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Combination of Pursuit Eye Movement Training With Prism Adaptation and Arm Movements in Neglect Therapy: A Pilot Study

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Objective. The aim of the present study was to determine if a combination of pursuit eye movement training to optokinetic stimulation (OKSP) and prism adaptation leads to greater improvement of neglect symptoms than a single application of OKSP. Additionally, the effect of ipsilesional arm movements during OKSP was tested. *Methods*. Ten patients with left-sided neglect due to unilateral right-sided vascular brain lesions were studied between 2 and 4.5 months after their stroke. Each patient received 4 different single-session treatments (each lasting 30 minutes): visual scanning treatment (control condition), OKSP, OKSP in conjunction with wearing base-left prisms inducing a shift of the visual field to the right by 10°, and OKSP in conjunction with the right to the left side. Severity of visuospatial neglect was assessed before and directly after each treatment with 4 standard neglect tests. *Results*. Visual scanning training improved neglect symptoms only slightly. Single OKSP stimulation led to significant improvements in all tests. OKSP in conjunction with prism adaptation was superior to the control condition in the cancellation task. The treatment condition requiring arm movements aggravated neglect symptoms in all tests. A comparison between treatments indicates best improvements may be achieved with OKSP without any additional treatment. *Conclusions*. The present results give evidence that OKSP significantly reduces symptoms of visuospatial neglect within 1 treatment session. The results suggest that patients should be prevented from performing ipsilesional movements during OKSP.

Key Words: *Hemispatial neglect—Optokinetic stimulation—Prism adaptation*.

Hemineglect denotes the impaired or lost ability to react to or process sensory stimuli presented in the hemispace contralateral to the lesioned cerebral hemisphere. Despite recovery from the most obvious signs of hemineglect in the first 3 months after the stroke, a considerable number of neglect patients—especially those with large right-hemispheric lesions—remains severely impaired in visual scanning, reading, and functional activities of daily living.[1,2] Furthermore, neglect patients have a delayed recovery from hemiplegia, often display postural problems, and suffer from a poorer long-term outcome than patients without neglect.[3,4] Few neglect patients recover in a way that allows them to live independently or even return to work.

Various rehabilitation approaches have been developed to improve recovery of patients with persistent unilateral neglect. These approaches can be divided into 2 categories: remediation procedures based on top-down mechanisms and those based on bottom-up mechanisms. Top-down rehabilitation procedures train patients to direct attention to the neglected side. Since the introduction of visual scanning training by Diller and Weinberg, it has been successfully shown that such top-down treatments reduce visual neglect.[5-8] However, a visual scanning training is often laborious, requires numerous treatment sessions, shows little transfer to activities of daily living, and has no effect on nonvisual neglect.[9-11] Another drawback of top-down procedures is that patients have to learn a compensatory strategy, which is—due to lack of awareness and cognitive deficits—often difficult for the acute patient. Consequently, treatments based on bottom-up mechanisms, which do not require explicit awareness of the deficit, may be more successful in these patients. Bottom-up rehabilitation procedures use sensory stimulation to enhance perception of the contralesional space. In the past decade, a variety of sensory stimulation techniques have been applied showing that virtually every aspect of neglect behavior can be improved significantly. All sensory stimulation approaches in neglect patients are based on the idea that neglect results from a disrupted transformation of spatial coordinates into a common frame of reference necessary for accurate orientation in space.[12] Because multiple sensory and proprioceptive information is fed into such a hypothetical reference frame, many of these afferent channels have been used to manipulate neglect symptoms by varying sensory input.

Vestibular stimulation by squirting iced or warmed water into the contralesional or ipsilesional ear, respectively,

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has been shown to ameliorate hemineglect.[13,14] Transcutaneous mechanical vibration and electrical neural stimulation, in which stimulation is applied to the contralesional neck muscles, induces partial remission of the visuospatial deficit.[11,15,16] In addition, Fresnel prisms have been shown to reduce visual neglect significantly.[17] In line with this finding, repeated optical manipulation in the form of prisms inducing a shift of 10° to the ipsilesional side lead to a lasting improvement of neglect symtoms.[18-20] The idea behind this treatment is that an optical deviation of the visual field to the ipsilesional side results in a systematic contralesional deviation of visuomotor responses.

