Cognitive, Affective, & Behavioral Neuroscience
2002, 2 (1), 37-51

Effects of callosal lesions in a model of letter perception

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During cognitive tasks, the cerebral hemispheres cooperate, compete, and in general, interact via the corpus callosum. Although behavioral studies in normal and *split-brain* subjects have revealed a great deal about the transcallosal exchange of information, a fundamental question remains unanswered and controversial: Are transcallosal interhemispheric influences primarily excitatory or inhibitory? In this context, we examined the effects of simulating sectioning of the corpus callosum in a computational model of visual letter recognition. Differences were found, following simulated callosal sectioning, in the performance of each individual hemisphere, in the mean activation levels of hemispheres, and in the specific patterns of activity, depending on the nature of the callosal influences. Together with other recent computational modeling results, the findings are most consistent with the hypothesis that transcallosal influences are predominantly excitatory, and they suggest measures that could be examined in future experimental studies to help resolve this issue.

Hemispheric interactions via the corpus callosum, the major interhemispheric pathway, are an important aspect of the neurobiological processing that underlies cognition. Many carefully designed experimental studies with normal individuals have identified conditions under which the cerebral hemispheres cooperate, compete, and exchange information, during various cognitive tasks (Davidson & Hugdahl, 1995). Observations from human and animal split-brain studies have also revealed that the corpus callosum is very important in integrating performance of the two cerebral hemispheres. Experiments done over many years have shown that, although chronically split-brain-patients may superficially appear normal, communication between their two hemispheres is actually largely compromised (Gazzaniga, 1995; Seymour, Reuter-Lorenz, & Gazzaniga, 1994). Various clinical syndromes also occur in ischemic strokes that produce partial callosal sectioning (Goroud & Dumas, 1995). In this paper, we are concerned with the effects of callosal lesions and the implication of those effects with respect to the nature of callosal connections.

Although split-brain and other studies have helped greatly to define the nature of the information exchanged between the hemispheres, some other aspects of transcallosal hemispheric interactions remain quite confusing. Here, we focus on a long-standing yet ongoing controversy about whether transcallosal hemispheric interactions are primarily excitatory or inhibitory in nature. Specifically, it is often assumed that transcallosal hemispheric interactions are primarily excitatory (Berlucchi, 1983; Caselli, 1991; Lassonde, 1986). This is because most neurons sending axons through the corpus callosum are pyramidal cells, and these mainly end on contralateral pyramidal and spiny nonpyramidal cells with asymmetric synapses (Hughes & Peters, 1992; Innocenti, 1986; Mountcastle, 1998). Such apparently excitatory monosynaptic connections, the interhemispheric transfer of information inferred from split-brain experiments (Zaidel, 1995), and diminished right-handedness associated with a larger corpus callosum all support this view. Furthermore, unilateral hemispheric lesions produce *transcallosal diaschisis*, a rapid depression of neural activity, oxidative metabolism, and cerebral blood flow contralaterally in the intact hemisphere, a phenomenon that is widely presumed to be due primarily to loss of monosynaptic excitatory influences via the corpus callosum (Fiorelli, Blin, Backchine, Laplane, & Baron, 1991; J. S. Meyer, Obara, & Muramatsu, 1993). However, the hypothesis that transcallosal influences are excitatory has long been and remains controversial. Several investigators have argued that transcallosal interactions are mainly inhibitory or competitive in nature (Cook, 1986; Corballis, 1991; Denenberg, 1983; Ferbert et al., 1992; Fink, Driver, Rorden, Baldeweg, & Dolan, 2000; B. U. Meyer, Roricht, Grafin von Einsiedel, Kruggel, & Weindl, 1995; B. U. Meyer, Roricht, & Woiciechowsky, 1998; Netz,

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Ziemann, & Homberg, 1995). Support for this latter view is provided, for example, by behavioral studies suggesting that cerebral specialization for language and other cognitive phenomena may arise from interhemispheric competition or "rivalry" (Cook, 1986; Fink et al., 2000), by a demonstration that transcallosal excitatory postsynaptic potentials are of low magnitude and are followed by more prolonged, stronger inhibition (Toyama, Tokashiki, & Matsunami, 1969), and by trans-cranial magnetic stimulation studies showing that activation of one motor cortex inhibits the contralateral one (Ferbert et al., 1992; B. U. Meyer et al., 1995; B. U. Meyer et al., 1998; Netz et al., 1995).

In the context of this "callosal dilemma" about the excitatory/inhibitory nature of callosal connections, a number of computational models, consisting of paired left and right cortical regions, have recently been developed to study hemispheric interactions and cerebral functional asymmetries (Cook, 1999; Cook & Beech, 1990; Jacobs & Kosslyn, 1994; Levitan & Reggia, 1999, 2000; Reggia, Gittens, & Chhabra, 2000; Reggia, Goodall, & Shkuro, 1998; Ringo, Doty, Demeter, & Simard, 1994; Shevtsova & Reggia, 1999, 2000; Shkuro, Glezer, & Reggia, 2000). Among other things, these neural network models have been very successful in demonstrating that a variety of underlying hemispheric asymmetries (such as asymmetries in region size, excitability, receptive field size, feedback intensity, or synaptic plasticity) can, in theory, lead to hemispheric specialization. However, these models have encountered a dilemma similar to that facing experimentalists: No single reasonable assumption about callosal influences that has been examined so far both leads to strong functional specialization/asymmetry and, at the same time, fits experimentally observed postlesion activation patterns. Specifically, in these computational models, the most substantial hemispheric specialization generally occurs when inhibitory callosal connections are used, whereas the postlesion drop in cerebral activation seen experimentally in diaschisis is captured only in models with excitatory callosal influences.

Here, we extend previous studies by examining the effects of simulated lesions to the corpus callosum on the performance of a computational model under various assumptions about corpus callosum influences, input stimuli, lesion completeness, and hemispheric asymmetries. In this work, we use a recently created neural model of letter identification consisting of left and right visual hemispheric regions interacting via a simulated corpus callosum. This model has previously been used to investigate conditions under which underlying asymmetries can lead to functional lateralization (Shevtsova & Reggia, 1999) and to demonstrate the extent to which, following unilateral focal damage to one cerebral hemisphere, the opposite intact hemisphere can be responsible for recovery (Shevtsova & Reggia, 2000). The effects of callosal sectioning are now studied in the acute (just following the lesion) and chronic (after retraining and recovery) phases, focusing on determining how the model's behavior differs, following lesions to the corpus callosum, depending on whether callosal influences are assumed to be excitatory or inhibitory.

In the following, we begin with a brief description of the intact model and then describe the method used to simulate partial and complete callosal lesioning. The effects of callosal sectioning on the model's performance and on its activation patterns when callosal connections are excitatory versus when they are inhibitory are then described, both for the letter stimuli used during training and for inconsistent or conflicting stimuli presented to each hemisphere. The model's postlesion behavior is found to differ substantially, depending on whether callosal influences are assumed to be excitatory or inhibitory. Overall, particularly in the context of other recent computational modeling studies, these results tend to support past arguments that transcallosal interhemispheric interactions are primarily excitatory and provide suggestions for measures that could be examined in future experimental studies to help clarify the nature of these interactions.

METHOD

A detailed description of the neural model used in this study is given elsewhere (Shevtsova & Reggia, 1999), so only a summary is given here. This is followed by a description of the input stimuli used, the measurements that were made, and how callosal lesions were simulated with the model.

