The Neural Basis of Visual Skill Learning: An fMRI Study of Mirror Reading

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The learning of perceptual skills is thought to rely upon multiple regions in the cerebral cortex, but imaging studies have not yet provided evidence about the changes in neural activity that accompany visual skill learning. Functional magnetic resonance imaging (fMRI) was used to examine changes in activation of posterior brain regions associated with the acquisition of mirror-reading skill for novel and practiced stimuli. Multiple regions in the occipital lobe, inferior temporal cortex, superior parietal cortex and cerebellum were involved in the reading of mirror-reversed compared to normally oriented text. For novel stimuli, skilled mirror-reading was associated with decreased activation in the right superior parietal cortex and posterior occipital regions and increased activation in the left inferior temporal lobe. These results suggest that learning to read mirror-reversed text involves a progression from visuospatial transformation to direct recognition of transformed letters. Reading practiced, relative to unpracticed, stimuli was associated with decreased activation in occipital visual cortices, inferior temporal cortex and superior parietal cortex and increased activation in occipito-parietal and lateral temporal regions. By examining skill learning and item-specific repetition priming in the same task, this study demonstrates that both of these forms of learning exhibit shifts in the set of neural structures that contribute to performance.

Introduction

It is now widely recognized that there are multiple memory systems in the brain that are functionally and neurally independent (Squire *et al.*, 1992; Cohen and Eichenbaum, 1993). Evidence from patients with amnesia due to medial temporal or diencephalic lesions, along with parallel evidence from studies of normal people, suggests a distinction between declarative memory, which supports performance on direct tests of memory that require recollection, and procedural (or non-declarative) memory, which supports performance on indirect tests of memory that do not require ecollection of previous episodes (Cohen and Squire, 1980; Graf and Schacter, 1985). Whereas declarative memory relies critically upon the medial temporal lobe and diencephalic structures, procedural memory is thought to involve widespread areas in the cerebral cortex, basal ganglia and cerebellum (reviewed in Poldrack and Gabrieli, 1997).

The procedural memory phenomena that are independent of the medial temporal lobe and diencephalic regions can be divided into several classes, including repetition priming and skill learning. Repetition priming (hereafter simply priming) is a facilitation or biasing of performance (speed or accuracy) with a stimulus on the basis of previous experience with the same or a closely related stimulus. Priming has been studied extensively using functional neuroimaging methods such as positron emission tomography (PET) and functional magnetic resonance imaging (fMRI). Priming in a visually cued word retrieval task (word-stem completion) is accompanied by reduced activation in the right occipital lobe (Squire *et al.*, 1992; Buckner *et al.*, 1995; Schacter *et al.*, 1996). Priming in a semantic classification task is accompanied by reduced activation in the left inferior prefrontal cortex using words (Demb *et al.*, 1995; Gabrieli *et al.*, 1996) and pictures (Wagner *et al.*, 1998). These data suggest that priming is associated with more efficient processing in regions that mediated original task performance with a stimulus.

Skill learning is measured as an improvement in the speed and/or accuracy of performance on a task with practice. Skill learning has been further divided into motor, perceptual and cognitive forms (Cohen and Eichenbaum, 1993). Imaging studies have examined the neural plasticity underlying motor skill learning in tasks such as sequential finger-tapping and rotary pursuit. A number of studies have found that activation of contralateral sensorimotor cortex increased in intensity or extent with the acquisition of motor skill. One difficulty in the interpretation of changes in activation with practice is that the duty cycle, or proportion of scan time taken up by task performance, can change as behavior becomes faster or more accurate. Changes in duty cycle could explain learning-related changes in activation in studies where the rate of movements was not controlled (e.g. Seitz *et al.*, 1990). However, learning-related increases have been found even when movement frequency was controlled across training (Grafton *et al.*, 1995; Karni *et al.*, 1995; Hazeltine *et al.*, 1997), suggesting that learning-related changes in motor cortex are not simply related to changes in duty cycle (e.g. Jenkins *et al.*, 1994). Instead, these learning-related changes may be related to experience-dependent cortical plasticity that has been observed in animals following motor training (Nudo *et al.*, 1996). Learning-related increases in activity have been observed also in the supplementary motor area (Grafton *et al.*, 1992, 1994, 1995; Hazeltine *et al.*, 1997) and basal ganglia (Seitz *et al.*, 1990; Seitz and Roland, 1992; Grafton *et al.*, 1995; Hazeltine *et al.*, 1997). These changes are thought to be related to the formation of motor programs for sequential actions.

Mirror-reading

The neural basis of perceptual skill learning has not yet been examined using neuroimaging methods. The present study examined the functional anatomy of visual skill learning in the mirror-reading task. In this task, examined extensively by Kolers (1968, 1975, 1976), words are presented in a mirror-reversed manner for the participant to read. Learning to read mirror-reversed text is a lengthy process; Kolers (1975) showed that learning in the task followed a negatively accelerated power function, and that performance continued to gradually improve even after two months of practice. This learning is also long-lasting; Kolers (1976) found that it lasted up to one year after initial training.

Current knowledge about the neural basis of skill acquisition in the mirror-reading task comes from neuropsychological

studies. Amnesic patients exhibit normal learning of mirror-reading skill, despite their inability to recognize previously presented items (Cohen and Squire, 1980; Martone *et al.*, 1984). Patients with Huntington's disease are mildly impaired at learning the mirror-reading skill (Martone *et al.*, 1984), whereas patients with Alzheimer's disease are not impaired at learning this skill (Deweer *et al.*, 1993). Learning of the mirror-reading skill is also normal in patients with cerebellar damage (Daum *et al.*, 1993). Thus, the acquisition of mirror-reading skill does not involve medial temporal and diencephalic brain regions damaged in amnesia or the association regions damaged in Alzheimer's disease, but may involve the basal ganglia structures damaged in Huntington's disease.

In the present study, participants performed mirror-reading in two separate fMRI scanning sessions, in between which they received training at mirror-reading. Because vocal speech during fMRI scanning can cause artifacts due to head motion, participants in this study performed lexical decisions (i.e. word/non-word decisions) on letter strings (e.g. violin, pring) presented during fMRI scanning, which alternated between blocks of plain text and blocks of mirror-reversed text. The non-words were pronounceable, so that the participant had to make decisions on the basis of lexical knowledge rather than rules of orthography.

