Table *Summary of patients identifying reason for IVIg therapy, number of previous treatments, and dosages and rates of infusions on the day of vascular events*

Case no.	Reason for IVIg therapy	Previous treatments, d	IVIg dose, g	Infusion rate, g/h	Symptoms	Radiologic findings
1	CIDP	3	15	4.2	L ptosis, facial numbness, aphasia, diplopia	L occipital parietal infarcts, L PCA thrombus
2	CIDP	5	25	8.1	R lower extremity pain and paresthesias	R popliteal occlusive thrombus
3	Polymyositis	13	80	12.3	Confusion, aphasia, and R facial weakness	L insular region infarct
4	Polymyositis	14	70	12.1	Confusion and memory difficulties	R parietal lobe infarct, R MCA thrombus

IVIg = IV immunoglobin; CIDP = chronic inflammatory demyelinating polyradiculoneuropathy; PCA = posterior cerebral artery; MCA = middle cerebral artery.

table). Although we were using Polygam exclusively, three different lots were used in these patients. The most remediable factor is the increase in serum viscosity, which is related to the amount of IVIg infused in a given time period. We have not had any further thrombotic events over a 12-month period since we attempted to minimize the viscosity changes by using only 5% solutions, limiting the maximum infusion rate to 15 g/hour, and using IVIg formulation with osmolality comparable to serum for patients with known vascular risk factors.

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CME Eye movements tell only half the story

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Article abstract—The dramatic improvements of neglect symptoms after prism adaptation (PA) have been interpreted as evidence that PA reorganizes higher levels of spatial representation. Here the authors demonstrate that while the exploratory eye movements of a patient with neglect were clearly shifted toward the left after PA, he still showed no awareness for the left side of the stimuli he was now actively exploring. PA modulates functions of the parietal lobe, such as eye movement control, but fails to influence the underlying mechanisms of neglect.

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Patients with neglect following right hemispheric brain damage behave as if half of their world has ceased to exist. Several studies have demonstrated temporary amelioration of neglect by sensory stimulation,[1] but it has been argued that these procedures modulate only the overt behavior measured by classic tests of neglect without actually getting to the root of the underlying disorder.[2] To test whether or

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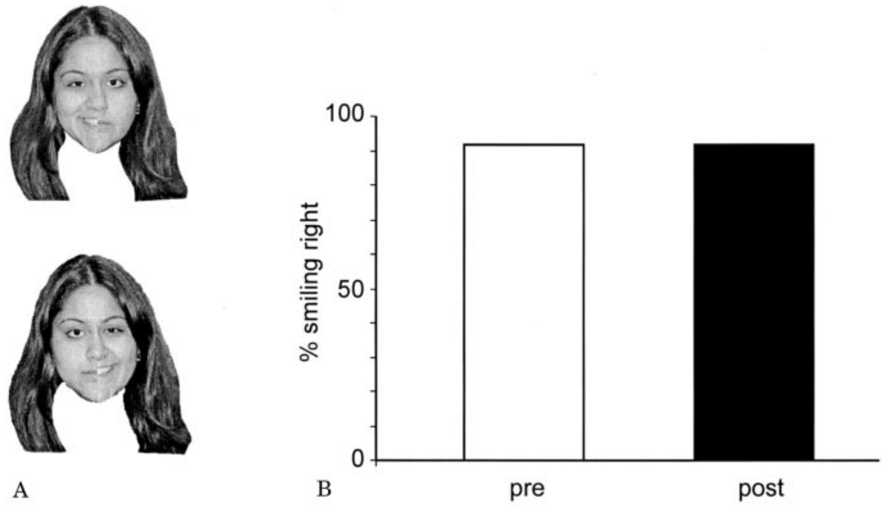

Figure 1. (A) Pair of chimeric faces. The patient had to choose which face was "happier" by saying "top" or "bottom." The two faces in one pair were arranged vertically such that no lateral bias occurred. Each pair was presented for 1.5 seconds. (B) Results of the perceptual task. Before (pre) and after (post) prism adaptation, the patient chose the face that was smiling on the right side in 91.67% of all trials (i.e., in 11 of 12 trials before and after prism adaptation).

not the same holds true for prism adaptation (PA), a patient with neglect was tested on two visual tasks before and after PA. The improvement generated by PA typically generalizes across many tests of neglect[3,4] (e.g., cancellation, line bisection, copying, and mental imagery), but none of these measures patients' explicit awareness of stimuli that are acted upon. For instance, the beneficial effect of PA on cognitive tasks such as mental imagery is not surprising because mental imagery of motor or visual tasks shares common neural mechanisms with overt motor behavior or visual perception.[5] In fact, perception and imagery access the same stored representation of the given stimulus. Thus, it still needs to be shown whether or not PA affects the awareness of a new stimulus that has not been previously encoded.