The intact model is trained to output the identity of letters that appear in various locations in its "visual field." Figure 1 shows the model's structure schematically. Each letter may be presented in any one of three positions of the 30×60 element input layer representing the visual field: the left and the right hemifields (LVF and RVF) and the center. Each hemifield of the input layer projects topographically onto the contralateral primary cortical layer. The orientation-sensitive neurons in the primary cortical layers extract and encode orientation of local edges in their receptive fields. Each primary layer projects onto the corresponding 20×20 associative cortical layer (fully connected). The input to each associative cortical neuron is a weighted sum of signals from the corresponding primary cortical layer, other elements of the same layer, and the opposite associative layer via homotopic callosal connections. Intralayer connections and dynamics are organized so that each associative cortical element receives excitatory inputs from nearby elements and inhibitory ones from more distant elements, resulting in a Mexican Hat pattern of activation in the associative cortical layers. Such dynamics, along with homotopic callosal connections and unsupervised learning of primary-to-associative connection strengths, generate an encoding of the input

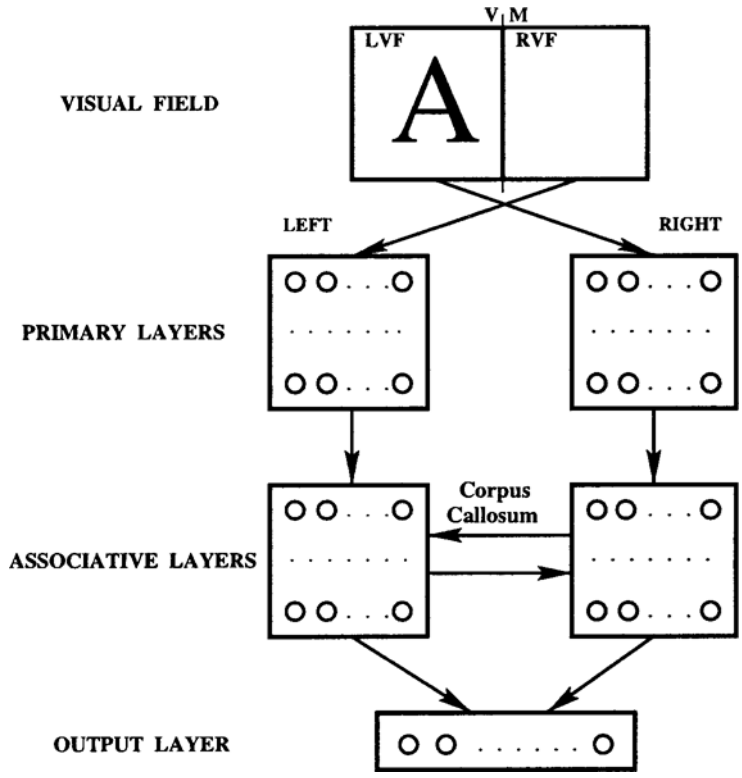

Figure 1. Architecture of the neural network model used in this study. VM, the vertical meridian; LVF, left visual hemifield; RVF, right visual hemifield.

stimuli in distributed activity patterns over the associative cortical layers. Both associative cortical layers project to an output layer. Each output element represents one input stimulus (a letter in a certain position in the visual field). A supervised (Widrow–Hoff) learning rule is used to modify associative-to-outputconnection strengths during training. Model performance is measured as a root-mean square error E of output element responses in terms of correctly classifying each input stimulus.

Using multiple versions of the basic model described above, we performed a series of computer experiments in order to examine the effects of callosal lesions on the model. Each independently performed simulation involved training a version of the model to recognize a set of letters presented one at a time in the LVF, the central position, and the RVF. Five different versions of the model were studied in which various left–right regional asymmetries were involved because of uncertainties concerning the actual underlying asymmetries in the biological visual cortex. Our intent in varying the nature and amount of left–right asymmetries was to verify that the results obtained concerning the effects of excitatory versus inhibitory callosal connections were qualitatively the same regardless of whether one assumed symmetrical or asymmetrical cortical regions. One model version had symmetric left and right hemispheric regions, whereas four others each had a single asymmetry: excitability of the associative cortical layers, size of the associative cortical layers, rate of unsupervised learning, or rate of supervised learning. For simplicity, we always arranged model asymmetries to favor the left cortical regions. With symmetric regions and with each cortical asymmetry, 2 separate model versions were done in which the callosal connections were either excitatory (callosal strength $c = 1.0$) or inhibitory ($c = -4.0$), making a total of 10 versions of the model used in the experiments.

With each version of the model, the pretraining error E ranged from 5.0 to 8.0. In each simulation, training continued until either E had been reduced to 0.05 or 1,000 presentations of the training stimuli had occurred. After training, each version of the model was able to identify correctly the input letters used during training (100% performance). Lateralization was measured as the difference in the contribution of the two hemispheres to performance. Specifically, after training was completed, the root-mean square error was measured under three conditions: with both associative layers connected to the output layer (E) and with each of the left and the right associative cortical layers alone connected to output elements (E^{L} and E^{R}, respectively). E^{L} and E^{R} allow one to evaluate the relative contribution of each individual hemisphere to overall performance and to measure

lateralization of that contribution. Lateralization was measured as $E^L - E^R$. Negative values of lateralization thus correspond to left lateralization, whereas positive values indicate right lateralization.

In the present study, after each version of the model described above had been trained to identify the training set of single letters, experiments with simulated lesions of the corpus callosum were done. Callosal lesions were varied in severity, with the percentage of connections "cut" in different simulations being 25%, 50%, 75%, 90%, or 100%, each lesion being done independently. Each lesion was introduced by assigning a certain percentage of randomly selected callosal connection weights between the two associative cortical layers to be 0 and holding these weights fixed thereafter. Following each lesion, training was continued either until full recovery had occurred with error reduced to 0.05 or until 1,000 new presentations of the training stimuli had occurred (the same criterion as that for the intact model). In each experiment, the root-mean square error evaluating model performance was measured before the lesion in the intact model, just after the lesion (the acute phase), and after retraining and recovery (the chronic phase), using E, E^L, and E^R.

With each model version, a set of additional experiments was done using *conflicting stimuli* that presented different information to each hemisphere (see Figure 2). Specifically, after training the model with a set of letters, two types of new stimuli not used during training were presented, including *chimeric letters* formed from two half-letters joined along the vertical meridian and presented in the central position in the visual field (Figure 2C) and *simultaneous different letters*, composed of two different letters presented at the same time in the LVF and the RVF (Figure 2F). These new stimuli were presented to the intact model after training was completed, in the acute phase just after a corpus callosum lesion was done and in the chronic phase after retraining and recovery, but were never used in training. They were always constructed from individual letters used during training.

SIMULATION RESULTS

In the following, we first describe in some detail the performance and activation patterns in the symmetric versions of the model, both pre- and postlesioning. Analogous results for the asymmetric versions of the model are then given for comparison. Postlesion shifts in the amount of activation in the individual hemispheres are also described.

Symmetric Case

In the symmetric version of the model, all the parameters are identical in both hemispheres, and the only difference is in the initial random distribution of primary-to-associative and associative-to-output connection weights. Figure 3 shows error as a function of callosal lesion severity, both acutely and after recovery, for inhibitory and excitatory callosal influences. The acute impairment of the full model in each case was found to be roughly proportional to the lesion severity—that is, acute postlesion performance was worse with larger callosal lesions. The symmetry of the hemispheric regions resulted in similar postlesion behavior of the left and the right hemispheric regions regardless of lesion severity. With inhibitory callosal influences, acutely, both individual hemispheres' errors increased a little with lesion severity, whereas with excitatory callosal influences, individual error measures remained almost unchanged. Note that a callosal lesion disrupts the full model acutely much more than it does either side alone. For both inhibitory and excitatory callosal influences, the model generally demonstrated full recovery after retraining, with both hemispheres participating in recovery roughly

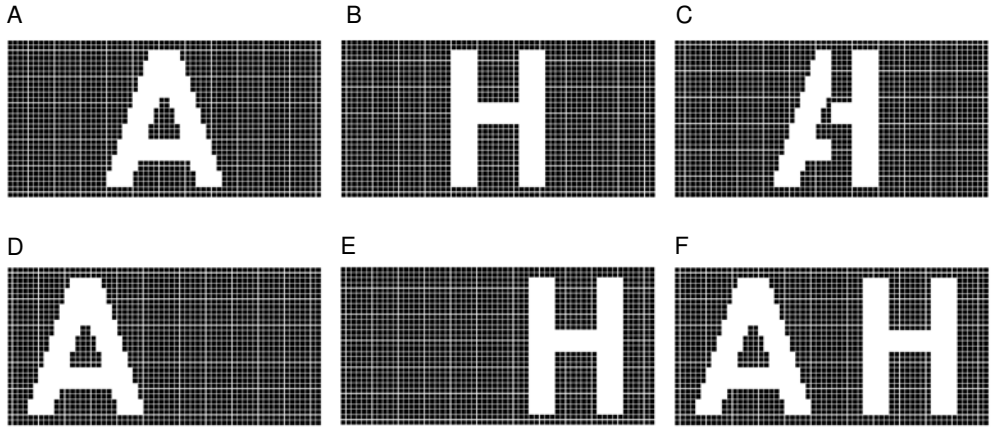

Figure 2. Sample input stimuli: (A, B) two letters, A and H, presented in the center of the visual field; (C) a chimera constructed from the two half-letters, A and H, joined along the vertical meridian; (D, E) two letters presented in the left visual field (LVF) and the right visual field (RVF), respectively; (F) two different letters presented in the LVF and the RVF simultaneously.