Another bottom-up technique showing positive effects on neglect symptoms is optokinetic stimulation (OKSP) with or without performing pursuit eye movements.[20-22] OKSP can be easily realized by means of visual displays of numerous stimuli moving coherently to the patient's neglected side. This technique positively affects several aspects of the neglect syndrome. Leftward OKSP temporarily reduces the ipsilesional line-bisection error, alleviates the ipsilesional deviation of the subjective visual straight ahead, and transiently decreases visual size distortion in neglect patients.[21,23-25] Moreover, OKSP effects are not limited to visual neglect. Vallar et al[16,26] described significant positive effects of leftward large-field OKSP on position sense in the contralateral and ipsilesional arm of patients with left-sided neglect.[16,26] Furthermore, grip strength could be temporarily improved in 2 patients with left-sided hemiparesis and left-sided neglect by observing large-field OKSP moving to the neglected side.[27] Finally, leftward OKSP temporarily reduces tactile extinction of the contralesional hand.[28] Interestingly, OKSP induced by high velocities is not necessary to obtain modulatory effects on neglect.[29] Beneficial effects occur also with low velocities of less than 10°/s and small stimulus displays.[23,30] Consistent with the transient improvements obtained during OKSP in nearly all aspects of the neglect syndrome, 2 recent treatment studies with repeated treatment sessions using this technique have also shown persistent therapeutic effects when patients were forced to make contralesionally directed pursuit eye movements.[31,32]

As various studies have shown positive therapeutic effects of all bottom-up methods, it can be speculated that a combination of these stimulation procedures might lead to a greater improvement than the single application of each technique. Instead of comparing stimulation techniques according to their general effect on visuospatial neglect, we are interested in exploring possible synergetic effects when applying 2 of these methods at the same time. OKSP, simply applied by using a computer showing moving stimuli on the display, as well as prism adaptation, only requiring a set of goggles fitted with prismatic lenses, are very easy to combine in clinical practice. In the present pilot study, we therefore decided to examine if a combination of OKSP and prism adaptation results in a greater improvement of neglect symptoms than using OKSP alone.

In addition to this question, we wanted to explore the influence of ipsilesional arm movements toward the neglected hemifield during OKSP. It is already known that activation of contralesional limbs ameliorate neglect symptoms.[33] Because 90% to 100% of acute neglect patients exhibit paresis of their contralesional arm and leg,[34] this method is only applicable to a small subgroup of patients with lesional sparing of the motor cortex and its efferents. Kinematic analyses of goal-directed arm movements with the ipsilesional, nonparetic arm have shown that neglect patients do not show any characteristic deviations in their hand paths during pointing movements compared with healthy controls or patients with right-sided lesions without neglect.[35] Chokron and Bartolomeo[36] found no significant correlation between left neglect and visuospatial motor response of the ipsilesional hand. In addition, physiological and kinematic studies in normal subjects show a tight coupling of eye position and arm position in space mediated by collicular structures,[37,38] and single-cell recordings in primates showed a bidirectional interaction between the oculomotor and manual-motor systems.[39,40] These findings led us to hypothesize that arm movements toward the contralesional hemispace might elicit an additional therapeutic effect leading to a homologous contralesional shift of eye position and a related attentional shift toward the contralesional side. Besides these theoretical considerations, there is clinical interest to know whether patients should be encouraged or prevented from using their ipsilesional arm during neglect therapy.

METHOD

Patients

Ten patients with large unilateral lesions due to cerebrovascular accidents of the right medial cerebral artery participated in the present study. Informed consent was obtained from all patients. All patients were recruited from the Neurological Clinic Bad Aibling. Brain lesions were confirmed by magnetic resonance imaging (MRI) scans, and lesioned areas were mapped onto a standard MRI template using MRIcro software.[41] Figure 1 shows lesion maps of all patients.

Each patient exhibited unilateral spatial neglect on admission, as assessed by a standard battery of neuropsychological tests including line bisection, Alberts's line cancellation, and the draw a clock face test. None of the patients had gaze paresis; 3 patients showed left-sided hemianopia in the Goldmann perimeter examination. All patients suffered from severe hemiparesis of the left arm and leg. Patient details and clinical test performances are shown in Table 1.

