Functional Cerebral Reorganization for Auditory Spatial Processing and Auditory Substitution of Vision in Early Blind Subjects

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Early blind (EB) individuals can recognize bidimensional shapes using a prosthesis substituting vision with audition (PSVA) and activate right dorsal extrastriate visual cortex during the execution of this task. The present study used repetitive transcranial magnetic stimulation (rTMS) to further examine the functional role of this structure in the successful use of the PSVA. Moreover, we investigated which auditory parameter used in the prosthesis (pitch, intensity, or spatial location) might contribute to this occipital activation. Results revealed that rTMS applied to right dorsal extrastriate cortex in EB subjects interferes with both the PSVA use and the auditory spatial location task but not with pitch and intensity discriminations. By contrast, rTMS targeting the same cortical areas in sighted subjects did not affect performance on any auditory tasks. Early visual deprivation thus leads to functional cerebral cross-modal reorganization in the processing of auditory information and auditory-to-visual sensory substitution. The findings also point to the specific involvement of the dorsal visual stream for auditory spatial processing in blind subjects. Moreover, this suggests that sensory substitution prostheses can be developed using these additional neural resources to perform tasks that partially compensate for the loss of vision.

Keywords: blindness, occipital cortex, plasticity, sensory substitution, transcranial magnetic stimulation

Introduction

There is increasing evidence that several of the exceptional abilities of sensory-deprived individuals are linked to the recruitment of cerebral areas deprived of their normal input. This is particularly true for people who lost their vision early in life, that is to say, during the critical time in development when cerebral plasticity is at its greatest (for reviews, see Bavelier and Neville 2002; Theoret and others 2004). Indeed, investigating cerebral reorganization, we showed that early blind (EB) individuals, compared with sighted control (SC) subjects, manifested higher metabolic levels in occipital (visual) areas (Wanet-Defalque and others 1988; Veraart and others 1990). Moreover, the similar oxygen-to-glucose ratios recorded in the visual areas of EB and SC subjects are in favor of an aerobic metabolism of EB's visual areas and thus related to neural activity (De Volder and others 1997). Since these preliminary works, a number of neuroimaging studies using various techniques have demonstrated task-dependent activation of occipital cortex (OC) during tactile (Sadato and others 1996; Buchel 1998; Burton, Snyder, Conturo, and others 2002; Pietrini and others 2004), auditory (Kujala and others 1995; Roder and others 1999; Leclerc and others 2000; Weeks and others 2000), memory (Roder and others 2001; Amedi and others 2003; Roder and Rosler 2003), and language-related (Roder and others 2000;

Burton, Snyder, Diamond, and Raichle 2002) processing in EB subjects. However, these neuroimaging studies only established an association between task execution and pattern of cortical activation without actually proving that the OC plays a causal role in the performance of the task. Chain of cause and necessity can be achieved only by reversely engineering the brain (Walsh and Cowey 2000). It has been demonstrated that a focal and transient disruption of the function of a targeted cortical region can be induced by transcranial magnetic stimulation (TMS). This method is therefore useful in determining whether and to what extent a specific brain region is necessary for perception (Walsh and others 1998). By applying TMS to the OC of blind subjects, previous studies established the relevance of the "visual" cortex for Braille (Cohen and others 1997, 1999) and language-related processing (Amedi and others 2004). Support of such causal link was further illustrated in the case of a proficient Braille reader, blind since birth, who became unable to read Braille, despite normal somatosensory perception, after bilateral occipital damage resulting from an ischemic stroke (Hamilton and others 2000). However, the functional relevance of OC in blind subjects has never been investigated for auditory processing.

At present, a number of laboratories are actively engaged in developing and testing auditory (Meijer 1992; Capelle and others 1998; Arno and others 1999; De Volder and others 1999; Arno, De Volder, and others 2001; Arno, Vanlierde, and others 2001; Pollok and others 2005; Renier and others 2005) and tactile (Bach-y-Rita and others 1969; Kaczmarek and others 1985; Sampaio and others 2001; Bach-y-Rita 2004; Ptito and others 2005) sensory substitution prostheses to attenuate the effects of visual deprivation (for review, see Bach-y-Rita and Kercel 2003). All these systems are designed to make use of the residual, intact senses to provide blind people with coded information related to lost perception in a rehabilitation paradigm (Veraart 1989). Our group has developed one such system, namely, a prosthesis for substitution of vision by audition (PSVA) (Capelle and others 1998). This system has proven its efficiency in blind individuals (Arno and others 1999; Arno, Vanlierde, and others 2001) and thus offers a unique tool for blind people to interact with the environment. Moreover, PSVA also offers an opportunity to study reorganization of the brain in general and the involvement of the OC in auditory processing in particular. The discrimination of visual stimuli using the PSVA was previously shown, with positron emission tomography (PET), to induce increased activation of the right dorsal extrastriate cortex (Brodmann area [BA] 18 or V2) in EB subjects compared with SC subjects (Arno, De Volder, and others 2001). This region is also known to be activated in EB during auditory location tasks (Weeks and others 2000).

The present study aimed at investigating whether this structure is necessary for the successful use of the PSVA by EB or

whether they simply constitute an epiphenomenon resulting from nonrelevant neuronal activations. For this purpose, we temporarily disrupted neural activity in the right dorsal extrastriate cortex using repetitive transcranial magnetic stimulation (rTMS), although EB and SC subjects discriminated various visual patterns by means of the PSVA. Moreover, participants carried out 3 control tasks, whose auditory properties are at the basis of the function of the prosthesis, namely, discrimination of pitch, intensity, and sound location. The effects of rTMS in auditory control tasks were expected to indicate which auditory processes contribute most significantly to occipital involvement in the PSVA use by our EB subjects.

Materials and Methods

Participants

Seven EB and 7 SC subjects participated in this study (see Table 1 for details regarding the blind subjects). The 2 groups were matched for age (range 22-54 years, mean ± standard deviation: 39 ± 11 for EB; 25-51 years, 33 ± 11 for SC), gender (5 men and 2 women), handedness (5 right handed, 1 left handed, and 1 ambidextrous in each group), and years of formal education (12 ± 4 years for the blind and 11 ± 5 for the sighted subjects). SC subjects were blindfolded while carrying out the various tasks. Given the important relationship between the age of onset of blindness and OC plasticity, we selected blind subjects who lost their sight early in life. However, one of our blind subjects, though having impaired vision from birth, became totally blind only at age 7. We decided to include her because Cohen and others (1999), using TMS, observed visual cortex involvement in nonvisual processing (Braille reading) in blind subjects who lost their sight as late as at the age of 14. When we compared the results of this blind participant with the rest of the blind group, we did not find any statistical differences in any of our experimental conditions.

The experimental procedures were approved by the Ethics committees of the Université de Montréal, the Notre-Dame Hospital, where the anatomical magnetic resonance images (MRIs) were obtained, and the Nazareth and Louis Braille Institute, an association for the blind, which helped recruit the blind participants. Experiments were undertaken with the understanding and written consent of each subject. Exclusion criteria included a history of neurological or psychiatric diseases, a family history of seizures, chronic headaches, pregnancy, implanted metal in the head, pacemaker, or defibrillator. None of the subjects were taking psychotropic medication at the time of testing.