Results from neuroimaging studies of priming suggest that learning-related changes should occur in brain regions involved initially in task performance. Because the mirror-reading task requires substantial visuospatial transformation, it was likely that regions in the dorsal visual pathway such as superior parietal cortex would be involved in the task and that activation in these areas would change with learning. The mirror-reading task also poses a difficult problem in object recognition, making it likely that the occipital and inferior temporal regions in the ventral visual stream would be active during task performance and show learning-related changes. In order to examine these areas, the current study imaged coronal slices through the rear portion of the brain, from the posterior commissure (PC) rearward to the occipital pole ($y = -25$ to $y = -95$ in the Talairach and Tournoux atlas [Talairach and Tournoux, 1988]). This choice of imaging region ensured coverage of the occipital lobe, posterior parietal cortex, posterior inferior temporal cortex and the entire cerebellum. An online registration technique (Desmond and Lim, 1997) was used to ensure that the same slices were imaged in the pre-training and post-training sessions. The goal of the study was to determine the areas that were activated during performance of the mirror-reading task, and additionally to determine the changes in functional anatomy that accompanied skill acquisition in the task.

In addition to examining general mirror-reading skill, the study also examined the nature of item-specific repetition effects in the mirror-reading task. As noted above, previous studies of repetition priming on verbal tasks have found reduced activations in task-related regions. Skill learning in motor tasks, on the other hand, has been associated with increased activation. The results from previous studies are difficult to integrate because skill learning and repetition priming were studied in different tasks. In addition, in previous studies of motor learning it is difficult to disambiguate skill learning and repetition priming because the same item (e.g. the same motor sequence) was studied repeatedly, and improvements in performance thus represent a combination of skill learning and item-specific learning. By examining skill learning and item-specific learning in the same task, the present study allows

Study Design

Scan Session 1 — 2 fmri runs: mirror-reversed vs. plain text

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Training — 3 mirror-reading training sessions on separate days, 360 trials each

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Scan Session 2 — 4 fmri runs:
2 mirror-reversed vs. plain text
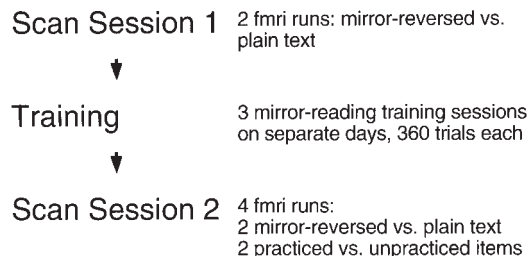2 practiced vs. unpracticed items

Figure 1. Diagram of study design.

a direct comparison of the differential patterns of neural plasticity associated with skill learning and repetition priming. The present study also extends the timescale of the examination from the scale of minutes used in most previous priming experiments (e.g. Raichle *et al.*, 1994; Demb *et al.*, 1995) to the scale of days, testing whether priming-related reductions found by previous studies rely upon short-term learning mechanisms (e.g. Karni *et al.*, 1995).

Materials and Methods

Participants
Participants were six right-handed volunteers from the Stanford community who participated for payment. All participants were native speakers of English. Informed consent was obtained from each participant prior to the experiment, and participants were screened for any possible contraindications prior to entering the MRI suite.

Materials
A list of 1080 words was drawn from the Francis and Kucera (1982) database; word frequency ranged from 10 to 100 occurrences and word length from five to seven letters. For each word, a matched pseudoword was created by changing one consonant in the word, with the constraint that the word remained pronounceable. Words from the list were randomly assigned to conditions within the experiment.

Procedure
The study consisted of two fMRI scanning sessions with three training sessions in between the fMRI sessions. Figure 1 presents a graphic description of the experimental procedure. In Scan Session 1, two functional scanning runs were taken. In each run, the participant performed a lexical decision (word/non-word) task on items presented in either plain text or mirror-reversed text during alternating blocks lasting 30 s each. In each block, five items were words and five were non-words, and participants were told to press a response key if the item appearing on the screen was a word. Items appeared for 2000 ms with a 1000 ms interstimulus interval (ISI). All items presented during Scan Session 1 were unique.

After Scan Session 1, the participant returned for three training sessions within the course of 2 weeks. In each session, the participant was presented with three blocks of 120 items; each of the items was presented in mirror-reversed format, and the participant performed lexical decision on the items. None of the training items had been presented in Scan Session 1. In each block, half (60) of the items were unique and were seen only once during training, while the other half were repeated in every block during training for a total of nine presentations; half of the repeated items were words and half were pseudowords, as was also the case for the new items in each block. Unlike the scanning session where items were presented for a brief period, during the training sessions the item remained on the computer screen until a response was made. The participant responded by pressing the '/' key for words and the 'z' key for non-words, unlike the scanning session where the participant made a go/no-go response for words.

After the three training sessions were completed, the participant

returned for Scan Session 2, which consisted of four fMRI runs. In the first two runs, a set of new words was presented with the mode of presentation (plain text vs. mirror-reversed text) alternating between blocks (i.e. the same procedure as in Scan Session 1). In the third and fourth runs, all items were presented in mirror-reversed format. Half of the items (unpracticed) had been presented once during the earlier scan session, while the other set of items (practiced) had been presented nine times during the training sessions, and the item type (unpracticed vs. practiced) was alternated between blocks of 10 items.

Stimuli were generated by a Macintosh computer and back-projected onto a screen located above the participant's neck via a magnet-compatible projector; the projected image appeared on a mirror mounted above the participant's head. Participants responded by pressing an optical switch with the right hand; in each case, the participant responded to the presentation of a word and withheld responses for non-words. The responses were collected by a computer interfaced with the optical switch using PsyScope (Cohen *et al.*, 1993).

fMRI Procedures

Imaging was performed with a 1.5 T whole-body MRI scanner (GE Medical Systems Signa). A receive-only whole-head coil was used for signal reception. Head movement was minimized using a 'bite-bar' formed with each participant's dental impression. A T_2*-sensitive gradient echo spiral pulse sequence (Meyer *et al.*, 1992) was used for functional imaging with parameters of TE = 40 ms, TR = 900 ms, flip angle = 70°, FOV = 36 cm and inplane resolution = 2.35 mm. Four spiral interleaves were obtained for each image, for a total acquisition time of 360 ms per image slice (3600 ms per image volume). The onset of the scanning run was controlled by the experimental presentation program via a TTL output, allowing precise synchronization of the stimulus presentation and scanner onset.