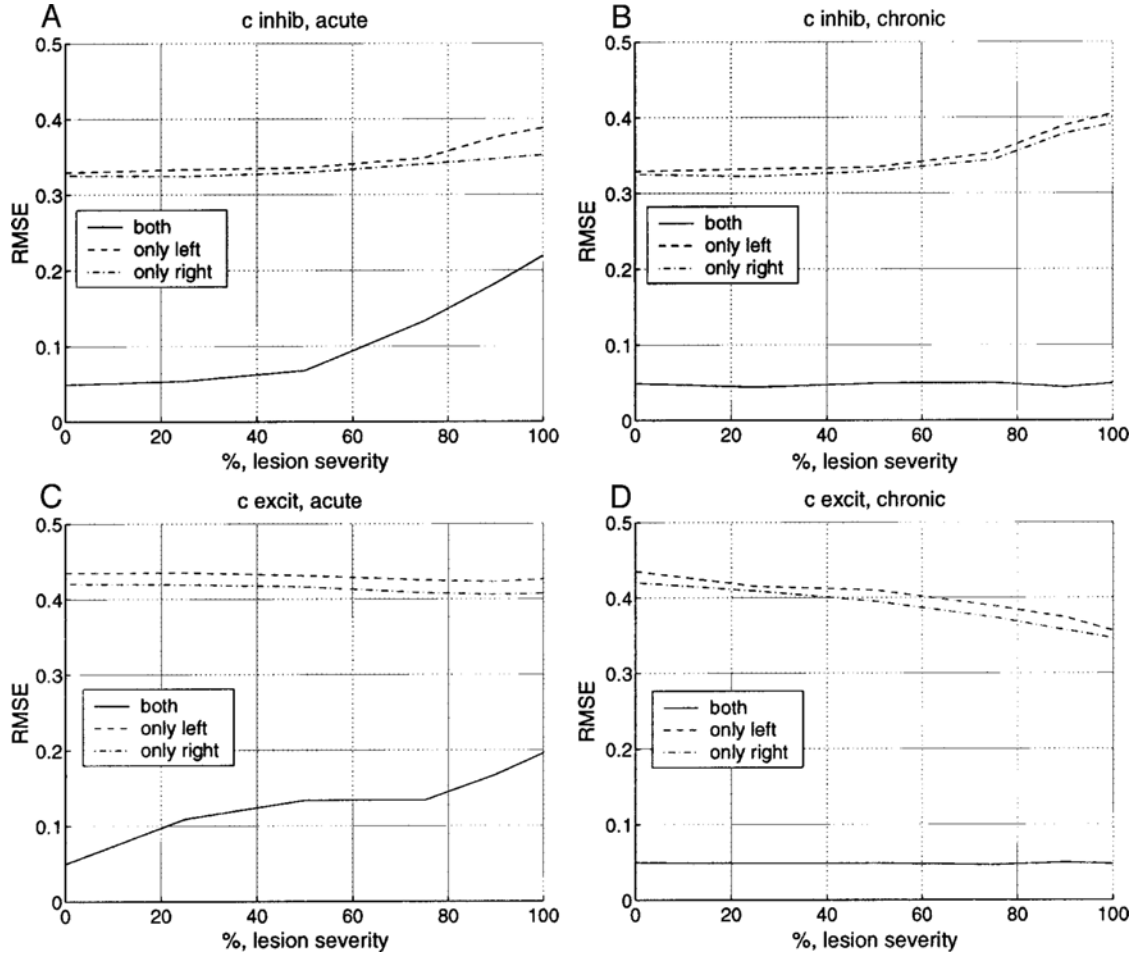

Figure 3. Root-mean square error (RMSE) versus corpus callosum lesion severity with the symmetric model for inhibitory (A, B) and excitatory (C, D) callosal influences. Error is shown in the acute phase immediately after lesioning (A, C) and after retraining and recovery (B, D) for the full model (*E*, solid line), the left associative cortex layer alone (E^{L}, dashed line), and the right associative cortex layer alone (E^{R}, dot–dashed line). Error measures are based on presentation of normal letter stimuli.

equally. However, with inhibitory callosal influences, the individual hemispheric errors did not reach their prelesion level, whereas with excitatory callosal influences, both hemispheres actually improved their individual performance, as compared with baseline.

The activation pattern in the left and right associative layers was examined with chimeric and with simultaneous different letter stimuli, both of which provide contradictory information to each hemisphere. Results are illustrated for a representative case based on the two letters A and H. Figures 4 and 5 show the distribution of activation over the left and right associative cortex layers before and after complete (100%) lesioning of the corpus callosum, both immediately after the lesion and after retraining and recovery. Figure 4 shows the results for inhibitory callosal influences, whereas Figure 5 shows the results for excitatory callosal influences. Results are shown both for regular A and H letter stimuli presented in the midline and for a chimera consisting of joined half-A and half-H.

In the intact model with inhibitory callosal influences, it may be seen that activation patterns in the left and the right hemispheric regions are somewhat complementary and antisymmetric for either letter, A or H, presented in the center of the visual field, and for the chimeric half-A/half-H stimulus also presented in the center of the visual field (Figure 4, IA–IC). When the half-A/half-H chimera is presented, the left associative layer activation pattern is very similar to that seen when a regular H is presented in the center of the visual field, and the right associative layer pattern is similar to that seen when a regular A is presented in the central position (Figure 4). Similar results are found with the acute postlesion version of the model (Figure 4, II). After a recovery period, it can be seen that weight changes during learning have led to substantial changes in the activation patterns (Figure 4, III).

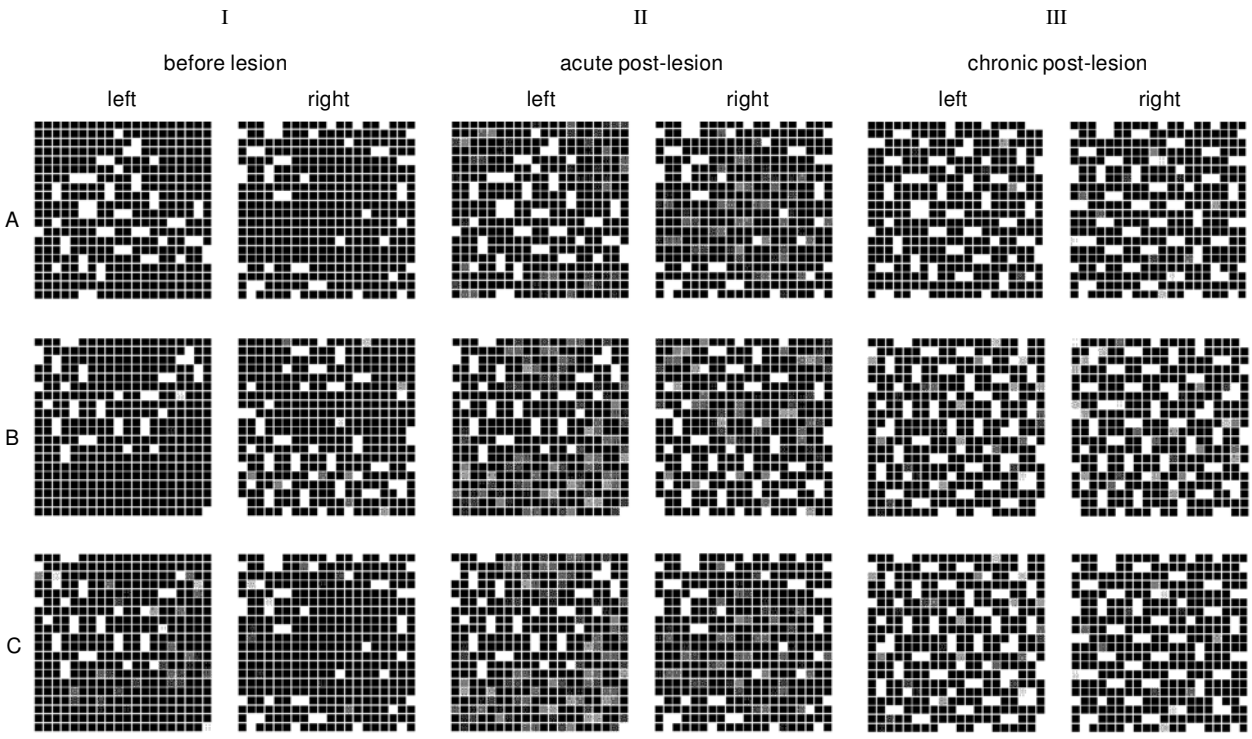

Figure 4. Activation patterns in the symmetric case with an inhibitory corpus callosum. Activation patterns in the left and right associative cortex layers while presenting (A, B) regular letter stimuli A or H, respectively, in the center of the visual field or (C) the chimeric stimulus half-A/half-H in the center of the visual field. Patterns are shown (I) before corpus callosum lesion, (II) immediately after 100% lesion (the acute phase), and (III) after retraining and recovery (chronic phase). Ten gray levels are used to demonstrate activation patterns: Black squares correspond to completely inhibited elements (activation zero), white squares show most excited elements, and gray squares of various intensity show intermediate activations.