The Sensory Substitution Device

The PSVA has been extensively described elsewhere (Capelle and others 1998; Arno and others 1999). Briefly, the use of PSVA requires the processing of complex sounds to extract auditory coded visual invariants (i.e., horizontal and vertical bars). A head-worn TV camera is used for online translation of visual patterns into sounds, which are then transmitted to the subject through headphones (see Fig. 1A). The image acquired by the camera is divided into pixels according to a high central and a low peripheral resolution to simulate an artificial retina (see Fig. 1B). Additional information is obtained from binaural intensity balance and phase differences. Visual frames, captured by the camera during the head movements of the PSVA use, generate in real time the corresponding complex sounds that allow recognition and location. Previous studies have demonstrated that blindfolded sighted and blind subjects using PSVA are able to recognize bidimensional visual patterns (see examples in Fig. 1C) (Arno and others 1999; Arno, Vanlierde, and others 2001).

Transcranial Magnetic Stimulation

We used a Magstim Rapid Stimulator (Magstim Company Ltd, Whitland, Wales, UK) with a maximum output of 2.0 T connected to a 7-cm figure-of-eight–shaped flat coil to deliver rTMS trains. The rTMS was applied over the right dorsal extrastriate OC (centered on BA 18). Coil positioning was obtained by using the Brainsight frameless stereotaxic system (Rogue Research, Montreal, Canada), which allows precise

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Table 1
Characteristics of the blind participants

EB	Age (years)	Educational level (years)	Visual perception	Sex	Handedness	Onset of blindness	Cause of blindness
1	25	11	None	M	R	Birth	Eyeballs did not develop
2	31	13	None	M	G	1 year	Glaucoma
3	36	16	Diffuse light	M	D	Birth	Leber's congenital amaurososis
4	42	22	None	M	D	Birth	Thalidomide victim
5	54	15	None	M	R	Birth	Mother accident during pregnancy[a]
6	24	16	None	F	A	Birth	Retinopathy of prematurity
7	24	16	None	F	R	7 years	Sturge–Weber syndrome[b]

Note: M, male; F, female; R, right handed; L, left handed; A, ambidextrous.
[a]no additional details available and [b]without neurological abnormalities.

Table 2
Error rate resulting from the subtraction of the performance in sham rTMS from real rTMS for pattern recognition using the PSVA and in the 3 auditory discrimination tasks

Blind subjects	PSVA	Intensity	Pitch	Location	Sighted subjects	PSVA	Intensity	Pitch	Location
1	0.1	0.07	−0.03	0	1	−0.09	−0.01	0.01	0.02
2	0.08	−0.01	0.05	0.06	2	−0.12	−0.03	−0.01	−0.03
3	0.02	0.03	0	0.04	3	−0.07	0.04	−0.05	0.01
4	0.06	−0.03	0.06	0.07	4	−0.02	0.02	−0.05	−0.01
5	−0.07	−0.01	0.03	0.01	5	0	0.08	−0.03	0.03
6	0.09	0.01	0.07	0.13	6	0	−0.13	−0.07	0.01
7	0.09	0.04	0	0.05	7	0.03	0.05	0.03	−0.01

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placement of the coil over the target brain area (see Fig. 2). We applied trains of 1200 biphasic sine-wave pulses at a frequency of 1 Hz (20-min stimulation) at 60% of the instrument output power for each subject. These parameters followed conventional guidelines for the safe use of rTMS (Wasserman and others 2000; Belmaker and others 2003).

The effect of 1-Hz rTMS leads to transient alterations of the activity of the stimulated area, which persist for several minutes after application of rTMS (Chen and others 1997; Boroojerdi, Prager, and others 2000) and results in behavioral interference with high-order perceptual functions (Kosslyn and others 1999; Lewald and others 2004; Merabet and others 2004). The effect of this rTMS mode is interpreted as being due to the residual physiological changes caused by the stimulation. The subsequent progressive disappearance of the disruption follows the functional recovery of the affected neuronal circuitry (Walsh and Pascual-Leone 2003). The use of such "distal (or off-line)" paradigm was particularly adapted to the design of the present experiment for several reasons. First, given that the use of PSVA requires the subjects to scan their environment by moving the head-worn TV camera, it was not possible to deliver the TMS during the task. Moreover, stringent temporal constraints were avoided because processing time to recognize one pattern with PSVA lasts about 70 s, which does not allow precise time locking between cognitive processing and magnetic stimulation like in the classical "online" single or even rTMS paradigms. Finally, separation between TMS period and behavioral tasks provides an opportunity to evaluate the contribution of a given cortical area in a specific task without the nonspecific effects (e.g., noise that accompanies the magnetic pulse and differences in auditory bone conduction) associated with online TMS (Robertson and others 2003). It further assures that the side effects of the TMS do not directly interfere with auditory discrimination in the PSVA and the 3 auditory control tasks.

The effect of rTMS was evaluated by comparing the performances of EB and sighted subjects in real and sham stimulation conditions. In the real stimulation condition, the magnetic field was oriented onto the target area. In the sham stimulation condition, the coil was held perpendicular to the scalp with the edge of the plastic block encasement touching the surface of the target area. We chose this method over stimulation of a different cortical region outside occipital areas to avoid difficulties arising from the involvement from any particular region during PSVA use. In previous studies (Arno, De Volder,
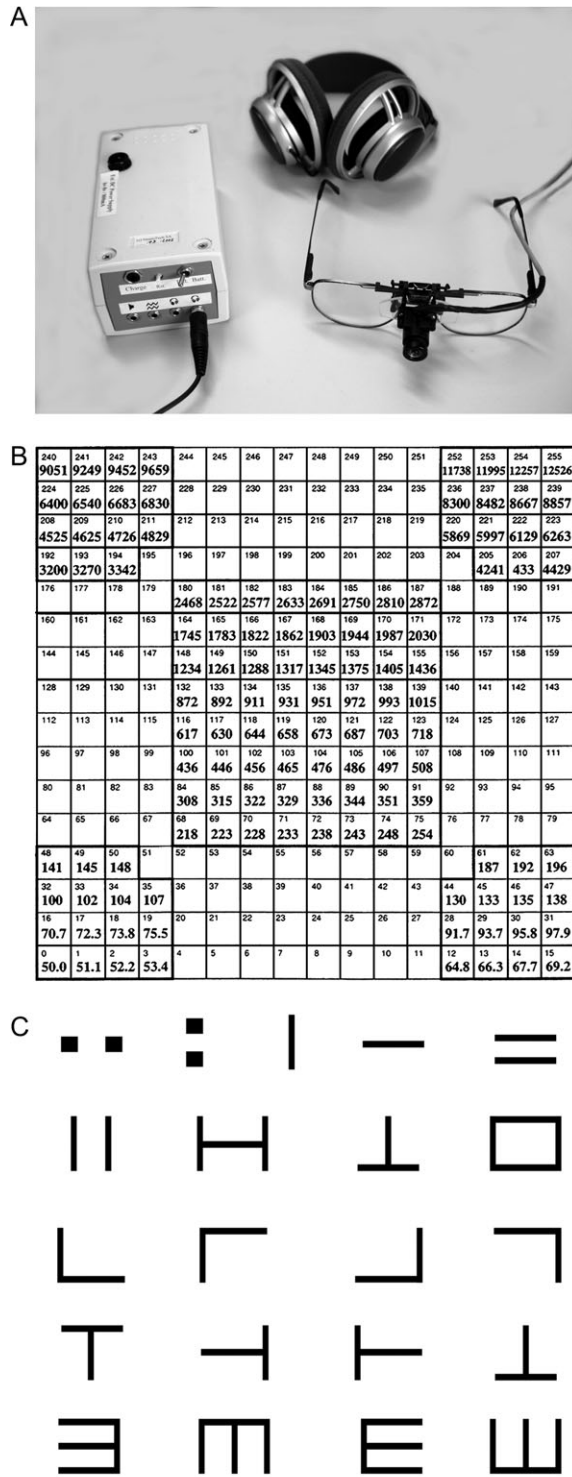
and others 2001; Renier and others 2005), when the authors compared activation foci during PSVA use and a "rest" condition, they observed the activation of a broad network outside the OC in blind and sighted subjects (due to working memory, executive, motor, and other components of the task) but without difference in intensity between the 2 populations. Moreover, in a pilot study, we also evaluated the effects of stimulating a ventral occipital area as control site. Unfortunately, we observed that stimulating this region generally induced scalp, face, and neck twitches, which became rapidly fairly uncomfortable for the participants and often resulted in headache. Given that these peripheral effects of TMS lasted for the whole stimulating period (20 min), we rejected the selection of this possible control site as ethically unacceptable.

