Effectiveness of Prism Adaptation in Neglect Rehabilitation
A Controlled Trial Study

Andrea Serino, PhD; Moreno Barbiani, PSY; Maria Luisa Rinaldesi, MD; Elisabetta Ladavas, Prof

Background and Purpose—This study was conducted to investigate the effectiveness on neglect recovery of a 2-week treatment based on prism adaptation (PA) in comparison to an analogous visuomotor training performed without prisms, ie, neutral pointing (NP).

Methods—Twenty neglect patients were divided into 2 matched groups, one was submitted to PA (PA group) and the other to NP (NP group) for 10 daily sessions over a period of 2 weeks. After the end of NP treatment, the patients in the NP group were also submitted to PA treatment. Neglect was assessed before and after each treatment and 1 month after the end of the PA treatment.

Results—Visuospatial abilities improved after both PA and NP treatment; however, the improvement was significantly higher in the patients in the PA group than in the patients in the NP group. Moreover, when the patients in the NP group were submitted to PA, they further improved up to the level reached by patients in the PA group, ie, to nonpathological scores. Long-lasting beneficial effects of PA were confirmed 1 month from the end of treatment.

Conclusion—The leftward recalibration of sensorimotor reference frames induced by PA is effective to obtain proper neglect recovery, although visuomotor training based on pointing might partially improve neglect symptoms. (Stroke. 2009;40:00-00.)

Key Words: clinical study ■ neglect ■ rehabilitation

He mispatial neglect is a common outcome after right hemisphere stroke and is characterized by a deficit in perceiving, orienting, and moving toward the left side of space, and such deficit is not due to basic perceptual or motor dysfunctions. Although some spontaneous recovery occurs in the majority of cases,1,2 neglect symptoms remain severe in many patients.1,2 Such symptoms may persist chronically3-4 with debilitating impact on everyday life.5 A variety of rehabilitation techniques have been explored6,7 and the prism adaptation technique (PA) in particular has been shown to ameliorate neglect symptoms in large populations of patients.8,9 PA requires the patient to perform a series of pointing movements toward a visual target while wearing prismatic goggles. These goggles induce a deviation of the visual field toward the right. To compensate, the patient has to orient the pointing movement toward the left, resulting in a leftward drift of sensorimotor coordinates. Several studies showed that this sensorimotor adaptation improves most neglect symptoms both for a short period of time after a single session of PA10-12 and for long term, up to 6 months after 2 weeks of daily treatment.13-15

However, the benefits of PA have recently come under 2 lines of criticism.7,16 First, studies showing long-term effects of PA did not include a proper control condition. Second, when a control condition was used, ie, pointing with neutral goggles (neutral pointing [NP]), 2 different studies obtained conflicting results. Rossetti and colleagues10 found no improvement in patients treated with neutral goggles, whereas Rosseaux and colleagues16 found comparable improvements after treatment with both prismatic and neutral goggles. These criticisms, together with other reports showing no improvement after PA for some tasks,17-20 or for some patients,13-15 cast doubt on the specific efficacy of PA above control conditions.

However, the fact that some neglect improvement can be obtained also after NP cannot be taken as an argument against the specific effectiveness of PA. During NP, patients perform a series of movements toward a visual target presented several times in the neglected hemifield. Such exercise per se might promote visuomotor coordination between the eye and hand21 which could partially reorient a patient’s visuomotor system toward the left. It is worth noting that a similar form of hand–eye coordination underlies PA with the crucial distinction that during PA, a systematic leftward recalibration of hand- and eye-centered reference frames is induced to compensate for the rightward optical deviation.14,22 Thus,
remediation of neglect might be obtained from either NP or PA, particularly if visuomotor training is undertaken for a sufficient amount of time. The crucial question is not simply whether remediation occurs, but whether the leftward recalibration induced by PA is specifically more effective in ameliorating neglect than the general visuomotor training provided by NP.