The recoding of the input stimuli as activation patterns is systematic: In each case, the most active neural elements in the intact and acute postlesion activation patterns are a proper subset of those in the chronic postlesion activation patterns (e.g., elements that are active in Pattern IA, left are essentially a proper subset of those in IIIA, left; the same holds for IB, left and IIIB, left, for IIA, left and IIIA, left, etc.). Although difficult to see by inspection, chronically postlesion, the left and right activation patterns remain largely complementary for each stimulus, as can be seen by the large euclidean distances between their activation patterns: |IIIA, left − IIIA, right| = 21.8, |IIIB, left − IIIB, right| = 23.0, and |IIIC, left − IIIC, right| = 23.6. The activation patterns with the chimeric stimulus are precisely what one would predict on the basis of the individual activation patterns with regular letters: For example, pattern IIIC, left is virtually the same as IIIB, left, whereas IIIC, right is virtually the same as IIIA, right (the euclidean distances in these two cases being 0.0).

With excitatory callosal influences, in the intact, acute postlesion, and chronic postlesion models, activity patterns are roughly uniformly distributed in all cases—that is, the left and right activity patterns are not initially divided into complementary regions, as occurred with inhibitory callosal influences. Nonetheless, the corresponding left and right activation patterns in all cases are quite different and substantially complementary. For example, the euclidean distance between the left and the right activation patterns in each of the nine pairs shown in Figure 5 was in the range of 24.8–26.6; |IA, left − IA, right| = 26.6 illustrates the large distances involved. Unlike with inhibitory callosal influences, there were no substantial changes chronically postlesion in any case in the activation patterns. For example, with a stimulus of A, the distances between the intact activation pattern and the acute and chronic postlesion patterns for the right cortical region were almost negligible (|IA, right − IIA, right| = 0.4, |IA, right − IIIA, right| = 0.8). The similarity between individual associative layer activation patterns while chimeric letters were presented and while each corresponding individual letter was presented was still present, however (e.g., |IA, right − IC, right| = 0.2, |IB, left − IC, left| = 0.6), both pre- and postlesion.

Figures 6 and 7 demonstrate patterns of neuron activation over the left and right associative cortex layers when regular letter stimuli were presented in the left or right visual hemifields or two different letters were presented simultaneously in both visual hemifields, before and after complete callosal sectioning (100% lesion of the corpus callosum).

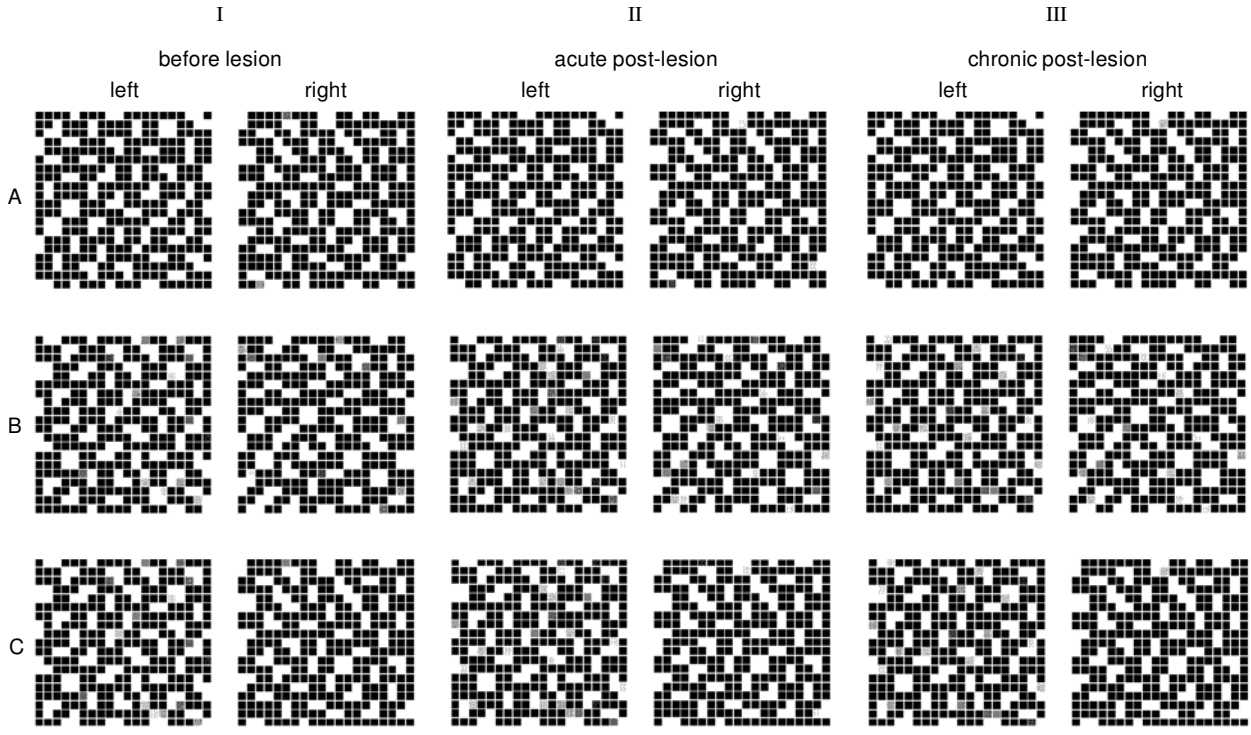

Figure 5. Activation patterns in the left and right associative cortex layers for excitatory callosal influences. Activation patterns in the left and right associative cortex layers while presenting (A, B) regular letter stimuli A or H, respectively, in the center of the visual field or (C) the chimeric stimulus half-A/half-H in the center of the visual field. Patterns are shown (I) before corpus callosum lesion, (II) immediately after 100% lesion (the acute phase), and (III) after retraining and recovery (chronic phase). Ten gray levels are used to demonstrate activation patterns: Black squares correspond to completely inhibited elements (activation zero), white squares show most excited elements, and gray squares of various intensity show intermediate activations.

With inhibitory callosal influences, it may be seen in Figure 6 that unilateral stimulus presentation results in unilateral activation in the associative layers: Only the associative layer that receives inputs from the contralateral primary visual layer becomes significantly active. This is true for the intact model and persists during both the acute and the chronic postlesion phases. When both A and H are presented in opposite halves of the visual field simultaneously with the intact-model, activation occurs in both associative layers (Figure 6, IC). However, instead of the resultant activation pattern being the sum of those seen with the individual stimuli presented above (IA and IB), substantial interference occurs, with somewhat complementary activation patterns appearing in the left and the right associative layers (IC), similar to that with the presentation of chimeric stimuli. After lesioning, activation in the left and right associative layers increases, and (as with chimeric stimuli) each associative layer's activation pattern resembles the corresponding pattern for unilateral stimulus presentation (Figure 6, IIC and IIIC).

As can be seen in Figure 7, with excitatory callosal influences, there is more of a bilateral component to information processing than there is with inhibitory callosal influences, although this is asymmetrical. In the intact model, bilateral conflicting letters produce similar, but not identical, activation patterns to those seen with presentation of the individual letters alone (e.g., distance $|IA, \text{right} - IC, \text{right}| = 1.9$ and $|IB, \text{left} - IC, \text{left}| = 2.1$ in Figure 7). Following complete callosal sectioning, these patterns become even more similar, with the same distance measures falling to 0.0.