Figure 1. Lesion maps for the 10 patients with visuospatial neglect, plotted onto a normal template brain using MRIcro software.[32] Affected areas (translucent gray) are plotted onto axial slices, with numbers indicating *Z*-coordinates in Talairach space.

Assessment of Treatment Effects

Four tests were used to investigate the efficiency of treatment on different aspects of the neglect syndrome. The test battery was performed immediately before and after each treatment session.

Line bisection. The line bisection test consisted of three horizontal lines each 20 cm in length, which were presented with identical left margins on a 29.7 × 21 cm sheet of paper. Patients were asked to bisect each line in the middle as accurately as possible. The mean aberration of all 3 bisections was calculated as test performance.

Cancellation test. Patients were presented with a high-density array of 300 geometric stimuli (240 distractors and 60 targets) on a 29.7 × 21 cm sheet of paper. The task was to cancel out the 60 targets with a pencil using the right hand. There was no time restriction. The number of omitted targets was counted.

Text reading. To examine transfer to a nontrained visual task, 8 parallel reading tasks were developed for the assessment of neglect dyslexia. Each text consisted of 180 words arranged in 20 lines with regularly indented margins on the left side (arial font, point size 12, double line spacing, printed on a 29.7 × 21 cm sheet of paper). Patients were instructed to read the text aloud as accurately as possible without using their finger. The number of correctly read words was scored. Missing and inaccurately read words were counted and subtracted from 180.

Tactile search task. The tactile search task was performed to investigate a possible cross-modal transfer effect. The

Table 1. Demographic and Clinical Data of Neglect Patients

Patient	Age, Sex	Months Since Lesion	Visual Field; Field Sparing (°)	Motor Function	Albert's Line Cancellation Omissions[a] (%)	Line Bisection Deviation L/R[b] (cm)	Clock Face[c] L/R
1	64, M	5	Left hemianopia, 10°	Hemiplegia	33	+5.1	1/0
2	74, M	3.5	—	Hemiplegia	36	+4.8	1/0
3	54, M	2.5	—	Hemiplegia	30	+1.1	1/1
4	55, F	3	—	Hemiplegia	52	+2.5	1/0
5	47, F	2.5	—	Hemiplegia	36	+2.8	1/1
6	66, M	2	Left hemianopia, 8°	Hemiplegia	44	+2.5	1/0
7	58, F	3	—	Hemiplegia	41	+1.1	1/0
8	60, M	4.5	—	Hemiplegia	50	+3.5	1/0
9	57, F	3	Left hemianopia, 10°	Hemiplegia	33	+3.7	1/0
10	53, F	2.5	—	Hemiplegia	47	+1.8	1/0

[a]Albert's line cancellation test: percentage of targets omitted.
[b]Line bisection: deviation to right (R, +) or left (L, –) of midpoint in centimeters.
[c]Clock face: 0, normal; 1, omission of numerals on the right (R) or left (L) side.

blindfolded subjects had to explore the surface of a rectangular board (120 × 60 cm). The surface consisted of 18 objects (eg, pen, button), which were evenly distributed in space (each third of the board comprised 6 objects). Patients were asked to find 9 of the 18 objects (3 specific targets in each third) within a time limit of 1 minute for each target. The examiner counted the number of correctly detected objects. For the pretreatment and posttreatment testing the patient had to find different objects.

Procedure

Each patient received 4 different single-session treatments: OKSP, visual scanning training (VST), OKSP in conjunction with wearing base-left prisms inducing a shift of the visual field to the right by 10° (OKSP + P), and OKSP in conjunction with following the visual stimuli by arm movements from the right to the left side (OKSP + A). Each treatment session lasted 30 minutes. The sequence of experimental conditions for each patient was different to prevent serial effects. All treatments were performed within 4 days. Hence, the patients received a different treatment every day, and measurements were carried out before and after the experiments.