Patient and methods. We tested one neglect patient 12 months after he experienced a hemorrhagic stroke of the right middle cerebral artery, leading to a temporoparietal lesion with minor extension into the frontal cortex. Within this lesion, a higher-density component was observed posteriorly in the region of the temporoparietal junction. The patient was 76 years old at the time of testing and over repeated assessments presented with clear signs of severe contralesional neglect as assessed by various cancellation tasks and figure copying (clinical details of the patient have been reported elsewhere).[6] Neuropsychological assessment was otherwise unremarkable.

We tested the patient on two tasks that allowed us to dissociate behavior from awareness. To examine his awareness of stimuli he is exploring, the first measure tested his ability to judge the "happiness" of 12 vertically arranged pairs of chimeric faces composed of half-smiling and half-neutral faces (figure 1 A). Patients with left neglect typically select the face in which the right half is depicted as smiling as the "happy" one (healthy subjects exhibit the opposite bias).[7] In addition to whether the patient showed this reversal, we were also interested in whether he noticed the chimeric nature of the stimuli at all and whether the rightward perceptual bias would persist after PA. To test his overt behavior, he was required to explore images of 12 normal and 6 chimeric faces, presented individually for 10 seconds each, while his eye movements were recorded. It is a common observation that patients with neglect do not always report the objects on which they fixate, indicating that they are not aware of what they are looking at. Thus, recording the eye movements and asking for a verbal report on the nature of the stimuli allowed us to explore both the overt behavior toward the faces and the perceptual awareness of the characteristics of those same faces. Eye movements were recorded at 60 Hz with the ASL model 501 eye tracker (Applied Science Laboratories, Bedford, MA). Successive points of measurement were defined as "fixations" if they fell into a moving window of 1° of visual angle and had a minimum duration of 150 milliseconds.

We tested the patient on tasks both before and after PA. As a baseline measurement,[3] he was also asked to make five pointing movements to his subjective straight-ahead position while blindfolded, a task on which he showed the expected rightward bias (figure 2 A). Then, while wearing prismatic lenses that created a rightward optical shift of 10°, he made 50 pointing movements to targets presented 10° left and right of the objective straight-ahead position. Afterward, he showed a clear leftward shift in his subjective straight-ahead pointing movements (see figure 2 A), indicating a successful adaptation to the rightward shift induced by the prisms.

In a separate session of PA conducted after the behavioral and eye movement chimeric faces tasks, the patient demonstrated substantial improvements on clinical cancellation tests of neglect (letter cancellation and bells test). A separate session was chosen for these tests to avoid the possible effects of fatigue. Before PA, he did not find any left-sided targets in the cancellation tasks, whereas after PA, he found 76.7% of the targets on the left side in the letter cancellation task and 86.7% of the targets on the left side in the bells test, again indicating a successful adaptation to the visual shift.

Results. Before PA, the patient showed a clear rightward perceptual bias, choosing the face depicted as smiling on the right side in 91.67% of all trials (see figure 1 B). This perceptual bias was accompanied by a clear rightward bias in his eye movements (see figure 2 B), such that 63 of 85 total fixations were to the right side of the chimeric faces (74.1% to the right side of the stimuli, 25.9% to the left side; see figure 2 C). His pattern of eye movements was then measured with the same stimuli after PA. As expected, his eye movement pattern had changed dramatically after PA (see figure 2 B), such that of 69 total fixations, now only 14 were on the right side of the chimeric faces, whereas 55 were on the left—a reversal of his preadaptation performance (20.3% to the right side of the stimuli, 79.7% to the left side; see figure 2 C). Statistical comparison of the number of fixations on the left and right sides of the chimeric faces before and after PA revealed a difference before and after PA (χ^2 [1] = 44.14, $p < 0.001$). In sharp contrast, the patient's perceptual bias remained unchanged. When he was now asked to judge the happiness of the chimeric faces, he chose the face that was smiling on the right side again in 91.67% of the trials (see figure 1 B).