In each experiment, ten 6 mm thick slices were acquired separately in the coronal plane. Placement of the slices was determined using a method for online registration of scanner coordinates into the coordinates of the Talairach and Tournoux (1988) atlas (Desmond and Lim, 1997). The slices were placed from 95 mm posterior to the anterior commissure (AC) to 25 mm posterior to the AC; the interslice interval varied between participants on the basis of the normalization parameters (range 1.0–2.5 mm). The use of the Desmond and Lim (1997) registration procedure allowed for the same set of slices to be obtained on multiple scanning occasions without the need for post-processing alignment (other than in-plane image translation and rotation). T_1-weighted flow compensated spin-echo anatomy images were acquired for each of the slices imaged in the functional scans.

A feature of the spiral acquisition technique is that off-resonance resulting from magnetic field heterogeneity or T_2^* variations causes only image blurring rather than spatial distortions as in echo-planar imaging or conventional gradient-recalled methods (Noll *et al.*, 1992). This blurring was corrected during reconstruction from a field map made using phase images obtained at two different echo times for each spatial slice (Irarrazabal *et al.*, 1996) Registration of the functional images and the spin echo anatomic images required no correction for distortion as is necessary with other imaging methods (such as EPI). Bulk head motion was controlled by the bite bar; residual bulk motion was corrected using an automated image registration algorithm for the in-plane dimensions (Woods *et al.*, 1992).

Data Analysis

Functional image processing was performed offline after transferring the raw data to a Sun SparcStation. After image reconstruction, functional images were motion-corrected using AIR 2.0 (Woods *et al.*, 1992). A set of functional images for use in the creation of composite images (as in Fig. 3*A*) was created by spatially smoothing the data in three dimensions with a Gaussian filter (6 mm full width at half-maximum), while the images presented for individual subjects (as in Fig. 3*B*) were created using unsmoothed functional data. The data were then analyzed using the cross-correlation method described by Friston *et al.* (1994). The activity of each pixel was correlated to a reference function obtained by convolving the square wave describing the task alternation with an estimate of the hemodynamic response function. These correlation values

were then normalized, and statistical parametric maps (SPM{Z}) were created using the normalized correlation values.

Composite SPMs were formed by warping the SPMs for each participant onto a reference template using the WARP_TRI procedure in IDL (Research Systems, Inc., Boulder, CO). Because the coronal templates in the Talairach and Tournoux (1988) atlas do not provide full coverage of the cerebellum, reference templates for each of the 10 slices were created using the inplane structural images of a single participant from the current experiment. After warping, the SPMs were averaged across participants, and a threshold was set at α = 0.05. In composite figures, thresholded SPMs are overlaid on warped structural images averaged across all participants.

Across-session statistical analyses were performed by creating paired difference images between the SPMs for each subject. Difference images were created by performing paired subtractions between SPMs for each subject after warping to the reference template and then averaging the difference images across subjects. The standard deviation of the difference map was set to $1/\sqrt{n}$, where n = 6 subjects, and this value was used to create a new difference Z map. This technique was validated by simulation using null hypothesis (rest) fMRI data, which showed that the technique resulted in the expected nominal level of false positives (J. Desmond, unpublished data).

Stereotactic coordinates for clusters of activation were obtained by aligning the coordinate system of the Talairach and Tournoux (1988) atlas to the averaged structural images. Only activations exceeding a cluster size threshold of four pixels are reported in the tables below. Reported coordinates correspond to the centroid of each cluster of activation.

Results

The alpha level for all analyses was 0.05. All P values for repeated-measures ANOVA reflect the Huhyn–Feldt correction for non-sphericity.

Response times during scanning were faster than those during training. This occurred because participants had unlimited time to respond to stimuli during training, a condition that led to high accuracy but slower responses. During scanning, stimuli were presented for a limited duration of 2000 ms with a 1000 ms ISI, forcing participants to respond more quickly and less accurately.

Behavioral Data: Training

Response times for the three mirror-reading training sessions are presented in Figure 2 for new items and items that repeated across blocks. A 2 (item type: new vs. repeat) × 9 (training blocks) repeated-measures ANOVA was performed on the response time data. Responses to repeated items (M = 1476) were faster than responses to new items (M = 2166), $F(1,5)$ = 399.2, MSE = 32 204. Response time decreased across training blocks, $F(8,40)$ = 19.15, MSE = 113 460. Separate tests for linear trend confirmed this decrease for both new items and repeated items (Ps < 0.001). There was a greater decrease in response times for repeated items than for new items, as signified by a significant item type × training block interaction, F(8,40) = 8.34, MSE = 26 887.

A 2 (item type: new vs. repeat) × 9 (training blocks) repeated-measures ANOVA was performed on mirror-reading accuracy. No effects were significant (Ps > 0.05), but the item type × training block interaction was marginally significant, $F(8,40)$ = 2.04, MSE = 0.0005 , P < 0.07. Separate tests for linear trend on new and repeated items showed no significant linear trend for new items (P > 0.29) but a significant increasing linear trend for repeated items (P < 0.001). These data confirm the response time results and rule out a speed–accuracy tradeoff.

Behavioral Data: Scan Performance

Response time and accuracy data for both scan sessions are presented in Table 1. The mirror vs. plain text data were

Table 1
Behavioral performance during Scan Sessions 1 and 2

		Response time		Accuracy	
		Plain	Mirror-reversed	Plain	Mirror-reversed
Scan Session 1	Run 1: MR vs. plain	768	1402	0.97	0.77
	Run 2: MR vs. plain	744	1400	0.99	0.83
Scan Session 2	Run 1: MR vs. plain	745	1372	0.99	0.86
	Run 2: MR vs. plain	728	1321	1.0	0.91
		Practiced	Unpracticed	Practiced	Unpracticed
	Run 3: practiced vs. unpracticed	996	1231	0.97	0.91
	Run 4: practiced vs. unpracticed	938	1214	0.98	0.91