Optokinetic stimulation with pursuit eye movements (OKSP). Visual stimuli were projected with a color TFT overhead display connected to a computer at a distance of 160 cm. Length and width of the stimulus array was 28 × 21° of visual angle. The patients were instructed to look at a computer-generated random display of 100 to 120 yellow dots (each 2 cm in diameter) on a dark blue background, all moving coherently toward the left with a speed of 5 to 10°/s. At random time intervals, the movement speed changed from 5°/s to 10°/s or the dot color changed from yellow to pink. Subjects had to detect these changes and inform the examiner. When changes of movement speed or color were detected correctly, settings were reset. This was done to keep patients' attention to the moving stimuli. Patients were also encouraged to make smooth pursuit eye movements toward the direction of the motion and return with their eyes repeatedly to the ipsilesional side of the stimulus array. No head movements were allowed. In this and all remaining treatment conditions, the head of the patient was not fixed mechanically but gross head movements were prevented by the therapist placing his hand at the rear side of the patient's head.

Control—visual scanning treatment (VST). In the control condition, patients received a visual scanning treatment using the same device and stimuli (see OKSP), yet with the important difference that all visual stimuli displayed on the screen remained *stationary*. Patients were instructed to count the stimuli in a systematic way starting at the top left and moving to the bottom right-hand side of the screen. Scanning strategies were repeatedly explained to the patient, and the timing of treatment was identical to that of the OKSP. Patients were encouraged to make eye movements and scan to the left side as far as possible. Head movements were not allowed (see above).

OKSP in conjunction with prism adaptation (OKSP + P). Before starting, patients put on a pair of goggles fitted with wide-field point-to-point prismatic lenses creating a rightward optical shift of 10°. Then patients were asked to point to a visual target presented at the body midline. This was repeated until the initially ipsilesionally directed pointing error diminished and the patient had entirely adapted to the visual shift (8-20 repetitions for all patients). Immediately after this adaptation procedure, OKSP started and visual stimuli were presented in the same way as described in the first

Table 2. Median Values of Improvement (+) or Decrement (−) in Test Performance[a]

	Improvement/Decrement, Pre–Post			
	Line Bisection	Cancellation Task	Reading (Words)	Tactile Search Test (Hits)
Control (VST)	+1.2 cm	+5.0%	+3	−0.5
OKSP	+1.8 cm (**$P = .024$**)	+9.5% (**$P = .012$**)	+15 (**$P = .014$**)	+0.5 (**$P = .024$**)
OKSP + prism	+1.4 cm ($P = .202$)	+8.6% (**$P = .045$**)	+8 ($P = .153$)	+0.5 ($P = .197$)
OKSP + arm movement	−0.6 cm ($P = .343$)	−5.5% ($P = .341$)	−9 ($P = .285$)	−0.5 ($P = .270$)

Abbreviations: VST, visual scanning training; OKSP, optokinetic stimulation.
[a] *P* values in brackets indicate the level of significance for comparisons between control (VST) and experimental conditions (Wilcoxon test for matched samples, two-sided including Bonferroni's α adjustment). Significant results are shown in boldface.

condition. Movement speed and color of the dots were intermittently changed as described for OKSP. Patients had to wear the goggles throughout the whole training session. Pretest and posttest were performed with the goggles removed. Head movements were not allowed (see above).

OKSP in conjunction with arm movements (OKSP + A). OKSP was carried out in the same way as already described with the difference that patients were instructed to pick out 1 or 2 of the moving dots and follow these dots with their outstretched right arm from the right to the left. When they reached the left margin of the array they had to return to the ipsilesional side and start a new trial. Patients were allowed to make short breaks (<15 seconds) whenever they felt exhausted by the arm movements. Head movements were not allowed (see above).

RESULTS

Nonparametric statistical analyses were performed using paired comparisons with Wilcoxon tests (two-tailed, $P < .05$, including Bonferroni's α adjustment for multiple testing), and multivariate Friedman rank tests were applied to all consecutive pretreatment measures. This was done to control for possible learning effects due to repeated interventions.

Friedman rank tests revealed no significant differences between pretreatment measures ($\chi^2(3) = 1.372$, $P = .712$ for the line bisection task; $\chi^2(3) = 4.418$, $P = .220$ for the cancellation task; $\chi^2(3) = 1.340$, $P = .720$ for the reading test; and $\chi^2(3) = 1.133$, $P = .769$ for the tactile search task).