Subjects wore earplugs during the stimulation period, which substantially attenuated the noise that accompanies the magnetic pulses, thus preventing auditory fatigue phenomena such as a noise-induced temporary auditory threshold shift (Quaranta and others 1998). Subjects were instructed to report any subjective sensations (visual, tactile, and/or auditory) evoked by TMS. The rTMS was well tolerated. Only one sighted subject reported having experienced phosphenes during the real stimulation condition. There was no evidence from the subjects' self-report that tactile or auditory sensations were evoked by magnetic stimulation in any groups.

Procedure

Before being submitted to the experimental conditions, all volunteers were trained to use the PSVA during two 2-h sessions. During all training and experimental sessions involving the use of the prosthesis, SC and EB subjects were seated in a table in front of a blackboard where patterns were displayed at a "viewing" distance of approximately 30 cm. SC subjects worked blindfolded.

The learning procedure, adapted from Arno and others (1999) aimed at developing a level of expertise with PSVA that would allow the subjects to recognize 2-dimensional visual patterns composed of vertical and horizontal bars. At the beginning of the first training session, the functioning of the device was explained to the subjects followed by the presentation of a single pixel to illustrate the procedure. The participants were then asked to explore the patterns within a maximum time of 120 s per pattern. Following this, they had to reconstruct the pattern using aluminum strips. Subjects were given tactile feedback regarding the similarity between their response and the actual pattern presented. They then reexplored the pattern and received additional verbal explanations about the code if necessary. Training began with the easiest stimuli (one pixel) and progressed to more complex ones (patterns composed by several horizontal and vertical bars). During training sessions, subjects had the opportunity to explore the patterns and to improve their ability to extract the auditory invariants related to horizontal and vertical bars within a pattern from other sounds provided by the device. They had to learn how to recognize the various components and, using head movement, to deduce the way they were organized. It was this self-induced movement that allowed extracting the auditory invariants and to recognize their organization. With training, the process of information extraction becomes more automatic. This results in a decrease in the overall processing time and a reduction of the working-memory load, enabling the users to recognize more complex patterns.

Subjects were subsequently submitted to 2 experimental sessions lasting about 2 h each and separated by at least 24 h. The first session was always devoted to the PSVA task, whereas the second dealt with the auditory discrimination tasks. Both experimental sessions included 20-min real and sham rTMS periods. Real and sham conditions were counterbalanced by beginning with real rTMS in 4 subjects and with sham rTMS in 3 subjects in both groups. Each rTMS period was immediately followed by a behavioral task lasting from 10 to 15 min. After the first rTMS period and the subsequent behavioral task, subjects were allowed a break of 40 min.

First Experimental Session: PSVA Tasks

After a real or a sham rTMS period, subjects put on the PSVA and began immediately a 2-dimensional pattern recognition task with the prosthesis. They were instructed to identify 8 patterns as fast and as accurately
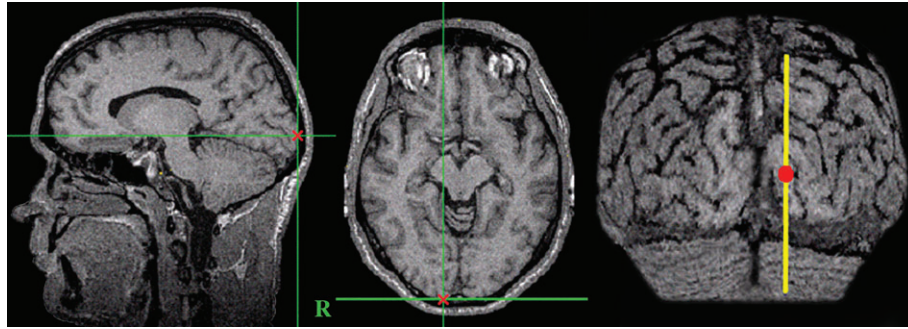
Figure 1. PSVA. (*A*) A head-worn video camera (fixed on glasses) allows online translation of visual patterns into sounds that are transmitted to the subject through headphones. (*B*) The artificial retina provided by the PSVA. The acquired image is divided into pixels according to a 2-resolution artificial retina scheme. The central part of the processed image or fovea has a 4-time higher resolution than the periphery. The coding scheme is based on a pixel-frequency association. Pixels in use are encompassed by a bold contour. Frequency is indicated in hertz in the lower part of the used pixels. A single sinusoidal tone is assigned to each pixel of the multiresolution image. The amplitude of each sine wave (the intensity of each sound) is modulated by the gray level of the corresponding pixel. The pattern moves on the grid according to the head movements of the subject, and the corresponding sounds of the activated pixels are transmitted to the subject in real time. (*C*) Examples of patterns used in the experiment.

240 9051	241 9249	242 9452	243 9659	244	245	246	247	248	249	250	251	252 11738	253 11995	254 12257	255 12526
224 6400	225 6540	226 6683	227 6830	228	229	230	231	232	233	234	235	236 8300	237 8482	238 8667	239 8857
208 4525	209 4625	210 4726	211 4829	212	213	214	215	216	217	218	219	220 5869	221 5997	222 6129	223 6263
192 3200	193 3270	194 3342	195	196	197	198	199	200	201	202	203	204	205 4241	206 433	207 4429
176	177	178	179	180 2468	181 2522	182 2577	183 2633	184 2691	185 2750	186 2810	187 2872	188	189	190	191
160	161	162	163	164 1745	165 1783	166 1822	167 1862	168 1903	169 1944	170 1987	171 2030	172	173	174	175
144	145	146	147	148 1234	149 1261	150 1288	151 1317	152 1345	153 1375	154 1405	155 1436	156	157	158	159
128	129	130	131	132 872	133 892	134 911	135 931	136 951	137 972	138 993	139 1015	140	141	142	143
112	113	114	115	116 617	117 630	118 644	119 658	120 673	121 687	122 703	123 718	124	125	126	127
96	97	98	99	100 436	101 446	102 456	103 465	104 476	105 486	106 497	107 508	108	109	110	111
80	81	82	83	84 308	85 315	86 322	87 329	88 336	89 344	90 351	91 359	92	93	94	95
64	65	66	67	68 218	69 223	70 228	71 233	72 238	73 243	74 248	75 254	76	77	78	79
48 141	49 145	50 148	51	52	53	54	55	56	57	58	59	60	61 187	62 192	63 196
32 100	33 102	34 104	35 107	36	37	38	39	40	41	42	43	44 130	45 133	46 135	47 138
16 70.7	17 72.3	18 73.8	19 75.5	20	21	22	23	24	25	26	27	28 91.7	29 93.7	30 95.8	31 97.9
0 50.0	1 51.1	2 52.2	3 53.4	4	5	6	7	8	9	10	11	12 64.8	13 66.3	14 67.7	15 69.2

