that assesses generalization to cognitive (including visual and auditory learning and memory) and functional outcome measures is the next step. Third, the amount and type of encouragement provided by the investigators should be standardized to the degree possible. Future work would also benefit from standardized ratings of subjective reports from participants. It will also be important to determine how task-related motivation can be further enhanced via program manipulation or study design (e.g., group vs. individual training). Finally, if UE training is shown to be effective in an RCT, future studies should also incorporate rehabilitation strategies such as vocational and social-skills training, to determine whether UE serves to enhance treatment responses to rehabilitation interventions, as suggested by Wykes et al. (2011).

In addition to future clinical trials, these case studies raise other research questions. For example, the effects of the intervention on visual cortex activity, and on connectivity between occipital and more anterior regions, should also be examined, given evidence of hypoactivity (Butler et al., 2013; Silverstein et al., 2009) and hyperactivity (Silverstein et al., 2015) within visual regions (depending on the task and participant characteristics), and of altered connectivity between the occipital lobe and other brain regions (Dima, Dietrich, Dillo, & Emrich, 2010; Dima et al., 2009), in schizophrenia.

As noted, a number of studies of a cognitive-remediation strategy that heavily emphasizes auditory sensory processing training, though not all, show promising effects on higher-level auditory and verbal functions in schizophrenia (Fisher et al., 2009; Fisher et al., 2010; Fisher et al., 2015; Keefe et al., 2012; Popov et al., 2011). Demonstration of similar effects with visual remediation could lead to the addition of a powerful new tool to the arsenal of cognitive interventions for individuals with schizophrenia.

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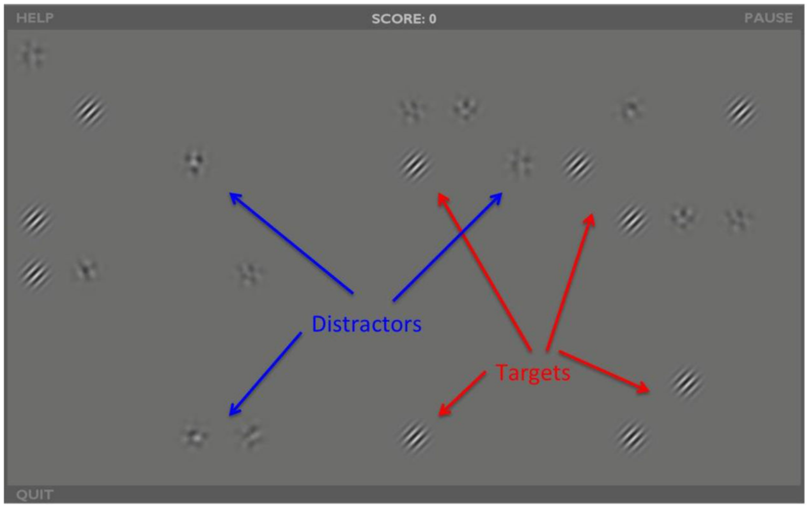

Figure 1.
Game screenshot. Static search with distractors. Participants are asked to select the targets, and ignore the distractors. As levels progress, distractors look more and more like targets. Of note, both targets and distractors are typically much lower contrast than they appear here. Figure reprinted with permission from Deveau, Lovcik, et al., 2014.

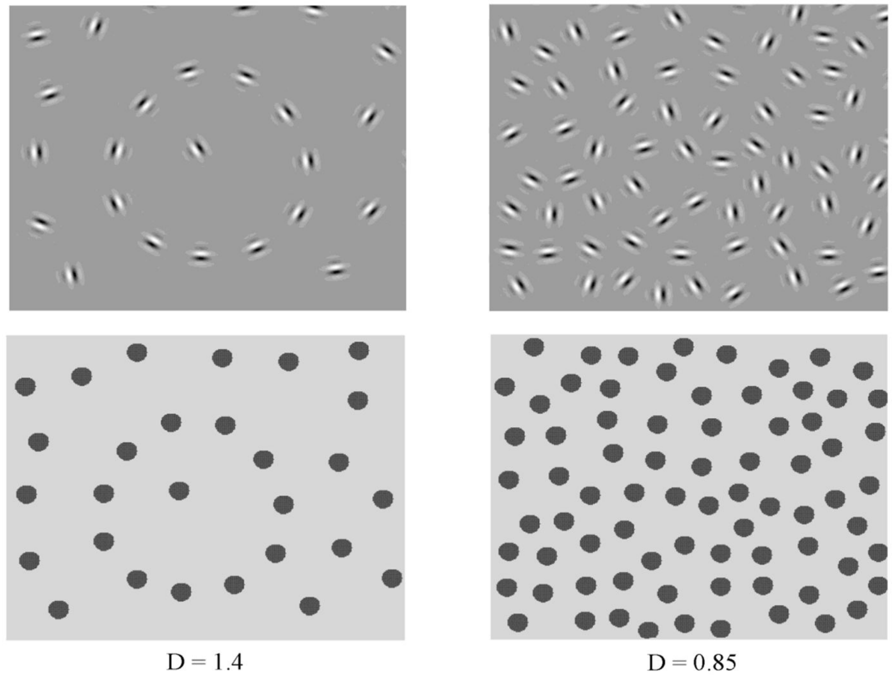

Figure 2.
Examples of Gabor-defined contours with different D values (D=ratio of mean background spacing and spacing between neighboring contour elements; i.e, left: D = 1.4, right: D = 0.85). In the bottom panels, Gabor elements were replaced by disks. Without orientation cues, the contour remains invisible at D < 1, and this is the range where perceptual organization depends on long-range spatial interactions. Note that these images only show the area around the contour. The actual test stimuli are much larger and consist of regions without contours (i.e., with background noise only). Figure reprinted with permission from Silverstein, Kovacs, Corry, & Valone, 2000.

Table 1

Results for Trained and Untrained Tasks Following UE Intervention

Case	Total # sessions	Mean exercises/ session	Mean levels/ session	CS % Improvement	Binocular Acuity Improvement	PO % Improvement
Mr. A	41	8.4	1	23%	0.2 logMAR[a]	15.4%
Mr. B	40	9.2	0.5	58%	0.2 logMAR[b]	7%
Mr. C	38	11	2.9	80.3%	0.2 logMAR[b]	no change

CS=contrast sensitivity and refers to peak contrast sensitivity; PO=Perceptual Organization;

[a] near acuity;

[b] far acuity;

Light gray column headings are trained tasks; dark gray are untrained tasks. 0.2 logMAR is two lines on a vision chart.