Table 2 summarizes the mean pre–post changes and statistical results for each treatment condition. There were only slight improvements in line bisection, cancellation, and reading and a decrement of 15% in the tactile search test for VST (control condition). Comparisons between experimental treatments and VST revealed statistically significant improvements for all 4 tests after OKSP ($z = -2.25$, $P = .024$ for line bisection; $z = -2.53$, $P = .012$ for the cancellation task; $z = -2.45$, $P = .014$ for reading errors; and $z = -2.25$, $P = .024$ for the table test). OKSP + P treatment showed a significant improvement for the cancellation task only ($z = -2.0$, $P = .045$). The combination of OKSP + A resulted in decrements of test performance between 3.5% and 20%. None of the differences between OKSP + A and VST were statistically significant.

Exposure to VST, OKSP, and OKSP + P led to an improvement in line bisection, whereas bisection error increased after OKSP + A. Figure 2 shows boxplots of pre–post changes for all treatment conditions.

Similar results were obtained for the cancellation task with best and statistically significant improvements for OKSP and OKSP + P and a slight decrement of test performance for OKSP + A (see Figure 3).

Figure 4 shows the results of the reading task. Again, OKSP was significantly superior to the control treatment, whereas OKSP + P improved the number of read words only slightly and OKSP + A reduced reading performance.

The pre–post difference of detected objects in the tactile search task varied only between −2 and +2. Nevertheless, OKSP led to a statistically significant improvement in the number of detected targets in this task when compared with VST. Figure 5 summarizes the results of the tactile search test.

DISCUSSION

Three main findings are apparent from this study. First, OKSP had a clear therapeutic effect within only 30 minutes of treatment in a variety of visual neglect tasks. The effects transferred to different tasks that were not trained, and a significant cross-modal effect was obtained in the tactile search task. Furthermore, OKSP was more effective than conventional visual scanning training. Second, a combination of OKSP and prism adaptation had no additional effect on test performance. Third, movement of the ipsilesional arm in conjunction with OKSP aggravated the neglect symptoms significantly.

In line with previous studies, which have shown transient effects of OKSP,[21-28] we could clearly demonstrate a short-term effect of pursuit eye movements to OKSP on visuospatial neglect. As repeated pretreatment

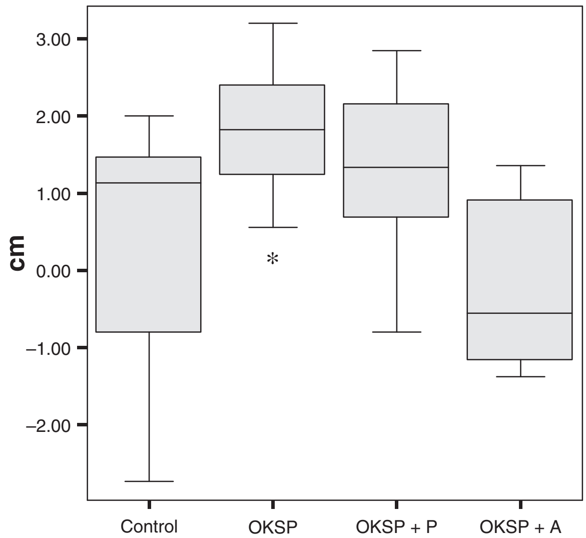

Figure 2. Boxplots of the results of the line bisection task. The lines in the box indicate the median values of pre–post treatment changes. The box contains 50% of the data, with the upper hinge indicating the 75th quartile and the lower hinge indicating the 25th quartile. The ends of the vertical lines show minimum and maximum values. Positive scores denote a leftward (contralesional) deviation from the pretreatment value; negative scores denote a rightward (ipsilesional) deviation from the pretreatment value. The asterisk indicates a statistically significant difference between VST and OKSP.