After all testing was completed, we asked the patient for his subjective impression both of the PA procedure and of the faces stimuli. Remarkably, he explicitly stated that he did not notice anything unusual about the faces stimuli or the induced visual shift caused by the prisms. Thus, before and after PA, he was aware of the fact that the stimuli he had been exploring consisted of full faces but was not aware of the fact that the emotional expression of the two halves of the faces did not match (this difference is immediately obvious to healthy observers).

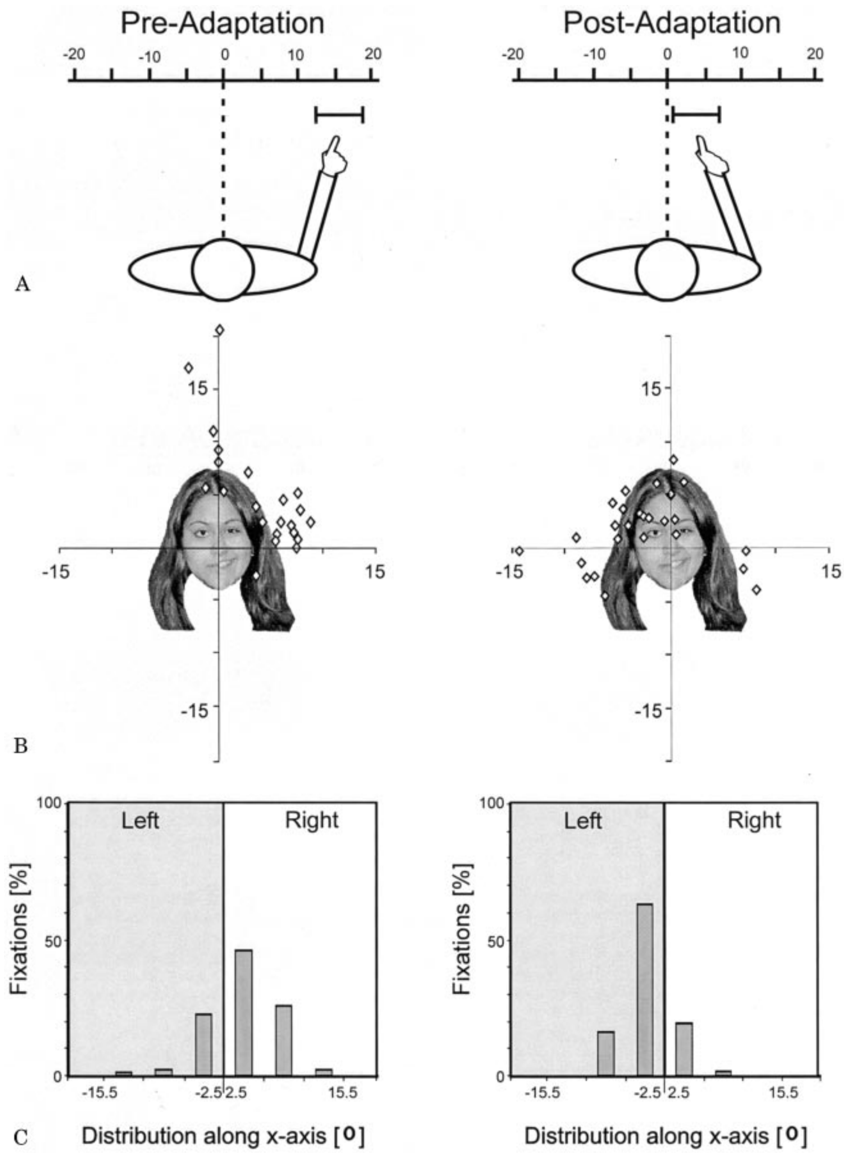

Figure 2. (A) Results of subjective straight-ahead pointing movements. Before prism adaptation, the patient's pointing movements deviated clearly toward the right side (mean 16.7°, SD 7.4°). After the exposure period, his subjective straight-ahead pointing movements almost coincided with the objective midline (mean 2.4°, SD 7.3°). (B) Fixations superimposed on a chimeric face stimulus. Fixations are depicted as diamonds. The faces in the eye movement task were presented individually for 10 seconds each and subtended approximately 13.2° horizontally and 14.9° vertically. (C) Distribution of fixations along the x-axis *before and after prism adaptation averaged across all chimeric faces (n = 6). Fixations are plotted in discrete 5° sectors along the* x-axis *starting from −2.5 and +2.5°. To compensate for minor head movements, we did not include fixations within a 5° sector around the patient's objective straight-ahead position in the statistical analysis.*