The aim of the present study is to directly compare the effect of a prism adaptation treatment with that of a treatment based on pointing with neutral goggles. Twenty neglect patients were pseudorandomly divided into 2 groups and assigned to either PA or NP treatment. Both treatments consisted of 10 daily sessions (5 sessions per week). Each session comprised 90 pointing movements toward a visual target presented in a variety of positions on the right, left, and at the center of the visual field. Throughout the sessions, patients in the PA group wore prismatic goggles deviating the visual field 10° toward the right, whereas patients in the NP group wore neutral goggles. At the end of treatment with neutral goggles, patients in the NP group underwent an additional 2-week treatment with prismatic goggles. Neglect was assessed at the time of admission, again after PA or NP treatment, and in patients in the NP group, for a third time after the treatment with prismatic goggles. To test long-term effects of prism adaptation, a follow-up evaluation was administered to all patients 1 month after their last treatment session.

We hypothesized that if repeated visuomotor training is useful per se in reorienting the sensorimotor system toward the left, an improvement of neglect should be found after both NP and PA treatments. However, if the leftward recalibration due to PA is specifically more effective in recovering neglect, greater improvement should be evident in the PA group than in the NP group. In addition, amelioration of neglect in the NP group after PA therapy should be greater than that obtained in the same patients after NP therapy. Finally, if the improvement in neglect after PA is long lasting, all patients should exhibit fewer neglect symptoms 1 month after the end of PA treatment.

Methods

Subjects

Twenty righthanded patients presenting with neglect after right hemisphere stroke were recruited to participate in the study at the Istituto di Riabilitazione Santo Stefano, MC, Italy. Patients were selected for the presence of hemispatial neglect after brain damage; the inclusion criterion was their pathological performance on the Behavioral Inattention Test (BIT) battery.23 Exclusion criteria were presence of widespread mental deterioration (Mini-Mental State Examination score <20) or psychiatric disorders. Ten patients (2 females) were assigned to the PA group and 10 females) to the NP group pseudorandomly with the last 4 patients distributed to match neglect severity between the 2 groups at the time of admission (see “Results”. Patients in the PA and NP groups did not differ in age (mean age: PA = 62 years, NP = 61; P = 0.78), education (mean years of schooling: NP = 9, PA = 10; P = 0.54) or in time after injury (mean months from injury NP = 10, PA = 5; P = 0.42). Patients were unaware of their group assignment; all were told only that they had been enrolled in rehabilitation treatment for their spatial attention deficits. There were no dropouts in either group. Patients gave informed consent to participate in the study, which was approved by the local ethics committee and conducted in accordance with the Declaration of Helsinki. Patients’ clinical and demographic data are presented in the Table.

Neglect Assessment

Hemispatial neglect was assessed with the BIT battery on both Conventional (BIT-C) and Behavioral (BIT-B) scales (mean range = 0 to 114; mean cutoff = 97), and with the Bell Cancellation Test.24 Patients’ neglect dyslexia was also evaluated, by using the reading test described by Ladavas and colleagues.25 BIT battery measure was chosen as the primary outcome of the treatment, whereas cancellation scores and reading accuracy were chosen as secondary outcomes. All tests were administered at the time of admission to the study, before any treatment (the baseline session), and again after 2 weeks of either PA or NP treatment (the posttreatment session). Patients in the NP group underwent a third evaluation at the end of PA treatment performed after their NP treatment. All patients underwent follow-up evaluation 1 month after the end of the PA treatment (the follow-up session). Testing sessions required approximately 3 hours per patient distributed over 2 days to minimize fatigue.

Treatment Procedure

PA treatment consisted of 10 daily sessions over a period of 2 weeks with sessions lasting approximately 30 minutes each. Patients were required to repeatedly point at a visual target with their right index finger while wearing prismatic lenses, which shifted their visual field 10° rightward (Société Peter, Lyon, France). Visual targets were presented 90 times 60 cm away from the patient’s midline subtending a total visual space of 50°. Thirty times, the visual targets were presented in a variety of positions in the patient’s right visual field, 30 times in the left and 30 times in the center, in random order. During the adaptation procedure, patients could see only the final part of their movement, ie, their index finger, enabling them to progressively correct the pointing errors induced by the prism.