It would be expected that after complete callosal lesioning, each individual hemisphere would perceive only its own part of the visual field and, for conflicting stimuli (chimeric or simultaneous different letters), could respond in favor of the corresponding letter stimulus, as occurred in experiments using conflicting picture stimuli with people who had undergone surgical section of the forebrain commissures (Levy, Trevarthen, & Sperry, 1972). In our simulations, this was persistently true with simultaneous bilateral different letters with either type of callosal influence. In other words, for such stimuli, each individual associative cortex layer activated the output node corresponding to the letter presented in the contralateral visual field much more strongly than it did other output nodes, regardless of type of callosal influence. With chimeric stimuli, the results were similar but more complex. With the intact full model, output elements for both letters forming the chimeric stimulus

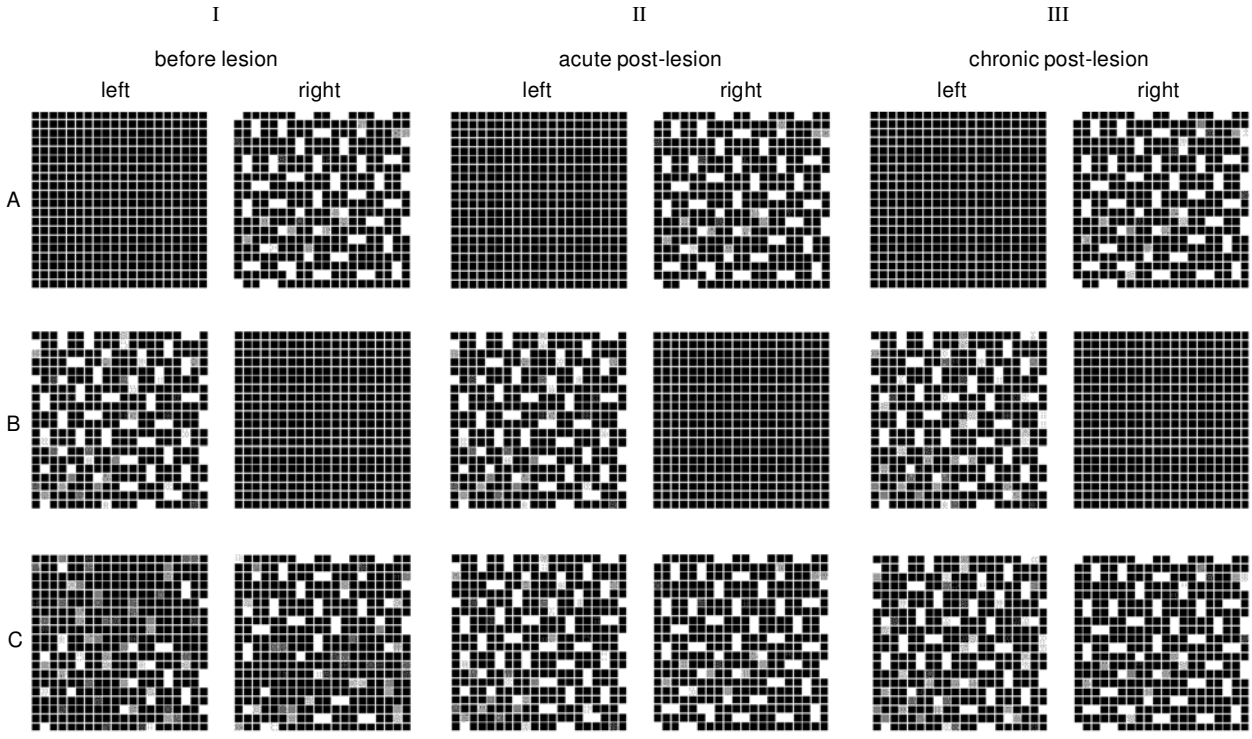

Figure 6. Activation patterns in the left and right associative cortex layers of the symmetric model with inhibitory callosal influences while presenting (A) the letter A in the left visual field (LVF), (B) the letter H in the right visual field (RVF), or (C) A in the LVF and H in the RVF simultaneously. Patterns are shown (I) before corpus callosum lesion, (II) immediately after 100% lesion (the acute phase), and (III) after retraining and recovery (chronic phase). Ten gray levels are used to demonstrate activation patterns: Black squares correspond to completely inhibited elements (activation zero), white squares show most excited elements, and gray squares of various intensity show intermediate activations.

were partially active (reflecting the fact that output elements were not competitive with one another), and there was often some partial activation of other incorrect outputs. When either hemisphere alone controlled the output, the correct output node for the half-letter that it saw (e.g., H in the midline for the left hemisphere when the half-A/half-H stimulus was used) was most active, but other output nodes could be partially active. Similar results occurred following callosal sectioning, with both inhibitory and excitatory callosal influences.

With partial lesioning of the corpus callosum, changes in performance and activation patterns were observed that were similar to but less pronounced than the complete lesioning results described above. Acute fall in performance of the full model was roughly proportional to the lesion severity with either type of callosal influence. In all cases, independently of lesion severity, the full model performance was completely restored in the chronic phase. Individual hemispheric performances in the model versions with inhibitory callosal influences worsened in the acute phase, and this was expressed more in the chronic phase. With excitatory callosal influences, individual hemispheric performances were almost unchanged in the acute phase and improved in the chronic phase. The latter was more evident with larger lesions. With partial callosal sectioning, in model versions with either type of callosal influence and for each type of input stimuli, the difference between activation patterns in the acute and the chronic phases was less evident than with complete callosal sectioning. For example, with inhibitory callosal influences, activation patterns for both chimeric and bilateral stimuli were mutually complementary in both the acute and the chronic phases.

Asymmetric Hemispheric Regions

Model versions with asymmetric hemisphere regions (asymmetric excitability, unsupervised learning rate, supervised learning rate, or size) were examined primarily as controls in order to determine whether the same differences observed in results with excitatory and inhibitory callosal connections were also present when the hemispheric regions were asymmetric rather than symmetric. The asymmetric versions generally demonstrated mild but consistent lateralization with inhibitory callosal influences. Simulations with these versions produced results qualitatively similar to those seen with the symmetric model. However, the results were modulated by the asymmetric functionality of the hemispheres. This

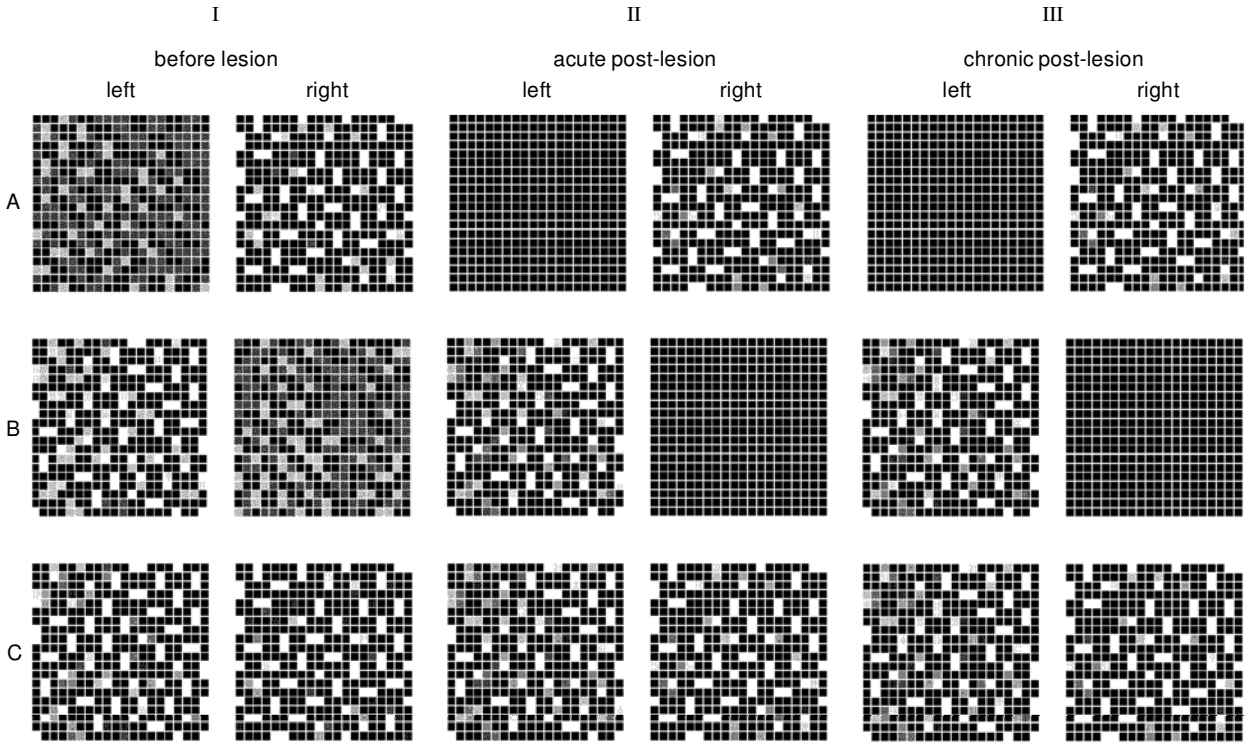

Figure 7. Activation patterns in the left and right associative cortex layers for excitatory callosal influences. Patterns are shown (I) before corpus callosum lesion, (II) immediately after 100% lesion (the acute phase), and (III) after retraining and recovery (chronic phase). Ten gray levels are used to demonstrate activation patterns: Black squares correspond to completely inhibited elements (activation zero), white squares show most excited elements, and gray squares of various intensity show intermediate activations.

was true for asymmetric performance for each different type of asymmetry. For brevity, the results are illustrated here just for the case in which the two associative cortical layers have different unsupervised learning rates favoring the left hemisphere (left, 0.01; right, 0.001); the results for all of the other cases were similar.