Response times during scanning were faster than those during training sessions (as shown in Fig. 2) because of the 2000 ms response window during scanning.
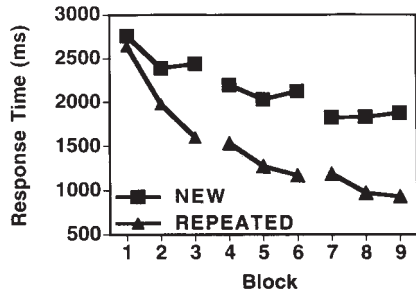

Figure 2. Response time data for mirror-reading training sessions.

analyzed using a 2 (Scan Session 1 vs. 2) × 2 (run 1 vs. run 2 within each session) × 2 (plain vs. mirror-reversed text) repeated-measures ANOVA (behavioral data for one participant in Scan Session 2 was not available, so ANOVAs were performed on only five participants). For response times, mirror-reversed items resulted in slower responses (M = 1368 ms) than did items presented in plain text (M = 745 ms), $F(1,4)$ = 225.79, MSE = 17 188. There were no other significant effects ($F < 1$). The non-significant effect of session suggests that the learning that occurred during training did not greatly affect response times in the scanner (though participants were 43 ms faster in the second session). The time limit placed on participants in the scanner and the go/no-go nature of the task may have led them to perform the task using a strategy in which increases in performance would be seen in accuracy rather than in response time. This lack of significant change in response time nearly rules out the notion that changes in brain activity from Scan Session 1 to Scan Session 2 were due to duty cycle changes following training.

There was a significant increase in accuracy between Scan Session 1 (M = 0.89) and Scan Session 2 (M = 0.94), $F(1,4)$ = 13.78, MSE = 0.03. There was also greater accuracy for plain text items than for mirror-reversed items, $F(1,4)$ = 31.58, MSE = 0.23. The session × task interaction was marginally significant, $F(1,4)$ = 6.80, MSE = 0.002, $P < 0.06$. This interaction reflected a greater increase in accuracy for mirror-reversed items (increase of 0.10) compared to plain text items (increase of 0.02), but is difficult to interpret given that plain text items were at ceiling. The accuracy data thus showed that training in the mirror reading task did significantly improve mirror-reading accuracy in Scan Session 2.

Performance in the unpracticed vs. practiced scans was examined using a 2 (run 1 vs. run 2) × 2 (practiced vs. unpracticed) repeated-measures ANOVA. For response times, unpracticed items were responded to more slowly (M = 1223 ms) than practiced items (M = 967 ms), $F(1,4)$ = 95.84, MSE = 3406. No other effects were significant ($Ps > 0.15$). The accuracy data confirmed the response time finding; accuracy was greater for practiced items (M = 0.98) than for unpracticed items (M = 0.91), $F(1,4)$ = 8.18, MSE = 0.002.

Imaging: Mirror-reading Performance
Areas activated during performance with mirror-reversed text compared to plain text are presented in Figure 3; locations of activations in Talairach space are listed in Table 2. The mirror-reading task led to widespread bilateral activation of occipital, parietal and inferior temporal regions. In the occipital lobe, extensive activation was centered on the cuneus, extending to the deep cortex of the calcarine sulcus and laterally to the lateral and middle occipital gyri. This activation extended forward along the lingual gyrus and bilaterally along the fusiform gyrus, along with bilateral pulvinar activation. In the parietal lobe, bilateral activation was noted in the posterior superior parietal lobule, along with extensive activation in the intraparietal sulcus. In the cerebellum, there were bilateral regions of activation in the superior cerebellar cortex along with activation in the right inferior cerebellar cortex. Regions of significantly greater activation for plain than for mirror-reversed text included the cuneus/precuneus along the midline, left inferior parietal cortex, right anterior superior parietal cortex and superior temporal gyrus bilaterally.

Imaging: Skill Learning
Figure 3 depicts several regions in which activity changed with practice from Scan Session 1 to Scan Session 2, and Table 3 presents the stereotactic locations of these changes. Significant skill-related increases were found in the left fusiform gyrus, precuneus, left superior parietal, right superior temporal gyrus and right cerebellum.

Significant learning-related decreases were found in posterior occipital areas including primary visual cortex, inferior and middle occipital gyri bilaterally, and in the right superior parietal cortex, along with the right pulvinar. Additional decreases were noted in the right inferior cerebellum and right inferior temporal cortex.