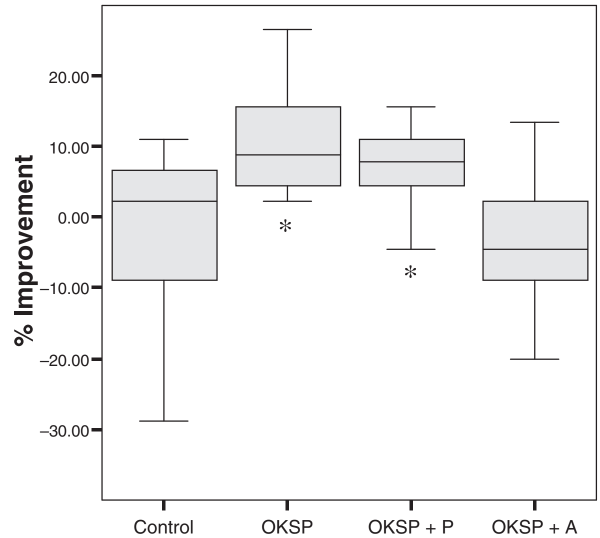

Figure 3. Boxplots of the results of the cancellation test. The lines in the box indicate the median values of pre–post treatment changes. The box contains 50% of the data, with the upper hinge indicating the 75th quartile and the lower hinge indicating the 25th quartile. The ends of the vertical lines show minimum and maximum values. Positive scores denote an increase of detection rate, and negative scores denote a decrease of detection rate. The asterisks indicate a statistically significant difference between VST and OKSP and VST and OKSP + P, respectively.

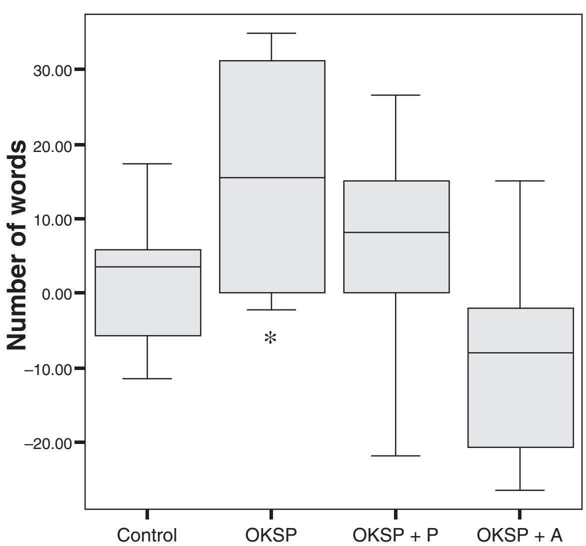

Figure 4. Boxplots of the results of the reading task. The lines in the box indicate the median values of pre–post treatment changes. The box contains 50% of the data, with the upper hinge indicating the 75th quartile and the lower hinge indicating the 25th quartile. The ends of the vertical lines show minimum and maximum values. Positive scores denote an increase in the number of words read, and negative scores denote a decrease in the number of words read. The asterisk indicates a statistically significant difference between VST and OKSP.

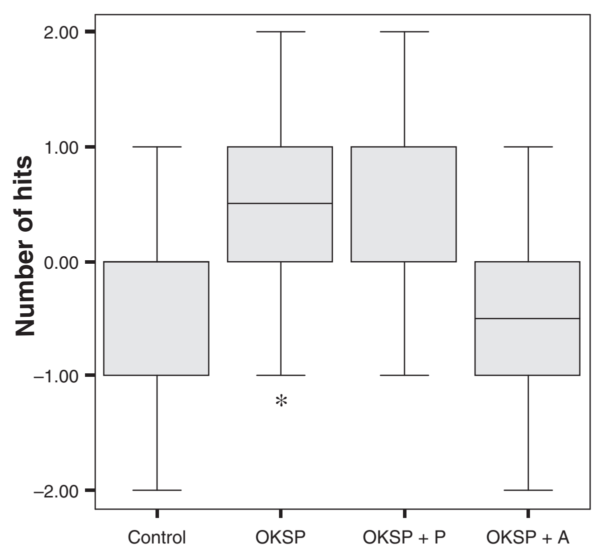

Figure 5. Boxplots of the results of the tactile search task. The lines in the box indicate the median values of pre–post treatment changes. The box contains 50% of the data, with the upper hinge indicating the 75th quartile and the lower hinge indicating the 25th quartile. The ends of the vertical lines show minimum and maximum values. Positive scores denote an increase in the number of hits, and negative scores denote a decrease in the number of hits. The asterisk indicates a statistically significant difference between VST and OKSP.