Figure 2. Location of the rTMS site on MRI. The stimulated site position (red cross) is shown on a saggital (left) and a transverse (middle) section of the brain. The stimulated site (red point) can also be seen on a 3-dimensional reconstruction of a subject's brain (right panel). This area corresponds to the right dorsal extrastriate OC (BA 18).

as possible. As soon as the subject recognized the displayed pattern, he/she was instructed to say "stop," and exploration time was recorded. The PSVA was then immediately switched off, and the subject was requested to reconstruct the pattern in a maximum of 30 s using aluminum strips laid on the table. After the 30 s period, the PSVA was automatically turned on again, and a new pattern appeared in front of the subject. Exploration time was limited to a maximum of 120 s per stimulus after which the PSVA was automatically turned off. The total time required to complete each condition of 8 patterns ranged from 10 to 15 min. In addition to exploration time, an accuracy score was computed to quantify the subject's performance. The accuracy score consisted of a weighted assessment rating each of the subject's responses on a scale from 0 to 1 according to their similarity with the actual stimulus as described in Arno and others (1999). None of the patterns presented to the participants during the experimental session were ever used in the training phase.

Second Experimental Session: Auditory Discrimination Tasks
Three sound discrimination tasks were administered. The order of these 3 tasks was counterbalanced across subjects in both groups, with 3 subjects starting with the "intensity discrimination," 2 with the "location discrimination," and 2 with the "pitch discrimination" task. During these tasks, subjects were seated in front of a perimeter of 7 speakers located at a distance of 1.2 m (see Fig. 4D). Subjects had to perform in succession 3 choice reaction time (RT) tasks involving pitch and intensity discrimination and a spatial location task. Each task consisted of stimulus pairs composed of a reference sound (200 ms duration, 440 Hz, 75 dBA, midsaggital location) followed 500 ms later by a 200-ms discrimination sound (one of the 6 possible sounds varying in pitch, intensity, or spatial location, depending on the task). In the pitch discrimination task, the 6 discrimination sounds had a pitch difference of a half tone and were centered on the reference sound in such a manner that 3 discrimination sounds were lower (370, 392, and 415 Hz) and 3 were higher (466, 494, and 523 Hz) than the reference sound. In the intensity discrimination task, the discrimination sounds had the same pitch and the same location as the reference sound but varied in intensity in steps of 1.5 dBA: 3 of the sounds were weaker (73.5, 72.0, and 70.5 dBA) and 3 were louder (76.5, 78.0, and 79.5 dBA) than the reference sound. In the spatial location task, the discrimination sounds had the same pitch and the same intensity as the reference sound but varied with regard to their location, 3 being on the left and 3 on the right side with respect to the reference with a relative angular difference of 7° from the subject (7°, 14°, 21° to the left and the right of the midsaggital reference).

For each discrimination task, the 6 possible pairs were randomly presented 15 times for a total of 90 pairs per task. The interstimulus interval (referring to the time between the end of the discrimination sound of a pair and the start of the reference sound of the next pair) varied between 500 and 2000 ms. Subjects were instructed to press a key positioned under their left index finger when the discrimination sound was lower, weaker, or on the left side compared with the reference sound and to press the key situated under their right index finger in response to a higher, stronger, and right-sided discrimination sound. They were asked to respond as quickly and accurately as possible. RTs

were recorded for each discrimination pair within 100–2000 ms postpresentation. Only RTs for correct responses were considered for analysis.

Results

PSVA Task
The effect of rTMS was evaluated by comparing the subjects' performance in real and sham stimulation conditions. An analysis of variance (ANOVA) performed on the subject's accuracy scores revealed a significant interaction between group and stimulation condition ($F_{1,12} = 8.79$, $P = 0.012$). Post hoc analyses showed a significant decrease in performance in the real compared with the sham stimulation condition in the blind group only ($P = 0.033$) (Fig. 3A). Furthermore, an ANOVA carried out on the exploration times yielded a significant interaction between group and stimulation condition ($F_{1,12} = 7$, $P = 0.021$). Post hoc analyses showed that the blind group required significantly longer exploration times in the real than in the sham stimulation condition ($P = 0.008$), whereas the SC did not show this response pattern (Fig. 3B). Transient disruption of the right dorsal extrastriate OC thus produced a significant decrease in performance during PSVA use.

Auditory Control Tasks
We examined which auditory parameters at the basis of the function of the prosthesis, namely, discrimination of pitch, intensity, and sound location, significantly contribute to this occipital involvement in the PSVA performance of the EB subjects. Separate 2 (group: blind, sighted) × 2 (stimulation conditions: sham, real) ANOVAs were performed for the 3 auditory discrimination tasks, first with the subjects' mean error rate and then with median RTs as the dependent variables. The ANOVA for the intensity discrimination task revealed a significant group effect ($F_{1,12} = 7.49$, $P = 0.018$), indicating that EB subjects made significantly fewer errors than the blindfolded SC subjects. However, no rTMS effects were seen for either group in this condition (Fig. 4A). In the pitch discrimination task, the analysis yielded a significant group × condition ($F_{1,12} = 7.65$, $P = 0.011$) interaction. Post hoc analyses did not, however, reveal significant rTMS effects in either group, therefore indicating that the interaction resulted from the fact that real rTMS produced opposite, albeit nonsignificant, effects in the 2 groups (Fig. 4B). Analysis of the data obtained in the location task yielded a significant rTMS conditions effect ($F_{1,12} = 7.83$, $P = 0.016$) and a significant interaction group × rTMS conditions
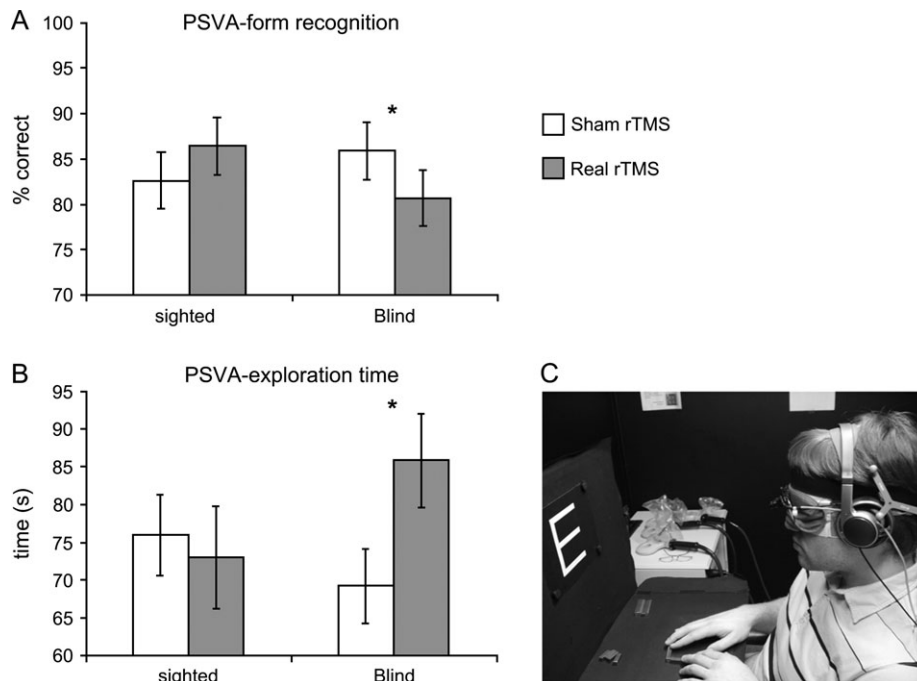
Figure 3. Performance of the 2 groups in the pattern recognition task using PSVA. Histograms represent (*A*) the average percentage of correct pattern recognition and (*B*) the mean exploration time taken to recognize the patterns. Error bars denote standard errors. The data indicate a significant decrease of recognition score and a significant increase of exploration time after real compared with sham rTMS in the blind group only. (*C*) Illustration of the experimental setup with a blindfolded SC using the PSVA (*$*P < 0.05$).