Figure 3. (*A*) Composite activation images for initial mirror-reading performance (Scan Session 1) along with images depicting skill-learning related changes in activation and item-specific activations. Data are presented for three slices in which activations of interest were present (y = −95, y = −79 and y = −56). Activations are significant at $P < 0.05$. (*B*) Activation image for a single participant depicting increase in fusiform gyrus activation and decrease in superior parietal activation from pre-training session to post-training session. Images were masked according to anatomical regions of interest (temporal lobe and superior parietal gyrus, respectively) in order to highlight changes in activation.
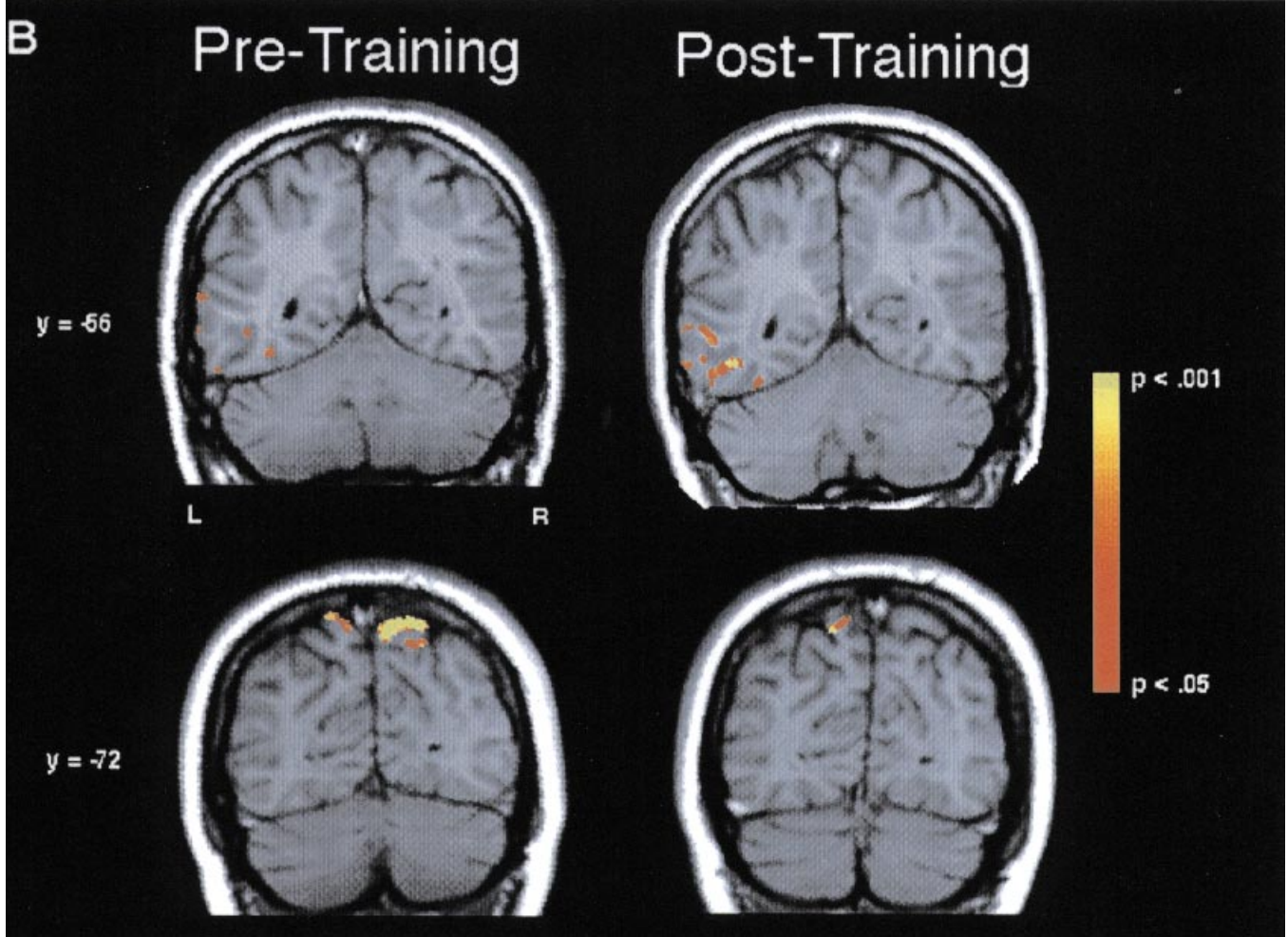
A

Mirror-Reading Task Activation

Skill-Related Learning

L R

Plain > Mirror ▮▮▮▮▮▮ Mirror > Plain

Learning-Related Increase ▮▮▮▮▮▮ Learning-Related Decrease

Item-Specific Learning

Practiced > Unpracticed ▮▮▮▮▮▮ Unpracticed > Practiced

B

Pre-Training **Post-Training**

y = -56

L R

p < .001

p < .05

y = -72
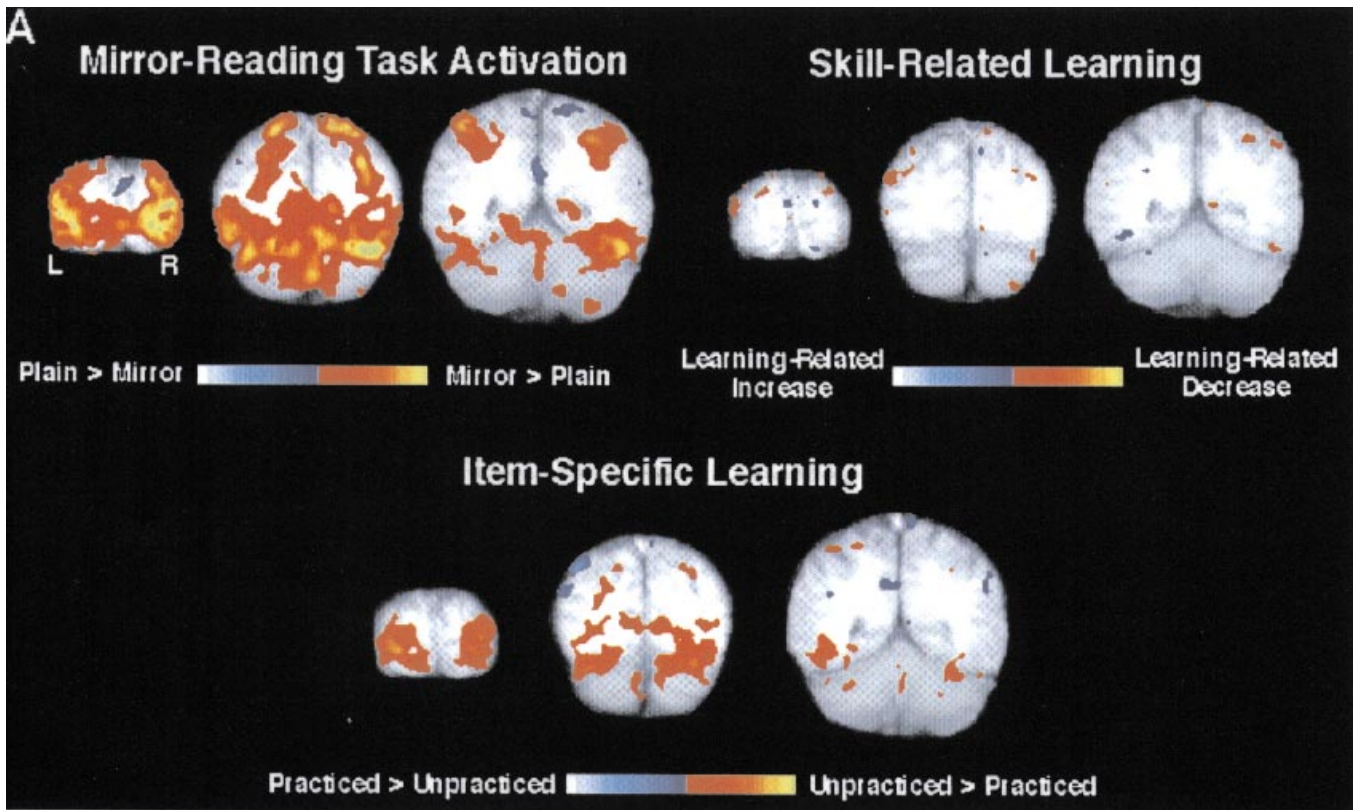
Table 2
Mirror-reading activations (from Scan Session 1)