Table. Demographic and Clinical Data for Patients Initially Submitted to PA and to NP

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Gender</th>
<th>Age</th>
<th>Education</th>
<th>Months From Illness</th>
<th>BIT at Admission (cutoff = 97)</th>
</tr>
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<tr>
<td>PA 1</td>
<td>M</td>
<td>61</td>
<td>23</td>
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<tr>
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<td>10</td>
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<tr>
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<td>3</td>
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<td>66</td>
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<td>6</td>
<td>75</td>
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<tr>
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<td>F</td>
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<tr>
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</table>

M indicates male; F, female.
To ensure that patients treated with prisms actually achieved a leftward correction of their visuomotor behavior, 2 indices of sensorimotor effects were measured: error reduction and after effect. Error reduction refers to the online correction of pointing movements during PA, whereas after effect refers to the amount of leftward deviation in pointing achieved after PA. These 2 indices are considered the hallmark of adaptation to prisms, and previous work has demonstrated that error reduction in particular is predictive of recovery from neglect.

To measure error reduction, during each PA session, patients’ pointing error was recorded by an expert therapist. Error was calculated as the deviation in the visual angle between the point and the target and was coded as positive for rightward deviance and negative for leftward. To assess after effect, before the first PA session and after each subsequent PA session, we measured pointing error toward 30 visual targets, on the left, right, and at the center, without vision of the pointing limb (see Serino and colleagues for details about PA procedure and apparatus).

NP treatment was administered using exactly the same procedures over the same amount of time with the exception that patients in the NP group performed their pointing exercises while wearing neutral goggles.

Results

Visuomotor Effects of Prism Adaptation: After Effect and Error Reduction

To demonstrate that the treatment with prisms actually induced a leftward correction in visuomotor coordinates, after effect and error reduction were measured in both groups of patients during PA.

To assess after effect, pointing accuracy (without vision of the pointing limb) recorded before the first session of PA was compared with pointing accuracy recorded after each PA session; to this aim, pointing error after all PA sessions was averaged. An analysis of variance (ANOVA) was conducted with the factors session (before PA and after PA) and group (PA and NP submitted to PA). A significant effect of session (F[1,18]=57.61; P<0.00001) demonstrates that pointing movements were accurate before any exposure to prisms (mean error=0.01° of visual angle), whereas after each PA session, patients showed a systematic deviation of their pointing toward the left (mean error, averaged across sessions=4°). Neither the effect of group nor the group-by-session interaction was significant (P>0.47). Together these results demonstrate that PA induced a systematic leftward deviation of pointing after prism exposure, ie, the after effect, and this effect was comparable in both groups of patients.

To demonstrate error reduction, ie, an online, gradual correction of pointing to compensate for the prism’s optical displacement, we analyzed pointing errors during each PA session as a function of exposure to the prisms. For each session, pointing errors were computed in the first 30 trials (T1), from Trial 31 to Trial 60 (T2), and in the last 30 trials (T3). An ANOVA was conducted with the within-subjects factors session (session of prism exposure from 1 to 10) and trial (T1, T2, and T3) and the between-subjects factor group. A significant effect of trial (F[2,36]=35.48; P<0.00001) demonstrates that pointing errors were progressively reduced from the first 30 trials of PA (T1=0.84°) to the middle trials 31 to 60 (T2=0.16), and to the last 30 trials (T3=0.09; P<0.002 in all comparisons). This result shows that patients wearing prisms typically exhibit an initial rightward deviation in their pointing, which is progressively reduced to compensate for the prismatic optical displacement. This adaptive behavior was implemented across sessions as shown by the significant 2-way interaction of session by trial (F[18,324]=6.25; P<0.0001). As Figure 1 clearly shows, pointing error was higher in the first trials of PA during the initial critical 10 trials (T1) for each session; pointing
error for T1 trials of the first session (1.78°) was higher than that recorded during T1 trials of all the other sessions (P<0.02 for all comparisons). Then pointing error for T1 trials progressively, slightly reduced across the second (1.28), third (0.97), and fourth (1) sessions and was stably and definitely reduced starting from the fifth session for the remaining 5 sessions; pointing errors for T1 trials was equivalent and close to zero for Sessions 5, 6, 7, 8, 9, and 10 (P>0.33 for all comparisons).

This time course in pointing performance during PA confirms previous findings from our group demonstrating a gradual error reduction effect across the first sessions of treatment. Error reduction was comparable between patients in the PA group and patients in the NP group undertaking PA, because neither the main effect of group nor any interaction among group, session, and trial were significant (P>0.67).

Conversely, as expected, NP treatment did not induce any systematic deviation of pointing behavior.