($F_{1,12} = 5.85$, $P = 0.032$). The post hoc analysis revealed that the blind subjects made significantly more errors in the real than in the sham rTMS condition ($P = 0.003$), whereas the controls did not show this pattern of results (Fig. 4*C*). Additional ANOVAs for the 3 auditory discrimination tasks were performed with median RT as the dependent variable. None of these analyses were significant. The absence of between-group or between-task differences on RTs suggests that the increase in error rate observed in EBs following rTMS in the sound location task did not result from a speed-accuracy trade-off effect. Table 2 shows the error rate resulting from the substraction of the performance in sham rTMS from real rTMS for pattern recognition using the PSVA and in the 3 auditory discrimination tasks.

Discussion

The results of the present study indicate that sighted and blind participants are able to rapidly learn to use the PSVA prosthesis to explore and discriminate 2-dimensional patterns on the basis of a real-time image-to-audition coding scheme. Although more extensive training strategies would be needed to recognize more complex shapes and objects (Arno and others 1999; Renier and others 2005), they nonetheless confirm that the prosthesis represents an interesting tool in a limited field attempting to develop instruments to compensate for sensory loss. Moreover, because the inhibition produced by applying 1-Hz rTMS over the right dorsal extrastriate cortex shown to be activated during prosthesis use leads to a decrement in performance in EB subjects but not in sighted ones, the results also suggest that EB subjects manifest effective functional reorganization of their deafferented visual cortex. We also investigated which auditory processes associated with the function of the prosthesis, namely, discrimination of pitch, intensity, and sound localization, contribute most significantly to this occipital in-

volvement in PSVA use in our EB subjects. We observed that the cortical disruption interfered with the auditory spatial location task but not with pitch or intensity discrimination. By contrast, rTMS targeting the same cortical areas in sighted subjects did not affect performance on any of the auditory tasks. We think that the failure of real TMS to affect discrimination of pitch and intensity in blind subjects and the absence of performance decrement in any of the tasks executed by sighted subjects prevents the interpretation that the impairment of perception was due to nonspecific effect of real compared with sham rTMS.

Several cognitive components are involved when users recognize visual patterns with PSVA (Arno, Vanlierde, and others 2001), and the present study only investigated a subset of the auditory features that are at the basis of the prosthesis. In fact, integration over time of different features is critical in form perception using PSVA. Extensive description of the code of the prosthesis and the mechanisms at play when subjects learn to use the system has been provided elsewhere (Capelle and others 1998; Arno and others 1999). However, because the rTMS disruption in auditory control tasks was selective only for spatial location in EB subjects, the results suggest the performance decrements observed in EB subjects are probably related to perturbations in the analysis of spatial components in auditory localization as well as in the PSVA task. This is attributable to the fact that perception with PSVA is mainly analytic and sequential and, given the small size of the perceptual field, requires a spatial arrangement of segments for recognition. Moreover, the intrinsic spatial component is also implemented in the PSVA code via an auditory binaural intensity balance allowing localization of "visual" patterns on the azimuth (Arno and others 1999; Arno, De Volder, and others 2001; Arno, Vanlierde, and others 2001). These results also allow us to draw two additional conclusions. First, because it is highly unlikely that practice with PSVA for only 4 h would have created new connections in
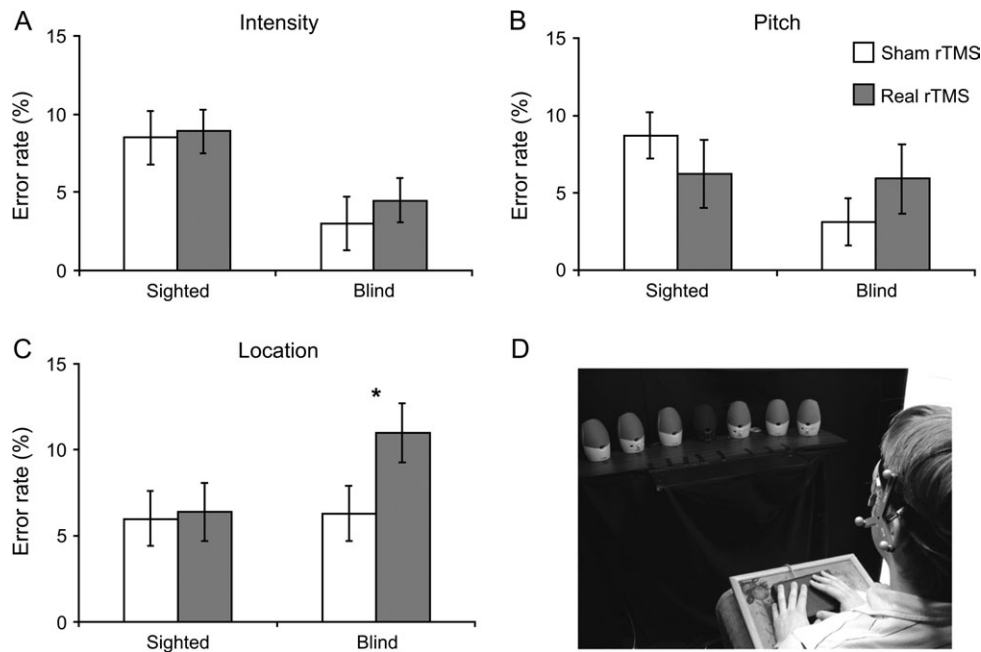
Figure 4. Performance of the 2 groups in the 3 auditory discrimination tasks. Auditory tasks involved discrimination of intensity (*A*), pitch (*B*), and spatial location (*C*). Histograms represent the average error rate after sham and real rTMS targeting the dorsal occipital stream. Error bars denote standard errors. The data show a significant increase of the error rate after real rTMS only in the blind group and selectively for the sound location task. (*D*) Experimental setup for the 3 auditory discrimination tasks (*$P < 0.05$).

the brain of blind subjects, the occipital involvement, suggested by our results, is probably best explained in terms of a functional reorganization that is already operational for specific nonvisual processing such as sound localization. Second, the results suggest that the right dorsal extrastriate cortex is part of the functional network involved in spatial processing in EB individuals.