values of all performed tests did not show any statistically significant differences, learning effects in the experimental tasks across the 4 days can be excluded. Nevertheless, the long-lasting therapeutic benefit of repetitive OKSP remains unclear. Pizzamiglio et al[29] compared a combination therapy of OKSP and visual scanning training with single visual scanning training. After 6 weeks of treatment, they found no difference between the 2 groups with respect to a variety of tasks, such as line bisection, line cancellation, letter cancellation, reading, the Wundt–Jastrow Area Illusion test, and a test of personal neglect. However, 2 recent treatment studies showed a significant and persistent reduction of neglect symptoms after repetitive treatment sessions of OKSP.[31,32] OKSP treatment was superior to conventional visual scanning training in digit cancellation, visuoperceptual and visuomotor line bisection, and visual size distortion and therapeutic effects generalized across tasks and remained stable in a 2-week follow-up.[31] A possible reason why Pizzamiglio et al did not find a treatment effect might be that they combined OKSP with a visual scanning training. Also, active pursuit eye movements were not part of their treatment procedure. The present study shows that significant improvements in neglect can be observed after only 30 minutes of OKSP training, which supports the hypothesis that focusing attention to the moving stimuli and actively performing eye movements to the neglected side are necessary to obtain a lasting treatment effect.

With respect to the possible mechanism of OKSP in neglect therapy, 2 hypotheses are currently advocated. The first hypothesis is based on the assumption that OKSP with slow velocities facilitates directing attention toward the neglected hemispace.[23] The improved attention allocation leads to subsequent improvements in all visual neglect tasks requiring systematic leftward exploration, as in cancellation, reading, size comparisons, or line bisection. This view is supported by the observation that forcing the patient's attention to the contralesional side produces a change in the degree of size distortion in patients with visual neglect.[42] Additionally, a recent functional MRI study by Sturm et al[32] showed significant improvements in different behavioral neglect tasks after OKSP, which correlated with activations of the posterior neural network deploying and directing attention to representations of extrapersonal space. Supplementary to these results, Doricchi et al[43] proposed a possible neural mechanism of action of OKSP, suggesting that leftward OKSP initially activates the undamaged left hemisphere and then —via callosal fibers—consecutively reactivates the damaged right hemisphere. Another possible neural mechanism underlying OKSP might be an optokinetic afternystagmus. Waespe and Henn[44] demonstrated that neurons in the monkey brain stem continue to fire for more than 30 seconds after termination of OKSP. As the brain stem was not damaged in any of our 10 patients (see Figure 1), this region might be involved in the recovery process in conjunction with the above-mentioned posterior attention network.[32]

Another compatible hypothesis is that OKSP facilitates the generation of a more accurate egocentric space representation by providing visual motion input to the disturbed spatial representation in neglect patients. As the visual motion system remains largely intact even after large cortical lesions, most of this system remains functional in neglect.[45] In accordance with this hypothesis, multiple activation sites in the lesioned and intact hemisphere were found with full-field OKSP in an imaging study of hemianopic subjects without neglect.[46] Thus, global directional motion—even in a blind or neglected hemifield—constitutes a strong modulatory input to the visual motion system in the dorsal visual stream, thereby influencing spatial attention and perception on a multimodal level.

In addition, there is also evidence that smooth pursuit eye movements to moving visual stimuli during OKSP might be an important modulating variable. Gur and Ron,[47] for instance, were able to demonstrate a significant improvement in functional visual tasks after a feedback-based training of smooth pursuit eye movements in patients with closed head trauma, but without neglect. A recent functional imaging study with healthy subjects showed that smooth pursuit eye movements and optokinetic nystagmus activate a largely overlapping neural network including the visual cortex, area MT, the frontal and supplementary eye fields, parietal cortex, and cerebellar regions of both hemispheres.[48]

Interestingly, a combination of OKSP and prism adaptation did not lead to a greater improvement than the sole application of OKSP. One reason for a missing add-on effect of prism adaptation might be that prism-induced gaze shifts and eye movements to optokinetic stimuli exploit the same neural mechanisms. Frassinetti et al[19] proposed that the effect of prism adaptation might be linked to the ocular system. This view is supported by studies showing that maneuvers inducing an eye deviation to the neglected side produce a temporary reduction in neglect.[13,14] Nevertheless, the effect of prism adaptation on the ocular system still remains to be proved.