Figure 8 shows model error as a function of lesion severity, both acutely and after recovery, for inhibitory and excitatory callosal influences. As with the symmetric version of the model, the severity of the full model performance deficit acutely was generally higher for more severe lesions with either type of callosal influence. With inhibitory callosal influences, individual hemispheric performances were slightly impaired acutely, whereas with excitatory callosal influences, the loss of callosal connections again led to decreased individual hemispheric errors. After retraining, full model performance was restored completely, regardless of the type of callosal influence. However, this long-term restoration with more severe callosal lesions was accompanied by substantial differences in individual hemispheric performances: With inhibitory callosal influences, long-term performance of the "dominant" (better performing) left hemisphere actually deteriorated even as the full model was "recovering," whereas with excitatory callosal influences, performance of each individual hemisphere tended to improve. These long-term changes, despite their left–right asymmetry, resembled those seen with the symmetric model.

Figure 9 shows lateralization versus lesion severity in the asymmetric unsupervised learning rate model. In the acute phase, lateralization was almost unchanged. Loss of callosal connections led to decreased lateralization in the chronic phase for both inhibitory and excitatory callosal influences. This supports the hypothesis that the corpus callosum plays an important role in functional lateralization.

Lesion Effects on Mean Activation Levels

Figure 10 shows the mean activation in the left and right hemispheric regions versus lesion severity for both inhibitory and excitatory callosal influences for the symmetric model version. With inhibitory callosal influences, mean activation increased bilaterally just following the lesion, because as callosal connections were sectioned, the hemispheres were disinhibited, thereby increasing their mean activation. This became even more pronounced in the chronic phase after retraining. On the other hand, with excitatory callosal influences, mean activation decreased acutely, and this decrease persisted during recovery. The decrease in mean activation reflected a loss of mutual excitation between the two hemispheric regions.

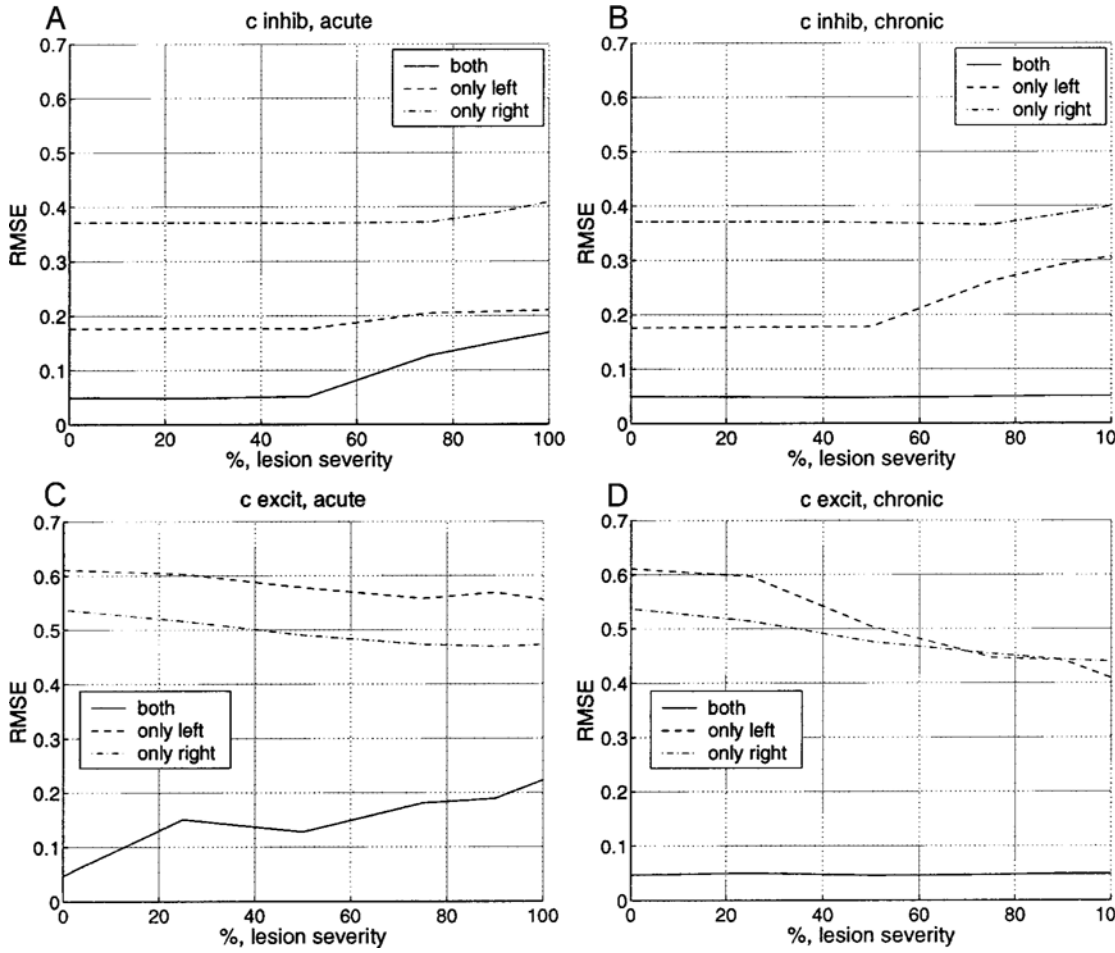

Figure 8. Root-mean square error (RMSE) versus corpus callosum lesion severity for the asymmetric unsupervised learning rate model (left, 0.01; right, 0.001) for inhibitory (A, B) and excitatory (C, D) callosal influences. Error is shown in the acute phase immediately after lesioning (A, C) and after retraining and recovery (B, D) for the full model (E, solid line), the left associative cortex layer alone (E^{L}, dashed line), and the right associative cortex layer alone (E^{R}, dot–dashed line).

The mean activation levels in the asymmetric models generally acted similarly to those of the symmetric model, with some differences owing to the underlying asymmetries. Usually, mean activation levels were initially higher on the dominant or better performing left side prior to lesioning, regardless of type of callosal influence (although this difference was most pronounced when callosal influences were inhibitory). With inhibitory callosal influences, the mean activation level of the left (dominant) hemispheric region remained almost unchanged or increased mildly after lesioning, whereas mean activation levels in the right hemisphere increased substantially, in both the acute and the chronic phases, for the four different underlying asymmetries we examined. With excitatory callosal influences, each hemisphere's mean activation levels decreased, both acutely and chronically. These changes in mean activity levels were thus similar to those seen with the symmetric versions.

DISCUSSION

In the study reported here, we examined the effects of corpus callosum lesions on performance and activation patterns of a simple neural network model of letter identification. The neural model used in this study is like many contemporary neural models in being both small and simplified, when compared with biological reality, and is concerned only with the single task of letter perception. Given this limited nature, caution must be exercised in deriving from the model any expectations concerning the general nature of interhemispheric interactions or hemispheric specialization or how individual hemisphere behavior may be altered following callosal sectioning and during subsequent recovery.