Numerous studies carried out in sighted people indicate that the dorsolateral extrastriate visual system is specialized for visuospatial processing (the "where" pathway) (Ungerleider and others 1984; Haxby and others 1991). Others have shown that the right hemisphere, more than the left, contributes to this type of visual processing (Heilman and others 1986). Our findings thus suggest that there exists an anatomofunctional correspondence between visual processing in sighted subjects and nonvisual processing in EB subjects in the analysis of space. Indeed, they indicate that the right dorsal "where" stream is also important for auditory spatial processing in EB subjects. This is in agreement with neuroimaging studies, which have underlined the role of occipitoparietal areas in nonvisual spatial processing in EB subjects, and particularly in the right hemisphere (De Volder and others 1999; Leclerc and others 2000; Weeks and others 2000; Arno, De Volder, and others 2001; Vanlierde and others 2003).

It might be argued, given the fact that rTMS was applied only to right extrastriate cortex, that its application to other visual areas might have produced similar effects. Despite ethical considerations, which limit application of the present TMS paradigm on ventral areas (see Materials and Methods), we think that this possibility is not probable. First, it must be remembered that the targeted cortex was the principal region activated in the PET scans when blind subjects, compared with sighted subjects, used PSVA (Arno, De Volder, and others 2001) and carried out auditory location tasks (Weeks and others 2000). Therefore, all visual cortex subregions are not equivalent in carrying out this type of auditory processing. Indirect support

also comes from studies demonstrating task-specific activation of the ventral stream during object-related nonvisual processing in EBs (Sadato and others 1996; Buchel and others 1998; De Volder and others 2001; Pietrini and others 2004; Burton and others 2005). Pitch and intensity discrimination rely on the analysis of stimulus qualities and seem to involve more ventral parts of the brain (Kujala and others 1995; Liotti and others 1998); rTMS on ventral areas would thus have disrupted blind subjects performance in these tasks.

Moreover, we do not presume that the right dorsal extrastriate cortex is the only site where blind subjects functionally process all visual-auditory sensory information related to substitution devices. In our case, this region was targeted because of its higher activation when blind subjects used PSVA compared with sighted one's (Arno, De Volder, and others 2001) and because the latter's operational mode mainly targets auditory spatial processing. Sensory substitution devices might activate different occipital cortical areas depending on the specific task performed (Poirier and others 2005; Ptito and others 2005; Renier and others 2005). Recent data obtained from a proficient blind user of another visual-to-auditory sensory substitution device suggest that the ventral visual stream was recruited to process shape information, whereas the dorsal visual stream contributes to location processing (Amedi and others 2005). Further research, using functional neuroimaging and/or rTMS, should attempt to dissociate occipital involvement in nonvisual processing between dorsal stream specialization for spatial processing and ventral stream involvement in shape processing.

In order to maximize TMS accuracy, we used a neuronavigational system in combination with a figure-of-eight coil so as to allow precise stimulation of the target area. However, even if effective stimulation is presumed to occur in a restricted area of cortex close to the center of the coil (Epstein and others 1990), spatial resolution of the TMS is limited and may have influenced adjacent cortical areas like V1, a region also found to be

functionally involved in nonvisual processing in EB (Cohen and others 1997; Amedi and others 2004). Moreover, accumulating evidence suggests that rTMS not only leads to direct effects at the site of stimulation but also affects functionally connected areas that are distant from the stimulation site (Paus and others 1997; Paus and Wolforth 1998). Direct disruption of right dorsal extrastriate area in EB subjects may thus have influenced other components of the network that could be involved in the PSVA utilization and/or in auditory -spatial discrimination (Weeks and others 2000). The absence of the rTMS effect in the sighted subjects suggests, however, that major functional reorganization of this network has taken place in blind subjects. It is thus difficult to ascertain if other areas of a broader network are also involved in the present task performance and future studies should specifically address this point.

Interestingly, rTMS did not interfere with performance of the sighted subjects on any of the auditory tasks. This result is in some disagreement with studies that have reported decreases in spatial processing in blindfolded sighted subjects after application of TMS over right extrastriate occipital region during tactile discrimination of grating orientation (Zangaladze and others 1999) as well as during an auditory -spatial task (Lewald and others 2004). It has been suggested that activation of these areas does not necessarily depend on the modality of the sensory input but rather on the nature of the information being processed (Pascual-Leone and Hamilton 2001) and thus that they should be considered to constitute a multisensory space-related network. In sighted subjects, however, vision is the most efficient sensory modality for spatial processing and would therefore dominate and modulate the spatial representation of other senses. One example for the preferential role of vision in spatial perception derives from the "ventriloquist illusion" (Bertelson and Radeau 1981), where sounds are commonly misallocated to their apparent visual source. Hence, the involvement of posterior brain areas in nonvisual spatial processing in sighted persons would probably only occur during the execution of extremely sensitive tasks (Zangaladze and others 1999; Lewald and others 2004; Merabet and others 2004) or when subjects are subjected to reversible visual deprivation through blindfolding (Boroojerdi, Bushara, and others 2000; Pascual-Leone and Hamilton 2001; Pollok and others 2005; Weisser and others 2005), which was not the case in the present study. In the case of blindness, on the other hand, the absence of competing visual input to the right dorsal extrastriate cortex could lead to an extension and/or functional enhancement of preexisting neural networks dedicated to nonvisual spatial processing, which remain relatively silent in sighted subjects.

The recruitment of deafferented visual areas is also often credited for the superior performance of EB subjects observed on a number of nonvisual tasks (see for review, Bavelier and Neville 2002). In the present study, however, a superior performance of the EB subjects was only observed for intensity discrimination and not for the other tasks. We think that the absence of superior performance in EB can be attributed to general lack of sensibility of the tasks. Previous studies using PSVA (Arno, Vanlierde, and others 2001), pitch discrimination (Gougoux and others 2004), and spatial localization (Lessard and others 1998; Roder and others 1999) have found a superior performance in EBs only in tasks with a high level of complexity or extended training. For example, the superiority of blind subjects in auditory -spatial tasks was reported in specific experimental conditions, involving, unlike the present one,

monaural listening (Lessard and others 1998) or sound processing in peripheral field (Roder and others 1999). In another study (Arno, Vanlierde, and others 2001), superior performance in EBs compared with SCs in a pattern recognition task using PSVA was observed after twelve 1-h training sessions. Thus, the shorter PSVA training period (4 h) and the simpler tasks used in our experiment probably account for the lack of superior performance in EB subjects in the present study.

When multifunctional visual rehabilitation is desired, invasive and noninvasive solutions can be investigated. Invasive neuro-prostheses rely on integrity of visual cortex function for the generation of visual phosphenes through electrical stimulation (for review, see Zrenner 2002; Veraart and others 2004). In contrast, in sensory substitution, information acquired with one sensory modality is used to accomplish a task, which is normally subserved primarily by another sensory modality. In doing so, it could take advantage of the cross-modal plasticity observed in early blindness whereby deafferented occipital areas provide the neural basis for behavioral compensation reported in nonvisual abilities in the blind (Amedi and others 2003; Gougoux and others 2005). We therefore think that sensory substitution devices in general and PSVA in particular are worthy of attention because this technique is noninvasive, and its principles follow the natural tendency of the brain to reorganize itself through the other modalities in order to compensate for the loss of a sensory system.