Region	Talairach coordinates (x,y,z)			Max Z
Significant mirror-reading increases				
Occipital cortex	−5	−87	+9	7.20
R cuneus	+10	−72	+15	2.52
L sup occipital/parietal	−23	−79	+28	6.52
R sup parietal	+24	−72	+39	5.85
L fusiform	−24	−64	−15	6.76
R fusiform/lingual gyrus	+19	−72	−10	7.03
L cerebellum	−33	−72	−33	2.94
R cerebellum	+23	−72	−35	4.24
Medial cerebellum	−6	−56	−6	3.33
R pulvinar	+14	−25	+13	3.04
L pulvinar	−8	−25	+9	3.18
Significant mirror-reading decreases				
Cuneus	+4	−95	+19	3.94
L inf parietal	−55	−64	+16	2.94
Precuneus	−2	−72	+32	4.65
	−6	−56	+59	2.72
R sup parietal	+22	−41	+69	3.06
L mid/sup temporal	−52	−33	+11	3.21
R mid/sup temporal	+66	−33	16	3.75

Table 3
Changes in activation related to skill learning

Region	Talairach coordinates (x,y,z)			Max Z
Significant skill-related increases				
Precuneus	0	−72	+40	4.87
L sup parietal	−3	−72	+53	3.58
R cerebellum	+34	−64	−33	3.67
L fusiform	−43	−56	−3	3.70
R sup temporal	+66	−32	+15	4.04
Significant skill-related decreases				
L lingual gyrus	−4	−87	−5	4.41
L mid/inf occipital	−38	−95	+13	4.73
	−19	−95	+20	3.82
	−44	−87	−3	4.29
	−47	−79	+21	4.38
R mid/inf occipital	+25	−95	+21	3.99
	+45	−87	+3	4.07
R cerebellum	+27	−79	−26	4.34
	+32	−48	−36	3.70
R sup parietal	+31	−56	+49	3.82
R inf parietal	+47	−64	+40	3.33
R inf temporal	+58	−41	−15	3.45
	+47	−56	−10	4.07
R pulvinar	+12	−33	−7	4.31

Table 4
Item-specific learning activations

Region	Talairach coordinates (x,y,z)			Max Z
Significant item-specific increases				
L sup parietal/occipital	−42	−79	+32	4.68
cuneus/precuneus	−2	−72	+27	3.99
R sup parietal/occipital	+50	−72	+26	3.16
Precuneus	+1	−64	+40	3.18
R sup parietal	+8	−56	+68	3.38
L mid/inf temporal	−67	−33	−10	4.24
R mid/inf temporal	+66	−25	−9	
Significant item-specific decreases				
L inf occipital	−23	−95	+2	5.12
R lingual/fusiform gyrus	+18	−79	−4	4.48
L mid occipital	−33	−87	+23	3.45
L cuneus	−16	−87	+12	2.62
L sup/inf parietal	−39	−56	+53	2.74
R sup parietal	+19	−25	+51	2.42
R intraparietal	+30	−64	+33	3.67
L intraparietal	−38	−48	+38	2.74
Medial cerebellum	+1	−64	−20	2.84
R cerebellum	+25	−72	−10	3.18
	+25	−64	−23	3.65
	+41	−64	−28	2.67
L cerebellum	−24	−64	−24	3.11
L fusiform	−31	−56	−8	2.30
	−28	−56	0	2.20
L pulvinar	−10	−25	+12	2.94

Imaging: Item-specific Effects

Figure 3 presents data comparing performance on practiced vs. unpracticed mirror-reversed items in Scan Session 2, with the locations of these activations presented in Table 4. Item-specific reductions were observed bilaterally in lateral occipital cortex, fusiform/inferior occipital gyrus, superior parietal cortex, cerebellar cortex, the left intraparietal sulcus and left pulvinar. Item-specific increases were observed bilaterally in the region of the parieto-occipital junction with more extensive activation on the left, as well as in the left middle/inferior temporal gyrus. Increases were also found in the medial cortex of the precuneus.

Discussion

This study found that mirror-reading involves a widespread network of cortical regions, and that skill learning in the mirror-reading task is accompanied by changes in the functional anatomy of the task. Specifically, skill learning resulted in decreased activation in occipital and right superior parietal regions and increased activation in left inferior temporal cortex. In addition, comparison of highly practiced items to new items revealed further item-specific reductions in activity for lateral occipital, left inferior temporal, intraparietal and cerebellar cortices, with item-specific increases in occipito-parietal and lateral middle/inferior temporal cortices.

Neural Basis of Visual Skill Learning

These results indicate that visual skill learning in the mirror-reading task involves a progression from visuospatial transformation to object recognition that reflects a transfer from initial reliance upon the right hemisphere dorsal visual stream to later reliance upon the left hemisphere ventral visual stream. Early in training, the participant may attempt to transform spatially the individual letters in the mirror-reversed word in order to match those letters to existing letter representations. While it is unlikely that mirror-reading involves mental rotation in the traditional sense (Koriat and Norman, 1985), there is probably significant overlap between the visuospatial processes involved in mental rotation and those involved in mirror-reading. It is notable that the right superior parietal regions activated during initial mirror-reading are also strongly activated during mental rotation, as are occipital visual areas (Cohen *et al.*, 1996; Rypma *et al.*, 1996).

Mirror-reading skill is letter-specific rather than being a general visual transformation skill; training on one half of the alphabet does not transfer to words constructed from the other half of the alphabet (Masson, 1986). This result suggests that during skill acquisition the participant forms new representations of individual mirror-reversed letters. PET studies of reading indicate that the cortical locus of these new letter representations may be the left inferior occipital and inferior

temporal cortices. Left fusiform gyrus and extrastriate cortex are activated in letter processing compared to the processing of false-font strings (Price *et al.*, 1996). Consistent with the hypothesis that learning in the mirror-reading task involves increased involvement of letter recognition processing, activation in the left fusiform gyrus increased with training in our study.