Our study has focused solely on examining the implications of assuming that transcallosal influences are excitatory versus inhibitory in nature. As was noted at the

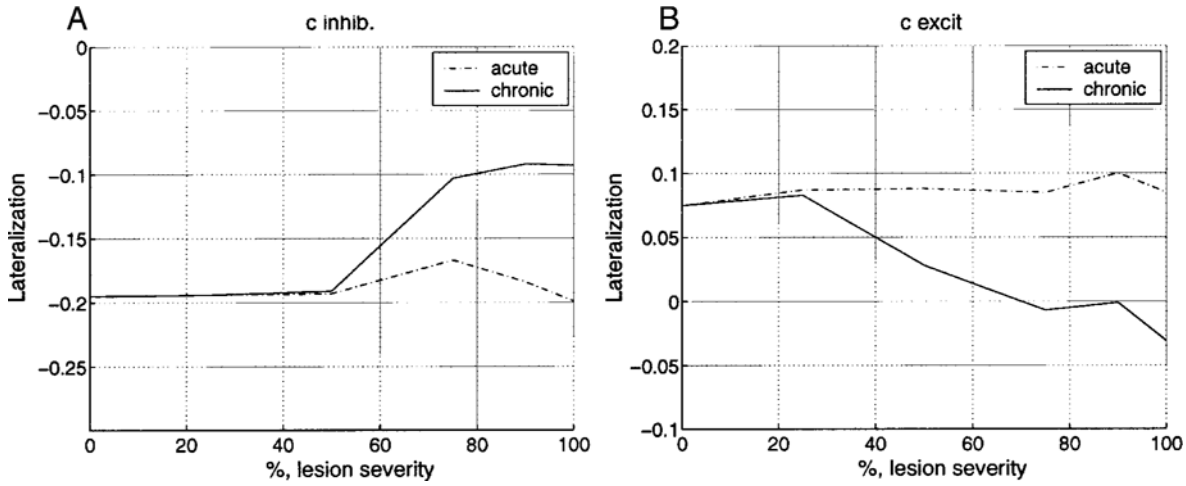

Figure 9. Lateralization versus corpus callosum lesion severity for the asymmetric unsupervised learning rate model (left, 0.01; right, 0.001) for inhibitory (A) and excitatory (B) callosal influences in the acute (dashed line) and chronic (solid line) phases. Note the different ranges for the vertical axes.

beginning of this paper, this issue has long been and continues to be controversial, despite substantial experimental data. Although a computational model such as ours cannot resolve such a controversy, it can contribute to its resolution by generating explicit predictions that may guide future experimental research. To our knowledge, the work described here is the first systematic examination of the effects of sectioning callosal connections in a neural model of interacting left- and right-hemispheric visual regions. The results indicate that, on the basis of the model, three specific experimentally testable predictions can be made about differences that are to be expected following callosal sectioning, depending on the excitatory/inhibitory nature of callosal connections.

Before looking at these specific predictions, we first note that some of the results obtained in the present study with different versions of our model were the same regardless of whether callosal influences were assumed to be excitatory or inhibitory. For example, in the acute phase following a callosal lesion, the performance of each version of the model that we examined was transiently impaired. This impairment was more pronounced the more severe the callosal lesion and was quite substantial with complete callosal sectioning. This acute postlesion impairment of performance is reminiscent of the acute disconnection syndrome (confusion, disorientation, unintelligible speech, etc.) that occurs following cerebral commissurotomy in humans (Bogen, Fisher, & Vogel, 1965). The acute postlesion impairment of the model suggests that one factor causing the transient postcommissurotomy confusional state may be the loss of interhemispheric transfer of information used jointly by the two hemispheres, since the impairment we observed was independent of the type of callosal influence.

Another behavior that was found regardless of type of callosal influence was that postlesion model performance rapidly and completely recovered to baseline levels. This recovery is interesting in the context of experimental observations that human split-brain subjects largely appear superficially to be normal after a recovery period. Of course, it is well known that such split-brain subjects have residual changes in their cognitive processing (some of which may be due to preexisting epilepsy and/or medication) and, furthermore, that these changes can be made especially evident when tested with carefully designed procedures that present different information to each hemisphere (Gazzaniga, 1995). This latter point was also true with our model, as can be seen from an examination of the model's reaction to chimeric stimuli and simultaneous different letters in opposite halves of the visual field. Each "hemisphere" in the model processed its portion of such stimuli largely independently, and had a selection been made of the identity of the input stimulus, each hemisphere would have favored a different stimulus. This is reminiscent of results obtained experimentally in split-brain subjects responding to chimeric figures, for example, when one hemisphere controls output (Levy et al., 1972).

The above results, found with the several variations of the model that we examined, are encouraging in suggesting that, however simplified the model is from reality, it does capture some fundamental aspects of postlesion behavioral observations. More interesting, however, are three differences in the effects of callosal sectioning that occurred in the model that depended on whether callosal influences were assumed to be excitatory or inhibitory, and we consider these next. These three differences are explicit and specific predictions of the model that could be looked for in future experiments to help clarify the nature of callosal influences.

First, the changes in the mean activation levels in the individual hemispheric regions depended primarily on the

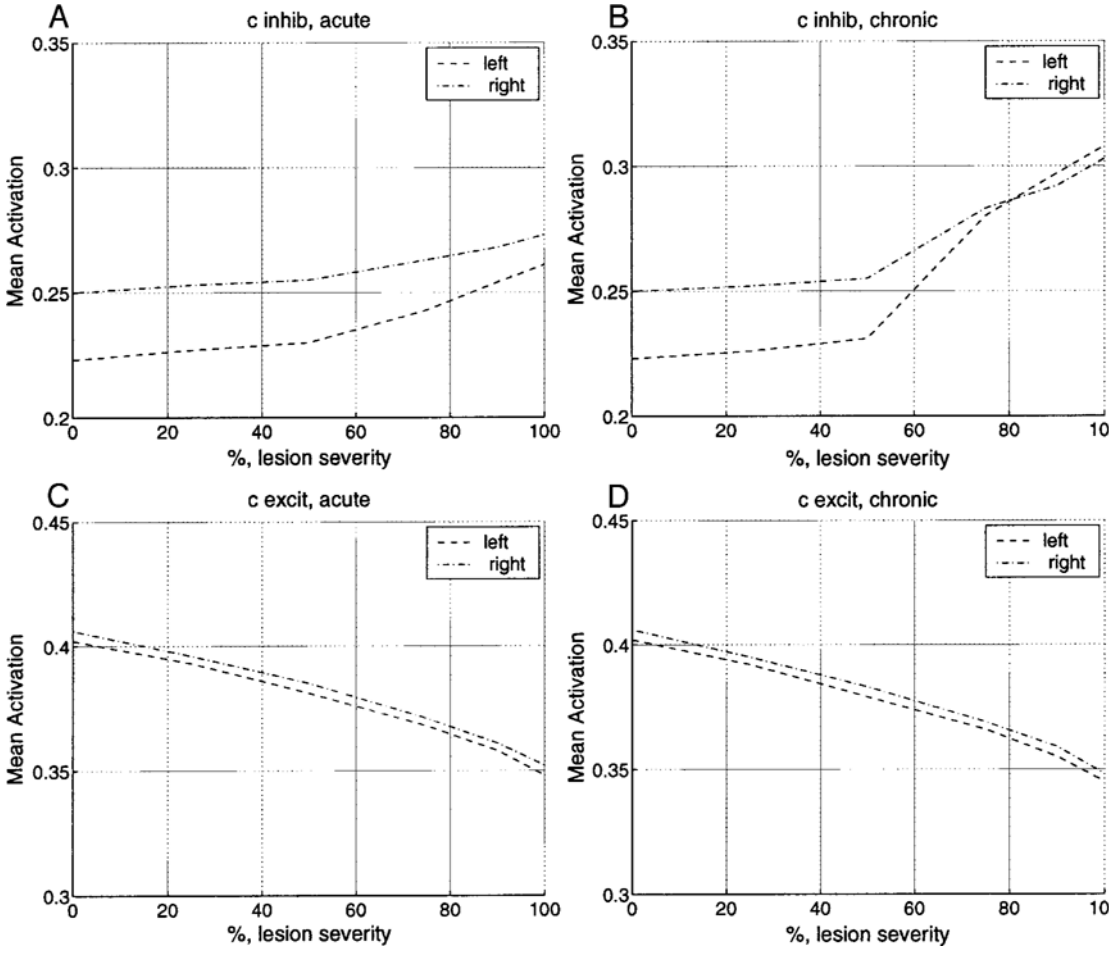

Figure 10. Mean activation versus corpus callosum lesion severity for the symmetric model for the left (dashed line) and right (dot-dashed line) associative layers. Mean activation is shown for inhibitory (A, B) and excitatory callosal influences (C, D) for the acute phase immediately after lesioning (A, C) and after retraining and recovery (B, D).

nature of the callosal influences. Sectioning of our model's callosal connections when callosal influences were excitatory led to acute bilateral depression of postlesion mean activation levels. In contrast, when callosal influences were inhibitory, increased activation was found in both hemispheric regions following callosal sectioning. Experimentally, regional cerebral blood flow and glucose metabolism have been found to decrease in both cerebral hemispheres following a unilateral stroke, presumably owing to loss of transcallosal excitation (Cappa et al., 1997; Dobkin et al., 1989). However, much less is currently known about the effects on hemispheric activity following corpus callosum ischemic infarct and/or corpus callosum sectioning. Limited experimental data indicate that bilateral depression of cortical metabolism, as measured by positron emission tomography, occurs in baboons following anterior corpus callosum sectioning (Yamaguchi et al., 1990), and a mild bilateral decrease of cerebral blood flow has also been found in swine following callosal sectioning (Andrews, Bringas, Alonzo, Khoshyomn, & Gluck, 1993). Thus, to the extent that coupling exists between neuronal activity and blood flow/oxidative metabolism, the mean activation changes following callosal sectioning observed with our model are most consistent with the hypothesis that callosal effects are predominantly excitatory. However, further experimental measurements of individual hemisphere metabolic activity prior to and following callosal sectioning, particularly in human subjects using contemporary functional imaging and other noninvasive methods for assessing regional cerebral blood flow, are needed to provide any confidence in this conclusion.