Notes

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References

Amedi A, Bermpohl F, Camprodon J, Fox S, Merabet L, Meijer P, Pascual-Leone A. 2005. Neural correlates of visual-to-auditory sensory substitution in proficient blind users. Proceeding of the 11th Annual Meeting of the Organization for Human Brain Mapping; 2005 June 12–16; Toronto, Canada. Neuroimage 26:747.

Amedi A, Floel A, Knecht S, Zohary E, Cohen LG. 2004. Transcranial magnetic stimulation of the occipital pole interferes with verbal processing in blind subjects. Nat Neurosci 7:1266–1270.

Amedi A, Raz N, Pianka P, Malach R, Zohary E. 2003. Early 'visual' cortex activation correlates with superior verbal memory performance in the blind. Nat Neurosci 6:758–766.

Arno P, Capelle C, Wanet-Defalque MC, Catalan-Ahumada M, Veraart C. 1999. Auditory coding of visual patterns for the blind. Perception 28:1013–1029.

Arno P, De Volder AG, Vanlierde A, Wanet-Defalque MC, Streel E, Robert A, Sanabria-Bohorquez S, Veraart C. 2001. Occipital activation by pattern recognition in the early blind using auditory substitution for vision. Neuroimage 13:632–645.

Arno P, Vanlierde A, Streel E, Wanet-Defalque MC, Sanabria-Bohorquez SM, Veraart C. 2001. Auditory substitution of vision: pattern recognition by blind. Appl Cognit Psychol 15:509-519.

Bach-y-Rita P. 2004. Tactile sensory substitution studies. Ann N Y Acad Sci 1013:83-91.

Bach-y-Rita P, Collins CC, Saunders FA, White B, Scadden L. 1969. Vision substitution by tactile image projection. Nature 221:963-964.

Bach-y-Rita P, Kercel W. 2003. Sensory substitution and the human-machine interface. Trends Cogn Sci 7:541-546.

Bavelier D, Neville HJ. 2002. Cross-modal plasticity: where and how? Nat Rev Neurosci 3:443-452.

Belmaker B, Fitzgerald P, George MS, Lisanby SH, Pascual-Leone A, Schlaepfer TE, Wassermann E. 2003. Managing the risks of repetitive transcranial stimulation. CNS Spectr 8:489.

Bertelson P, Radeau M. 1981. Cross-modal bias and perceptual fusion with auditory-visual spatial discordance. Percept Psychophys 29:578-584.

Boroojerdi B, Bushara KO, Corwell B, Immisch I, Battaglia F, Muellbacher W, Cohen LG. 2000. Enhanced excitability of the human visual cortex induced by short-term light deprivation. Cereb Cortex 10:529-534.

Boroojerdi B, Prager A, Muellbacher W, Cohen LG. 2000. Reduction of human visual cortex excitability using 1-Hz transcranial magnetic stimulation. Neurology 54:1529-1531.

Buchel C. 1998. Functional neuroimaging studies of Braille reading: cross-modal reorganization and its implications. Brain 121(Pt 7):1193-1194.

Buchel C, Price C, Friston K. 1998. A multimodal language region in the ventral visual pathway. Nature 394:274-277.

Burton H, McLaren DG, Sinclair RJ. 2005. Reading embossed capital letters: an fMRI study in blind and sighted individuals. Hum Brain Mapp 27:325-339.

Burton H, Snyder AZ, Conturo TE, Akbudak E, Ollinger JM, Raichle ME. 2002. Adaptive changes in early and late blind: a fMRI study of Braille reading. J Neurophysiol 87:589-607.

Burton H, Snyder AZ, Diamond JB, Raichle ME. 2002. Adaptive changes in early and late blind: a fMRI study of verb generation to heard nouns. J Neurophysiol 88:3359-3371.

Capelle C, Trullemans C, Arno P, Veraart C. 1998. A real-time experimental prototype for enhancement of vision rehabilitation using auditory substitution. IEEE Trans Biomed Eng 45:1279-1293.

Chen R, Classen J, Gerloff C, Celnik P, Wassermann EM, Hallett M, Cohen LG. 1997. Depression of motor cortex excitability by low-frequency transcranial magnetic stimulation. Neurology 48:1398-1403.

Cohen LG, Celnik P, Pascual-Leone A, Corwell B, Falz L, Dambrosia J, Honda M, Sadato N, Gerloff C, Catala MD, Hallett M. 1997. Functional relevance of cross-modal plasticity in blind humans. Nature 389:180-183.

Cohen LG, Weeks RA, Sadato N, Celnik P, Ishii K, Hallett M. 1999. Period of susceptibility for cross-modal plasticity in the blind. Ann Neurol 45:451-460.

De Volder AG, Bol A, Blin J, Robert A, Arno P, Grandin C, Michel C, Veraart C. 1997. Brain energy metabolism in early blind subjects: neural activity in the visual cortex. Brain Res 750:235-244.

De Volder AG, Catalan-Ahumada M, Robert A, Bol A, Labar D, Coppens A, Michel C, Veraart C. 1999. Changes in occipital cortex activity in early blind humans using a sensory substitution device. Brain Res 826:128-134.

De Volder AG, Toyama H, Kimura Y, Kiyosawa M, Nakano H, Vanlierde A, Wanet-Defalque MC, Mishina M, Oda K, Ishiwata K, Senda M. 2001. Auditory triggered mental imagery of shape involves visual association areas in early blind humans. Neuroimage 14:129-139.

Epstein CM, Schwartzberg DG, Davey KR, Sudderth DB. 1990. Localizing the site of magnetic brain stimulation in humans. Neurology 40:666-670.

Gougoux F, Lepore F, Lassonde M, Voss P, Zatorre RJ, Belin P. 2004. Neuropsychology: pitch discrimination in the early blind. Nature 430:309.

Gougoux F, Zatorre RJ, Lassonde M, Voss P, Lepore F. 2005. A functional neuroimaging study of sound localization: visual cortex activity predicts performance in early-blind individuals. PLoS Biol 3:e27.

Hamilton R, Keenan JP, Catala M, Pascual-Leone A. 2000. Alexia for Braille following bilateral occipital stroke in an early blind woman. Neuroreport 11:237-240.

Haxby JV, Grady CL, Horwitz B, Ungerleider LG, Mishkin M, Carson RE, Herscovitch P, Schapiro MB, Rapoport SI. 1991. Dissociation of object and spatial visual processing pathways in human extrastriate cortex. Proc Natl Acad Sci USA 88:1621-1625.

Heilman KM, Bowers D, Valenstein E, Watson RT. 1986. The right hemisphere: neuropsychological functions. J Neurosurg 64:693-704.

Kaczmarek K, Rita P, Tompkins WJ, Webster JG. 1985. A tactile vision-substitution system for the blind: computer-controlled partial image sequencing. IEEE Trans Biomed Eng 32:602-608.

Kosslyn SM, Pascual-Leone A, Felician O, Camposano S, Keenan JP, Thompson WL, Ganis G, Sukel KE, Alpert NM. 1999. The role of area 17 in visual imagery: convergent evidence from PET and rTMS. Science 284:167-170.