**Effects of Prism Adaptation and Neutral Pointing on Neglect Recovery**

To study the specific effect on neglect recovery of PA treatment in comparison to NP treatment, we compared the baseline and posttreatment results from the PA and NP groups on the BIT battery, the cancellation tasks, and the reading test. Furthermore, to test whether patients in the NP group could obtain a further amelioration of neglect if treated with prisms, the results of patients in the NP group were compared at baseline, post NP treatment, and after subsequent PA treatment. Finally, to study the long-term persistence of the PA effect, scores from all patients were compared at the baseline, post PA treatment, and in the follow-up session 1 month after the end of the PA treatment. For sake of brevity, only significant effects are discussed, and when necessary, results from Newman-Keuls post hoc comparisons are presented.

**Neglect Recovery After Prism Adaptation and Neutral Pointing Treatment**

An ANOVA conducted on BIT scores with within-subjects factors of scale (conventional and behavioral) and session (baseline and posttreatment) and between-subjects factor of group (PA and NP) showed a significant effect of session (F[1,18]=42.95; P<0.000001; η=0.70); patients’ scores were higher posttreatment (mean score=88; SD=14) than at the baseline (mean=73; SD=16). This result needs to be interpreted in the light of the significant 2-way group×session interaction (F[1,18]=4.77; P<0.05; η=0.21); scores for patients in the PA group strongly improved from before (mean=75; SD=11) to after PA (mean=95; SD=6; P<0.0002). A moderate improvement was also found in scores for patients in the NP group before (mean=71; SD=17) and after NP (mean=81; SD=20; P<0.02). Importantly, although scores of patients in the PA group and those in the NP group did not differ at baseline (P=0.17), BIT scores posttreatment were significantly higher in patients submitted to PA than in patients submitted to NP (P<0.0006; see Figure 2). Considering patients’ individual data, all patients from the PA group improved after the treatment, whereas 8 of 10 patients in the NP group improved after the treatment.

Furthermore, it is noteworthy that, whereas after PA, scores for patients in the PA group were not different from the cutoff score of the BIT (mean cutoff BIT-C and BIT-B=97; one-sample t test [1,9]=−1.15; P=0.27), after NP, scores for patients in the NP group remained significantly under the cutoff score (one-sample t test [1,9]=−2.58; P=0.04). Considering patients’ individual data, 6 of 10 patients from the PA group obtained BIT scores above the neglect cutoff score, whereas only one of 10 patients from the NP group obtained a score above the cutoff.

A further ANOVA, with the factors group and session, was conducted on patients’ scores in the 3 cancellation tasks (mean percentage of correctly cancelled items in the left hemispace in the Bell Cancellation Test and the Star and Letter Cancellation subtests from the BIT). The effect of session was significant (F[1,18]=31.63; P<0.0001; η=0.64; baseline: mean=41%, SD=23%; posttreatment=65%, SD=25). More importantly, the 2-way group×session interaction was significant (F[1,18]=5.15; P<0.04; η=0.23). Post hoc comparisons showed that both patients in the PA group and those in the NP group improved after treatment (PA group: baseline mean=39%, SD=24; after PA mean=73%, SD=18; NP group: baseline mean=54%, SD=24; after NP mean=75%, SD=18).
Finally, an analogous ANOVA conducted on the percentage of correctly read letter strings in the reading task showed a significant effect of session \((F[1,18]=23.56; P<0.0002; \eta^2=0.57)\); reading accuracy was higher posttreatment \((mean\ accuracy=78\%; SD=26)\) than at the baseline \((mean=72\%; SD=25)\). More importantly, the 2-way group \(\times\) session interaction was significant \((F[1,18]=4.78; P<0.04; \eta=0.22)\). Post hoc tests revealed that in the PA group, reading accuracy was higher posttreatment \((mean=76\%; SD=23)\) than at baseline \((mean=67\%; SD=23; P<0.0003)\), whereas in patients in the NP group, the difference between baseline \((mean=77\%; SD=27)\) and posttreatment \((mean=81\%; SD=28)\) was not significant \((P=0.08)\). Considering patients’ individual data, all patients from the PA group improved after the treatment, whereas only 5 of 10 patients from the NP group improved.