Primary visual cortices were also significantly more active during mirror-reading than during the reading of plain text. Given current knowledge about the kinds of features that are encoded at the level of primary visual cortex, it is unlikely that this activation reflects processing of different sets of features in mirror-reversed and plain items. Rather, this activation probably reflects attentionally mediated increases in basic featural processing. Corbetta *et al.* (1990) and Haxby *et al.* (1994) have shown that the activity of visual cortical regions is increased by focal visual attention, and it is likely that reading the mirror-reversed words required significantly greater and more sustained visual attention. Alternatively, this increase may simply represent prolonged perceptual processing in the mirror reading condition, given the longer response times for mirror reading compared to reading plain text.

Item-specific Learning
Recent studies of item-specific learning (or repetition priming) effects have found process-specific decreases in activation of task-related cortical regions for both perceptual (e.g. Squire *et al.*, 1992; Buckner *et al.*, 1995) and semantic (e.g. Raichle *et al.*, 1994; Gabrieli *et al.*, 1996) tasks. Each of these studies examined repetition priming in a single testing session with a relatively short retention interval (of the order of minutes). The results of the present study, in which reductions in cortical activation were found for practiced items relative to unpracticed items, extend these previous findings by showing that similar reductions occur when priming is tested across a delay of days.

Item-specific practice led to a reduction in activation in the left inferior temporal cortex, in a region that overlapped with the region exhibiting a skill learning-related increase in activity. This result converges with previous findings of priming-related reductions in activity for task-related regions, but extends those findings by demonstrating priming-related reductions in a region that was not initially involved in task performance but became involved as skill learning progressed. These priming-related reductions in activity may have occurred because of the repetition of either individual reversed letters or letter clusters (cf. Masson, 1986). This result suggests that the neural signature of repetition priming may change as skill progresses; the present experiment did not examine repetition priming early in the course of skill learning, so additional studies are necessary to examine this question.

Practice on repeated stimuli during the training sessions may have led participants to adopt a word-level identification strategy for these items, in contrast to the letter-level identification strategy used for unpracticed stimuli. The increase in inferior temporal activation for unpracticed relative to practiced items may reflect a greater reliance upon letter-based processing for unpracticed items. The increase in activation in the left occipito-temporo-parietal area observed for practiced items relative to unpracticed items suggests that such whole-word processing may have occurred. The processing of practiced items may also have been facilitated by explicit memory for studied words; participants may have explicitly remembered the item and its associated response, eliminating the need for letter-by-letter reading of the mirror-reversed stimulus and thus reducing the involvement of letter-level processing regions.

The adoption of a whole-word identification strategy for practiced items may also have affected the eye movements necessary to perform the task. Because mirror-reversed words read right-to-left, the participant has to overcome the strong tendency to read from left-to-right, and overriding this tendency requires deliberate control of eye movements. Activity in the intraparietal sulcus was greater for unpracticed items relative to practiced items, and this region is known to be involved in the direction of eye movements. Activation of the intraparietal sulcus has been found in other tasks where participants performed directed eye movements (Petit *et al.*, 1996) and an analogous region in monkeys, known as LIP, is known to encode the intention to make an eye movement (Andersen, 1995). It is tempting to suggest that repeated items may have been identified in a whole-word fashion rather than a letter-by-letter fashion, perhaps reducing the need for rightward eye movements. This is clearly speculative, and resolution of this issue will require further experimentation.

The cerebellar activation observed bilaterally for unpracticed relative to practiced items is puzzling, especially given that these same cerebellar regions did not exhibit learning-related changes. These results may reflect an increased working memory load for unpracticed compared to practiced items. While practiced items could often be recognized without reading the entire word, unpracticed items would require letter-by-letter reading which would require keeping decoded letters in working memory. Alternatively, the results may reflect an increased need for sequencing, which would be required to assemble the individually-decoded letters into a whole string. Both of these alternatives are consistent with recent imaging findings (on working memory: Fiez *et al.*, 1996; on sequencing: Sadato *et al.*, 1996; Wessel *et al.*, 1996).

Relation Between Skill Learning and Repetition Priming
Previous imaging studies of skill learning and repetition priming have suggested that these two forms of learning exhibit different neural signatures. Skill learning has been associated with increases in activation; in contrast, priming has been associated with decreases in activation. However, in these previous studies skill learning has been primarily investigated in motor tasks whereas repetition priming has been investigated in perceptual and conceptual verbal tasks. It was thus unclear whether this contrast was due to a difference between skill learning and repetition priming or between motor tasks and verbal tasks. The present study compared skill learning and repetition priming in the same task, which is necessary in order to make direct comparisons between the two forms of learning (R.A. Poldrack, unpublished). The results of the present study show that skill learning and repetition priming may both be characterized by patterns of increases and decreases in task-related neural activation, and that some of these changes may occur in the same brain regions for both skill learning and repetition priming.

The present results seem to rule out any explanation of differences between repetition priming and skill learning that is based upon a distinction between short-term and long-term learning mechanisms. In a previous study, Karni *et al.* (1995) found that short-term learning in a motor task was associated with decreased activity in motor cortex, while long-term learning was associated with increased activity. The Karni *et al.* (1995) data suggested that the decreases found for repetition priming may have been the result of short-term learning (of the

order of minutes to a few hours) whereas the increases for skill learning were the result of long-term learning (of the order of hours to days). However, in the present study both skill learning and item-specific learning were tested over an interval of several days and thus both represent long-term learning. The fact that item-specific learning was associated with decreased activation at this timescale demonstrates that these effects do not rely upon the short timescale of all previous imaging studies of priming. Alternatively, differences in the patterns of neural change for skill learning and repetition priming may be related to differences in the effect of changes in strategy.

Changes in neural systems accompanying skill learning may be seen as a result of changes in cognitive strategy for task performance. For example, in the mirror-reading task the strategy for task performance may change from effortful spatial transformation of reversed letters to a less effortful retrieval of reversed-letter representations from memory (cf. Masson, 1986). This change in strategy need not be intentional on the part of the subject, and could arise from competitive cognitive mechanisms (e.g. Logan, 1988). The increases and decreases associated with skill learning might thus reflect changes in reliance upon the different sets of neural networks invoked by the changing cognitive strategies.