Another reason for a missing add-on effect of the prisms might be that patients in our study were only initially required to perform a pointing task. The hypothesis that prism adaptation is based on visuomotor interaction is supported by a positron emission tomography study demonstrating that improvement of left neglect after prism adaptation is correlated with a modulation of neural activity in the right cerebellum, the left thalamus, the left temporooccipital cortex, the right posterior parietal cortex, and the left medial temporal lobe.[49] In addition, the activation of the cerebellum was strongly correlated with improvements in the Behavioral Inattention Test, suggesting that activation of this area reduces left neglect by facilitating the recruitment of an intact brain area responsible for controlling normal visuospatial output. According to the forward model, the cerebellum is a likely site for comparing the predicted consequences of an action, through an efferent copy of cortical origin.[50] This, in turn, implies that prism-induced modifications of exploratory eye movements without recruiting neural motor circuits may not lead to a visuospatial recalibration in neglect. According to this hypothesis, no add-on effect could be expected from the simultaneous application of OKSP and prism adaptation.

In addition, there is evidence that prism adaptation often shows its strongest effects about 2 hours after administration.[18] An add-on effect of prism adaptation, therefore, could have been missed simply by measuring test performance directly after the treatment.

Nevertheless, as the effectiveness of several bottom-up methods has been approved, the idea of combining these methods to improve the therapeutic effect should be continued in further studies. Sequentially tailored treatments where patients receive a first bottom-up treatment for 10 minutes, followed by a second bottom-up treatment for another 10 minutes, might be a promising approach. OKSP is a method that can be easily combined with other bottom-up methods such as neck muscle vibration, limb activation, or transcranial magnetic stimulation. Likewise, the application of a prism adaptation training could be combined with neck muscle vibration or transcranial magnetic stimulation.[11,51-53]

The idea that following the moving stimuli with the intact arm might serve as an anchor stimulus, helping the patient to focus attention on the dot pattern, could not be affirmed. In contrast, ipsilesional arm movements extinguished the OKSP-induced treatment effect completely. This result has practical implications for the rehabilitation of the neglect syndrome. As a result of our results, patients should be prevented from performing movements of their ipsilesional arm during neglect therapy. According to the work of Robertson and North,[54] the movement of a hand in space activates the ipsilateral half of the personal and peripersonal spatial sector. This is achieved because limb movements activate motor circuits in the contralateral hemisphere. Related to a left-sided neglect syndrome, movements of the left hand activate the lesioned hemisphere, which then reduces neglect. In our study, movement of the right hand in space should have activated motor areas of the nondamaged left hemisphere, thereby directing visuospatial attention to the right hemispace, which obviously resulted in an aggravation of neglect symptoms.

Another possible explanation for a lack of treatment effects under this condition might be that patients focused their attention on the index finger of the right hand, thus missing the full-field stimulation. It is known that neglect patients have limited capacities for dividing attention.[55] Following the moving stimuli with their arm and eyes was the only dual task applied in this study. Therefore, it cannot be ruled out that the divided attention condition led to a decrease in performance. However, this result clearly demonstrates that the effect of OKSP and possibly any other bottom-up treatment can be influenced negatively by any simultaneously applied task. This argues for the isolated or at least sequential use of OKSP and other treatments in neglect therapy.

In summary, contralesional pursuit eye movements to moving visual stimuli presented via conventional PC technology provides a promising therapeutic technique for patients with visuospatial neglect. The present study did not intend to show long-lasting positive effects of single treatment sessions on visuospatial neglect. Instead, we were interested to evaluate therapeutic after effects when 2 neglect treatments are combined. Such combined treatments might be more effective than the single application of each stimulation procedure alone. As resources and outcome of neglect therapy are limited, such combined strategies might be useful in clinical practice.

In the future, randomized treatment studies will have to elucidate the precise mechanisms of action and evaluate other cross-modal therapeutic effects beyond the tactile search effect shown in our study. The effects of bottom-up therapeutic techniques seem to be superior to those obtained with top-down compensatory strategies, such as visual scanning training, or gain similar improvements in a considerably shorter period of time.

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