It might be noteworthy that patients in the PA group obtained lower reading accuracy scores than patients in the NP group at the baseline assessment. This difference can be explained considering that neglect dyslexia is a secondary symptom of neglect present in some patients and not in others. Thus, because patients’ assignment to either group was performed pseudorandomly, considering only BIT scores, the 2 groups were not perfectly matched for a secondary measure of neglect such as reading abilities. One might object that the different effect of the treatment on neglect dyslexia in the 2 groups was due to their different performance at the baseline; indeed, the lack of any improvement in patients in the NP group could be due to a ceiling effect. However, this argument can be discharged considering that when patients in the NP group were subsequently submitted to the PA treatment, they actually improved in reading scores. Thus, even if patients in the NP group started from a higher level of performance, they still obtained a significant benefit from the PA treatment.

In summary, although a moderate improvement of visuospatial abilities was found in both groups of patients, the improvement was higher in patients undergoing PA than in those undergoing NP. Furthermore, BIT scores from the PA group, but not from the NP group, after the treatment were not below the neglect cutoff score. Patients in the PA group achieved a posttreatment score on the BIT battery not differing from the cutoff score. These results demonstrate the specific effectiveness of PA in ameliorating symptoms of neglect. For this reason, at the end of the first phase of the study, patients in the NP group were also treated with PA, and their visuospatial abilities were compared among the assessments performed at the admission, after NP, and after PA.

### Additional Effect of Prism Adaptation in Patients Undergoing Neutral Pointing

An ANOVA performed on BIT scores in patients in the NP group, with 2 within-subjects factors of session \((baseline, post-NP, and post-PA)\) and scale \((BIT-B and BIT-C)\), showed a significant effect of session \((F[2,18]=25.42; P<0.000001; \eta=0.85)\). In comparison to the baseline session \((71)\), patients’ scores improved both after NP \((81; P<0.02)\) and after PA \((mean=98; SD=11; P<0.0002)\); however, the scores obtained after PA were significantly better than those after NP \((P<0.0005; see Figure 2)\). Importantly, only after PA, scores for the patients in the NP group were not below the BIT cutoff score \((t[19]=0.17; P=0.83)\). Moreover, although after NP only one patient obtained a BIT score above the neglect cutoff, after PA, 6 patients obtained BIT scores above the cutoff.

The ANOVA conducted on cancellation tasks scores with the factor session showed similar results; the main effect of session was significant \((F[2,18]=13.52; P<0.0003; \eta=0.77)\). Post hoc tests showed that although an improvement was found between baseline \((42\%)\) and post-NP \((57\%; P<0.05)\) scores, the improvement was much stronger after PA \((mean=77\%; SD=18; P<0.008 for both comparisons)\). Finally, the ANOVA conducted on reading accuracy scores showed a significant effect of session \((F[2,18]=7.58; P<0.005; \eta=0.60)\); reading accuracy was not significantly different before \((77\%)\) and after NP \((81\%; P=0.09)\), whereas it was significantly higher after PA \((mean=85\%; SD=24; P<0.05 for both comparisons)\).

### Long-Term Effects of Prism Adaptation

Finally, to confirm that the recovery from neglect due to PA was long-lasting, patients’ visuospatial abilities assessed before any treatment and after the treatment with PA were compared with the results of the follow-up assessment performed 1 month after PA. Patients from both groups were included in this analysis. An ANOVA conducted on BIT scores with the within-subjects factors of scale \((Conventional and Behavioral)\) and session \((baseline, post-PA treatment, follow-up)\) and the between-subjects factor of group \((PA and NP)\) showed a significant effect of session \((F[1,18]=41.2; P<0.00001; \eta=0.81)\); patients’ scores at the follow-up assessment \((mean=93; SD=11)\) were significantly higher than those at the baseline \((72; P<0.0002)\) and did not differ from those obtained after PA \((95; P=0.51)\). An ANOVA performed on cancellation scores with the factors group and session showed similar results; the main effect of session was significant \((F[1,18]=39.82; P<0.00001; \eta=0.75)\) and post hoc comparisons revealed that patients’ results at the follow-up assessment \((mean=77\%; SD=9)\) were both better than those at the baseline \((41\%; P<0.00002)\) and not different than those after PA \((75\%; P=0.60)\). Analogously, an ANOVA conducted on reading accuracy scores showed a significant effect of session \((F[1,18]=10.61; P<0.0003; \eta=0.61)\), and post hoc confirmed that patients reading ability at the follow-up session \((mean=84\%; SD=24)\) was better that at baseline \((74\%; P<0.0004)\) and similar to that immediately after PA \((83\%; P=0.32)\). Neither the main effect of group nor any interaction of group with other factors reached
This is the first study that directly compares the effects of a 2-week treatment based on PA with those of 2 weeks of visuomotor training performed without prismatic goggles, ie, NP. The results clearly show that the repetition of pointing movements toward visual stimuli improved visuospatial performance in both patients treated with PA and with NP. However, the improvement was significantly stronger when the pointing was performed under the exposure to prismatic goggles, because neglect amelioration was higher in patients treated with PA than in those treated with NP. Furthermore, to obtain a comparable recovery from neglect, the patients in the NP group needed further treatment with prismatic goggles. Only after treatment based on PA did both groups of patients achieve BIT scores similar to the cutoff. This recovery was maintained at least 1 month after the end of the treatment in both groups of patients, confirming the long-lasting beneficial effects of PA described in previous findings from our group.14,15