Repetition priming, on the other hand, may be less affected by changes in strategies and more reliant upon facilitation within the individual neural networks involved in task performance. For example, the neural networks involved in feature detection and visual analysis could exhibit priming-related decreases in activity for previously encountered groups of features. At the neuronal level, priming-related decreases in activation may reflect decreased competition in neural networks subserving feature detection via strengthening of interfeature connections. This decrease in the level of competition could lead to faster and less metabolically demanding processing. However, if the underlying neural networks involved in the task change with skill as a function of strategy-driven process shifting, then priming may exhibit different loci of neural change from early learning to later performance.

Language and Mirror-reading
One surprising finding of the present study was the relative paucity of activation for plain text compared to mirror-reversed text. On the basis of previous studies of word and letter processing (e.g. Petersen et al., 1990; Price et al., 1996), one would have expected greater activity in a number of letter-form and word-form areas during plain-text reading compared to mirror-reading, because the mirror-reversed stimuli are visually dissimilar to normal text. However, the opposite result was found: posterior occipital and inferior temporal areas were consistently more active during the mirror-reading task than during the reading of plain text. Thus, the present findings suggest that the extrastriate regions uncovered in previous studies of orthographic processing may not be automatically related to this type of processing. Rather, these regions may be activated whenever the participant treats a stimulus as a word, and activation effects in these regions may reflect an interaction of attention with the underlying visual cortical representations. Consistent with this suggestion is the finding that posterior visual regions that are active during the processing of words are also active during the processing of pseudowords (Petersen et al., 1990; Price et al., 1996).

The most extensive area found to be significantly more active during reading of plain text was in the precuneus. A similar but more anterior region was found by Price et al. (1996) to be active during the presentation of words compared to letters. Thus, this area may be related to word processing in the plain text condition. However, activation of medial posterior regions has also been found during the baseline condition in explicit memory tasks (Buckner et al., 1996) and working memory tasks (Fiez et al., 1996), so it is tempting to ascribe a more general explanation to such activation.

Relation to Theories of Skill Learning
A number of interpretations have been suggested for changes in functional neural activity that accompany skill learning. *Representational plasticity* involves changes in the cortical representations for the acquired skill. For example, increases in the extent of motor cortical activity with motor skill learning may reflect the same sorts of representational plasticity that have been observed by neurophysiologists (Weinberger, 1995; though see Karni et al., 1995). *Process switching* involves shifting from reliance upon one set of processes to reliance upon another set of (more efficient) processes; this explanation predicts both increases and decreases in activation with skill acquisition. For example, Raichle et al. (1994) argued that practice effects in the verb generation task involved switching from an effortful generation process (associated with decreasing inferior frontal, cingulate and right cerebellar activations) to an automatic associative retrieval process (associated with increasing insular activation). *Teacher circuits* are neural networks that provide error feedback or guidance to other brain regions, and that become less involved in task performance as skill is acquired. The cerebellum is a classic example of a region thought to act as a teacher circuit, and the frontal lobe has also been suggested as having such a function (Schrager et al., 1996).

The results of the present study suggest that learning-related changes during mirror-reading may be best explained by process switching, namely a change from visuospatial transformation (mediated by right superior parietal cortex) to object recognition (mediated by left inferior temporal cortex). Previous imaging studies have provided strong evidence for these functional mappings; right parietal cortex is involved in a number of visuospatial tasks (Cohen et al., 1996; Petit et al., 1996) and left inferior temporal cortex is involved in a number of object recognition tasks (Haxby et al., 1994; Price et al., 1996). This evidence argues against the ascription of teacher functions to these areas, though we cannot discount the activity of other regions outside our imaging window as having teacher functions. Functional reorganization of cortical representations also cannot be ruled out on the basis of the present results.

Localizing Learning
The primary goal of imaging changes in brain activation associated with skill learning or repetition priming is to discover the loci of neural plasticity that underlie such procedural memory phenomena. This goal is difficult to achieve for two reasons. First, performance on any task involves a distributed network of neural regions. Changes in some of these areas reflect learning-related plasticity that drives facilitation on the task; these can be called primary learning-related changes, to the extent that they directly index the location of the critical neural plasticity. However, as a consequence of these primary mnemonic changes, activation may change in other areas where no learning-related plasticity occurs. These changes in activation are secondary to the neural plasticity that drives facilitation in the task, and reflect the effect rather than the cause of

facilitation. For example, the development of a new high-level visual representation (a primary change) might lead to increased efficiency of identification, which in turn leads to a decrease in the amount of visual processing that must be performed by primary visual cortex (a secondary change). A central problem in the study of learning using neuroimaging methods is to distinguish changes in activation that reflect primary local plasticity from those that reflect secondary changes in performance.

Second, skill learning and repetition priming are both related to changes in behavioral performance, often characterized by decreased response time. While the changes associated with repetition priming are often small, changes in response time due to skill learning can be substantial. Changes in response time can change the duty cycle of a task. Such changes in duty cycle can result in increases or decreases in neural activity that are secondary to the neural plasticity underlying learning, and these changes can occur both in regions that exhibit local learning-related plasticity and also in regions that do not exhibit such plasticity. It is thus desirable to test learning using tasks where duty cycle does not change appreciably with practice, as in tasks where learning occurs as increased accuracy rather than decreased response time.

The issue of duty cycle does not figure significantly in the interpretation of the skill learning findings in the present experiment, because there was not a significant change in response time from Scan Session 1 to Scan Session 2. Learning instead took the form of increased accuracy for mirror-reversed items in Scan Session 2 compared to Scan Session 1, suggesting that the changes in activation are genuinely associated with learning rather than with changes in duty cycle. Large differences in response time were evident between practiced and unpracticed items in Scan Session 2, leaving these data open to issues of duty cycle changes. For both skill learning-related and item specific practice-related changes in activation in the present study, questions remain as to whether the changes represent primary plasticity or secondary changes in regions that do not exhibit local plasticity.

Conclusions

The present study used fMRI to examine the neural basis of visual skill learning in the mirror-reading task. Mirror-reading was associated with widespread activation of occipital, inferior temporal and superior parietal cortices. Skill learning in the task was associated with increases in left inferior temporal activation and decreases in right superior parietal activation. These data are consistent with a progression from reliance upon right-hemisphere dorsal stream visuospatial processes to a reliance upon left-hemisphere ventral stream object recognition processes. Further research must investigate the roles of other regions, such as basal ganglia and frontal lobes, that may also be involved in skill learning in the mirror-reading task.

Notes

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