Discussion. Taken together, these results show that despite full exploration of a stimulus array after PA, the deficit in awareness of the left side still persists. This finding challenges accounts of spatial neglect that attribute the disorder to deficient scanning strategies of the contralesional side of stimuli or to a deficient attentional disengagement from the ipsilesional side.[8] These functions are subserved by the parietal lobe, and PA unarguably improves these important components of the neglect syndrome but does not improve the underlying awareness problem. According to recent findings, the neural substrate of spatial neglect is located in the superior temporal gyrus (STG)[9] rather than the parietal lobe. The STG is activated during the encoding of object identities and spatial locations.[10] If these processes fail after the STG is lesioned, incoming stimuli will not reach explicit awareness. This loss of perceptual awareness is not ameliorated by PA, which modulates actions directed toward stimuli but cannot influence the deficit in their internal representations. Further research (e.g., group studies, brain imaging studies) will be needed to examine explicitly the different contributions of the inferior parietal lobe and the STG to the neglect syndrome.

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CME

Prism adaptation can improve contralesional tactile perception in neglect

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Abstract—The authors show that prismatic adaptation can reduce tactile inattention in stroke patients with unilateral neglect. Four patients with visuospatial neglect and tactile extinction underwent 10-minute application of 20° right-shifting prismatic lenses during pointing. This improved contralesional tactile perception in all patients, even for a task requiring no exploration or spatial motor responses. This finding suggests a potential role for prismatic adaptation in the rehabilitation of multiple sensory modalities in patients with neglect.

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Unilateral neglect is common after right hemisphere lesions. Neglect patients ignore stimuli on the contralesional (usually left) side of space and body.[1] Some patients may show extinction, whereby single stimuli can be perceived on each side, but contralesional stimuli go undetected during bilateral stimulation.[2] Rehabilitation of visuospatial neglect has proved challenging, but recent work suggests striking effects from prism adaptation (PA).[3] Prismatic lenses induce an optical deviation toward the ipsilesional side for several minutes, while patients perform pointing movements with the ipsilesional hand toward visual targets. To correct for the visual shift induced by the lenses, patients must make motor corrections toward the contralesional side during each pointing movement. At the same time, they receive visual feedback on any inaccuracy further to the ipsilesional side than usual. Once prisms are removed, patients show a directional pointing error toward the contralesional side (prism aftereffect).[3] This aftereffect can be particularly long-lasting for neglect patients[3-6] as compared with PA in subjects, and critically is accompanied by improvements in visuospatial neglect lasting several hours or days.[5]

Prism adaptation has been shown to improve several visuospatial neglect symptoms, including visual search or drawing,[3] neglect dyslexia,[4] personal neglect, and haptic[7] and visuomotor tasks.[5] However, it remains unknown whether the beneficial effect of PA can directly affect perception in neglect patients or rather modulates primarily active exploration strategies (which may even affect visual imagery).[6] It also remains unknown whether PA can modulate the somatosensory deficits associated with neglect.[8] To address these issues, we tested whether PA can ameliorate tactile extinction.

Methods. Four patients with right hemisphere damage (figure) and tactile extinction were studied after giving written consent. The Ethics Committee of the Homerton Hospital in London (UK) previously approved the study. All patients showed some degree of neglect on standard tests (table 1). Tactile perception was assessed experimentally using electromagnetic solenoids (Trans Dimension, USA) to deliver single unseen 100-ms taps on the index finger pad of either hand. Patients placed their hands in their lap while fixating a cross centered on a monitor in front of them. Tactile stimuli could be delivered unilaterally to either the right or left hand (18 per side for Patients 2 and 4, 12 for Patients 1 and 3) or to both hands simultaneously (18 for Patients 2 and 4, 24 for Patients 1 and 3) in an intermingled sequence. Six "catch" trials

See also pages 1734 and 1826

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