The improvement obtained after the NP treatment might be surprising and partially explained as a consequence of nonspecific effects such as familiarity with the testing measures, general stimulation, or even a placebo effect. However, these effects alone cannot completely account for the NP improvement, because in previous studies, control patients, who were submitted to physiotherapy and general cognitive stimulation, did not show any improvement in successive evaluations for neglect.13–15 Therefore, the improvement found after NP might depend on a form of visuomotor training embedded in the NP procedure. Indeed, the procedure requires the patient to plan and perform a series of movements toward a visual stimulus, which is occasionally placed within the neglected hemifield. It is well known that pointing relies on a form of visuomotor coordination between the hand and eye21; thus, the NP procedure might train the patient to orient his or her sensorimotor system toward the left side of space when a visual stimulus is presented there. If this orienting behavior is reinforced by repetition of the procedure, like in the present study, visuomotor training itself might result in partial amelioration of neglect.

The same type of visuomotor exercise is also required during PA, tapping into a similar synergy between the hand and eye. However, in contrast to NP, PA promotes a systematic deviation of eye-centered and hand-centered reference frames toward the left.14,22 To compensate for the visual field displacement induced by prisms, patients during adaptation implicitly deviate their motor programs toward the left, thereby implementing a leftward recalibration into their sensorimotor systems. These adaptive effects are demonstrated by the presence of both error reduction and after effect during and after prism exposure, respectively.22 As a consequence of this sensorimotor adaptation, patients’ visuospatial abilities improve substantially, pushing their scores above the neglect cutoff.

Future researchers might shed light onto the mechanism underlying the specific effect of PA in comparison to NP. Previous studies from our own group14,15,26 for instance, showed that PA induces a leftward deviation not only of hand movements, but also of eye movements, and that the amount of eye movements deviation after PA was predictive of neglect recovery. Thus, we proposed that neglect recovery by PA is, at least partially, mediated by a leftward resetting of the oculomotor system due to the eye–hand coordination during pointing. Future studies might investigate whether the effect of PA on the oculomotor system can explain the specific benefit on neglect recovery due to PA in comparison to NP.

Finally, findings from the present study might also reconcile the apparent contradiction between the Rossetti et al10 and Rosseaux et al16 findings (see the beginning of this article). A single session of pointing could induce some amelioration of neglect; this effect might in some patients be similar to that obtained after a single PA session given that the 2 procedures share some common mechanisms. However, after the first treatment session, the PA effects require repetition to be stably implemented and to produce a general benefit for the majority of patients. This conclusion is supported by the increase in the error reduction effect across successive sessions as demonstrated in the present study. Moreover, previous findings from our laboratory14,15 showed that the amount of error reduction achieved during the first treatment sessions was predictive of recovery from neglect. Thus, the time course of error reduction effect across successive exposures to prisms might be an important factor to consider to evaluate the effectiveness of PA on different patients. Data concerning error reduction are not reported by either Rossetti et al10 or by Rosseaux et al16; therefore, these differing findings might result from individual differences in patients’ ability to rapidly adapt to prisms. The present study compensates for this variety in adaptation and demonstrates a specific effect of PA by virtue of the repetition of the training sessions, the assessment of different visuomotor effects, the correct balancing between the 2 groups of patients, and the additional PA training administered to the patients initially treated with NP.

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References


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