The second difference observed in the model between conditions in which callosal influences were excitatory and those in which they were inhibitory involved the performance of the individual hemispheres when each was examined alone during the postlesion recovery period. Performance of the full postlesion model always eventually returned to prelesion levels, regardless of callosal influences. However, with inhibitory callosal influences,

following complete callosal sectioning, the performance of each individual hemisphere *deteriorated* initially, and this deterioration tended to worsen with time, even as the performance of the full model improved during the chronic recovery period. In contrast, with excitatory callosal influences, acutely postlesion, the performance of each individual hemisphere tended to *improve* (even as the full model's performance deteriorated transiently), and this improvement in the individual hemisphere's performance increased during the chronic recovery period. This suggests a way—albeit a difficult one that would require the use of special equipment, such as a tachistoscope—to collect further data relevant to determining the nature of human callosal influences: follow the performance of the individual hemispheres over time during recovery from surgical sectioning of the corpus callosum. If, as the subject recovers, performance on tasks that assess the behavior of the individual hemispheres deteriorates, this would provide support for the hypothesis that callosal influences are inhibitory. Conversely, if individual hemisphere performance were to improve, that would support the hypothesis that callosal influences are excitatory.

The third observed difference, depending on callosal influences, involved asymmetries in the patterns of activation in left- and right-hemispheric regions. Even prior to lesioning, there was a difference in activity patterns. With inhibitory callosal influences, presentation of a midline stimulus prior to lesioning was associated with regions of inactive cortical elements that were fairly circumscribed, and the regions of inactivity on the left were complementary to those on the right (see, e.g., Figure 4). During the recovery period following callosal sectioning, the easily identifiable regions of inactivity vanished, even though the individual elements that were active remained largely complementary. In contrast, with excitatory callosal influences, no clearly identifiable regions of cortical inactivity were observed prior to lesioning with midline stimuli, and very little change in activation patterns occurred following callosal sectioning (see, e.g., Figure 5). These differences in activation patterns and pattern changes predicted by our model, depending on the type of callosal influence, could be searched for experimentally in animal callosotomy studies in which contemporary multielectrode and optical recording methods are used.

Another important issue is how the model reacted to callosal lesioning when there were underlying hemispheric asymmetries (unequal excitability, size, or learning rates) leading to partial lateralization. Since the lateralization of visual object recognition is currently incompletely understood and variable (Cummings, 1985; Hellige, 1993), and for character identification specifically may depend on the context in which the letters are viewed (Hellige, Cowin, & Eng, 1995; Hellige & Webster, 1979), we considered separately the cases in which the visual association cortex is assumed to be symmetric and the cases in which it is assumed to be asymmetric. Study of specific hemispheric region asymmetries was motivated by experimental evidence that a variety of corresponding left and right cortical regions can differ in their relative size (Geschwind & Levitsky, 1968), cortical circuitry (Galuske, Schlote, Bratzke, & Singer, 2000; Scheibel et al., 1985), neurotransmitter levels (Tucker & Williamson, 1984), and excitability by external stimuli (Macdonell et al., 1991). The key finding in our model in this regard is that the same three postlesion differences for excitatory versus inhibitory callosal connections (differences in individual hemispheric region mean activation levels, time course and nature of recovery, and activity patterns) observed when the hemispheric regions were symmetrical and without function lateralization were found in the lateralized versions of the model for each of the different underlying asymmetries. Thus, these three differences are fairly robust, in this sense, and do not depend on assuming initially symmetric hemispheric regions.

Furthermore, it was found that in asymmetric versions of our model, diminished lateralization was often present following callosal sectioning. The decrease in lateralization in the asymmetric versions of the model was not present in the acute phase, appearing only over time, indicating that it was a result of synaptic changes in the chronic recovery period, a period during which learning was triggered by the model's acute performance impairment. Most interesting is the observation that this diminished lateralization occurred regardless of the type of callosal influence (excitatory or inhibitory) assumed to be present. The postlesion loss of lateralization when inhibitory callosal influences were used is not surprising, given past models that have shown that transcallosal inhibition generally increases lateralization (Levitan & Reggia, 2000; Reggia et al., 1998; Shevtsova & Reggia, 1999). However, this finding is somewhat unexpected with excitatory callosal influences, and it suggests that even excitatory callosal influences can facilitate hemispheric specialization. Past arguments that hemispheric specialization depends on having inhibitory callosal influences lose some of their force in the context of these results.

In summary, the three specific differences described above produce suggestions for further experimentation, since ultimately the excitatory/inhibitory nature of transcallosal hemispheric interactions will be resolved through such experimentation. However, our sense from the present study and other recent computational modeling studies is that the computational evidence is increasingly supportive of the notion that callosal influences are excitatory. Not only do excitatory callosal influences explain the cerebral metabolic changes of diaschisis seen with stroke and callosal sectioning, but they have also provided a better account for some poststroke clinical findings (e.g., Rizzo & Robin, 1996) when these have been studied computationally (Shevtsova & Reggia, 2000). But if one accepts this hypothesis, it leaves open the question of how marked lateralization, such as occurs with language, can occur in the context of excitatory callosal influences, because in the past, qualitative hemispheric specialization has consistently proven easier to

obtain in computational models when callosal influences are assumed to be inhibitory.

One way that marked hemispheric specialization might arise in the presence of excitatory callosal influences, at least in some cases, is from asymmetrical sensorimotor experiences on the two sides. For example, this occurs in the cortical motor maps of individuals who read braille with only one hand (Pascual-Leone, Wasserman, Sadato, & Hallett, 1995). However, it is difficult to relate asymmetries from braille reading to many other situations in which hemispheric specialization exists but environmental asymmetries are not readily apparent. Another possibility, given past experimental evidence that brainstem and thalamic regions substantially influence cortical functionality, is that hemispheric specialization and asymmetries in function (readily produced in earlier models having transcallosal inhibition, but not excitation) and the postlesion changes of cerebral diaschisis (readily produced in past models having transcallosal excitation, but not inhibition) could both be accounted for if excitatory callosal influences are complemented by a *subcortical* mechanism for cross-midline competition/rivalry in afferent pathways. The existence of cross-midline inhibitory influences is well established in biological subcortical afferent pathways (Appell & Behan, 1990; Hilgetag, Kotter, & Young, 1999; Popper & Fay, 1992), may be viewed as consistent with findings in visual cuing effect studies of attentional mechanisms in human callosotomy subjects (Berlucchi, Aglioti, & Tassinari, 1997; Mangun et al., 1994), and has also in the past formed a central part of some computational models of paradoxical lesion effects and visuospatial neglect (Hilgetag et al., 1999). We thus recently hypothesized that excitatory callosal influences plus subcortical cross-midline inhibitory mechanisms might provide the best fit to experimental data in a single model (Reggia, Goodall, & Levitan, 2001; Reggia, Goodall, Shkuro, & Glezer, 2001). Initial simulations with models of nonvisual systems different from the model examined in this paper have provided support for this hypothesis, demonstrating for a language-related task that both strong lateralization and diaschisis-like changes in postlesion activation can be produced in a single computer model with excitatory callosal connections, as long as strong subcortical cross-midline inhibition is present (Reggia, Goodall, et al., 2001), and that experimentally observed cortical map asymmetries can also be explained, in part, by the presence of subcortical cross-midline inhibitory influences when callosal influences are excitatory (Reggia, Goodall, & Levitan, 2001).

Finally, another possibility meriting consideration is that callosal connections might be a mixture in time and space of excitatory and inhibitory effects, similar to what has sometimes been observed with cortical sensory afferents (Stemmler, Usher, & Niebur, 1995). One might even postulate that the human low-level sensory cortex could have excitatory callosal connections, whereas association areas could have inhibitory ones, and this idea has recently formed the basis of a neural model with which hemispheric interactions were investigated (Cook, 1999). It is possible that these or other subtle forms of brain organization might ultimately be revealed under more complicated testing paradigms.

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(Manuscript received June 5, 2001;
revision accepted for publication February 8, 2002.)