Kujala T, Huotilainen M, Sinkkonen J, Ahonen AI, Alho K, Hamalainen MS, Ilmoniemi RJ, Kajola M, Knuutila JE, Lavikainen J. 1995. Visual cortex activation in blind humans during sound discrimination. Neurosci Lett 183:143-146.

Leclerc C, Saint-Amour D, Lavoie ME, Lassonde M, Lepore F. 2000. Brain functional reorganization in early blind humans revealed by auditory event-related potentials. Neuroreport 11:545-550.

Lessard N, Pare M, Lepore F, Lassonde M. 1998. Early-blind human subjects localize sound sources better than sighted subjects. Nature 395:278-280.

Lewald J, Meister IG, Weidemann J, Topper R. 2004. Involvement of the superior temporal cortex and the occipital cortex in spatial hearing: evidence from repetitive transcranial magnetic stimulation. J Cogn Neurosci 16:828-838.

Liotti M, Ryder K, Woldorff MG. 1998. Auditory attention in the congenitally blind: where, when and what gets reorganized? Neuroreport 9:1007-1012.

Meijer PB. 1992. An experimental system for auditory image representations. IEEE Trans Biomed Eng 39:112-121.

Merabet L, Thut G, Murray B, Andrews J, Hsiao S, Pascual-Leone A. 2004. Feeling by sight or seeing by touch? Neuron 42:173-179.

Pascual-Leone A, Hamilton R. 2001. The metamodal organization of the brain. Prog Brain Res 134:427-445.

Paus T, Jech R, Thompson CJ, Comeau R, Peters T, Evans AC. 1997. Transcranial magnetic stimulation during positron emission tomography: a new method for studying connectivity of the human cerebral cortex. J Neurosci 17:3178-3184.

Paus T, Wolforth M. 1998. Transcranial magnetic stimulation during PET: reaching and verifying the target site. Hum Brain Mapp 6:399-402.

Pietrini P, Furey ML, Ricciardi E, Gobbini MI, Wu WH, Cohen L, Guazzelli M, Haxby JV. 2004. Beyond sensory images: object-based representation in the human ventral pathway. Proc Natl Acad Sci USA 101:5658-5663.

Poirier CC, De Volder AG, Tranduy D, Scheiber C. 2005. Neural changes in the ventral and dorsal visual streams during pattern recognition learning. Neurobiol Learn Mem 85:36-43.

Pollok B, Schnitzler I, Stoerig P, Mierdorf T, Schnitzler A. 2005. Image-to-sound conversion: experience-induced plasticity in auditory cortex of blindfolded adults. Exp Brain Res 167:287-291.

Ptito M, Moesgaard SM, Gjedde A, Kupers R. 2005. Cross-modal plasticity revealed by electrotactile stimulation of the tongue in the congenitally blind. Brain 128:606-614.

Quaranta A, Portalatini P, Henderson D. 1998. Temporary and permanent threshold shift: an overview. Scand Audiol Suppl 48:75-86.

Renier L, Collignon O, Poirier C, Tranduy D, Vanlierde A, Bol A, Veraart C, De Volder AG. 2005. Cross-modal activation of visual cortex during depth perception using auditory substitution of vision. Neuroimage 26:573-580.

Robertson EM, Theoret H, Pascual-Leone A. 2003. Studies in cognition: the problems solved and created by transcranial magnetic stimulation. J Cogn Neurosci 15:948-960.

Roder B, Rosler F. 2003. Memory for environmental sounds in sighted, congenitally blind and late blind adults: evidence for cross-modal compensation. Int J Psychophysiol 50:27-39.

Roder B, Rosler F, Neville HJ. 2000. Event-related potentials during auditory language processing in congenitally blind and sighted people. Neuropsychologia 38:1482-1502.

Roder B, Rosler F, Neville HJ. 2001. Auditory memory in congenitally blind adults: a behavioral-electrophysiological investigation. Brain Res Cogn Brain Res 11:289-303.

Roder B, Teder-Salejarvi W, Sterr A, Rosler F, Hillyard SA, Neville HJ. 1999. Improved auditory spatial tuning in blind humans. Nature 400:162-166.

Sadato N, Pascual-Leone A, Grafman J, Ibanez V, Deiber MP, Dold G, Hallett M. 1996. Activation of the primary visual cortex by Braille reading in blind subjects. Nature 380:526-528.

Sampaio E, Maris S, Bach-y-Rita P. 2001. Brain plasticity: 'visual' acuity of blind persons via the tongue. Brain Res 908:204-207.

Theoret H, Merabet L, Pascual-Leone A. 2004. Behavioral and neuroplastic changes in the blind: evidence for functionally relevant cross-modal interactions. J Physiol Paris 98:221-233.

Ungerleider LG, Desimone R, Galkin TW, Mishkin M. 1984. Subcortical projections of area MT in the macaque. J Comp Neurol 223:368-386.

Vanlierde A, De Volder AG, Wanet-Defalque MC, Veraart C. 2003. Occipito-parietal cortex activation during visuo-spatial imagery in early blind humans. Neuroimage 19:698-709.

Veraart C. 1989. Neurophysiological approach to the design of visual prostheses: a theoretical discussion. J Med Eng Technol 13:57-62.

Veraart C, De Volder AG, Wanet-Defalque MC, Bol A, Michel C, Goffinet AM. 1990. Glucose utilization in human visual cortex is abnormally elevated in blindness of early onset but decreased in blindness of late onset. Brain Res 510:115-121.

Veraart C, Duret F, Brelen M, Oozeer M, Delbeke J. 2004. Vision rehabilitation in the case of blindness. Expert Rev Med Devices 1:139-153.

Walsh V, Cowey A. 2000. Transcranial magnetic stimulation and cognitive neuroscience. Nat Rev Neurosci 1:73-79.

Walsh V, Ellison A, Battelli L, Cowey A. 1998. Task-specific impairments and enhancements induced by magnetic stimulation of human visual area V5. Proc R Soc Lond B Biol Sci 265:537-543.

Walsh V, Pascual-Leone A. 2003. Transcranial magnetic stimulation: a neurochronometrics of mind. Cambridge: MIT Press.

Wanet-Defalque MC, Veraart C, De Volder A, Metz R, Michel C, Dooms G, Goffinet A. 1988. High metabolic activity in the visual cortex of early blind human subjects. Brain Res 446:369-373.

Wasserman EM, Greenberg BD, Murphy DL, Nguyen MB, Smith MJ. 2000. A relationship between personality traits and cortical synaptic transmission measured with transcranial magnetic stimulation. Ann Neurol 48:420.

Weeks R, Horwitz B, Aziz-Sultan A, Tian B, Wessinger CM, Cohen LG, Hallett M, Rauschecker JP. 2000. A positron emission tomographic study of auditory localization in the congenitally blind. J Neurosci 20:2664-2672.

Weisser V, Stilla R, Peltier S, Hu X, Sathian K. 2005. Short-term visual deprivation alters neural processing of tactile form. Exp Brain Res 166:572-582.

Zangaladze A, Epstein CM, Grafton ST, Sathian K. 1999. Involvement of visual cortex in tactile discrimination of orientation. Nature 401:587-590.

Zrenner E. 2002. Will retinal implants restore vision? Science 295:1022-1025.