

The Relationship of Three Cortical Regions to an Information-Processing Model

John R. Anderson¹, Yulin Qin¹, V. Andrew Stenger², and
Cameron S. Carter²

Abstract

■ This research tests a model of the computational role of three cortical regions in tasks like algebra equation solving. The model assumes that there is a left parietal region-of-interest (ROI) where the problem expression is represented and transformed, a left prefrontal ROI where information for solving the task is retrieved, and a motor ROI where hand movements to produce the answer are programmed. A functional magnetic resonance imaging (fMRI) study of an abstract symbol-manipulation task was performed to articulate the roles of these three regions. Participants learned to associate words with instructions for transforming strings of letters. The study manipulated the need to retrieve these instructions, the need to transform the strings, and whether there was a delay

between calculation of the answer and the output of the answer. As predicted, the left parietal ROI mainly reflected the need for a transformation and the left prefrontal ROI the need for retrieval. Homologous right ROIs showed similar but weaker responses. Neither the prefrontal nor the parietal ROIs responded to delay, but the motor ROI did respond to delay, implying motor rehearsal over the delay. Except for the motor ROI, these patterns of activity did not vary with response hand. In an ACT-R model, it was shown that the activity of an imaginal buffer predicted the blood oxygen level-dependent (BOLD) response of the parietal ROI, the activity of a retrieval buffer predicted the response of the prefrontal ROI, and the activity of a manual buffer predicted the response of the motor ROI. ■

INTRODUCTION

As exemplified by the classic research of Sternberg (1969), information-processing models have frequently been used to predict latency. They postulate a series of cognitive components like memory retrieval and motor programming that are involved in the performance of a task and offer theories about the factors that control how long these components take. Brain imaging research has tried to identify brain regions that instantiate such components and has studied how the activation of these regions varies with manipulations of complexity. This article will describe how to bring these two traditions together in precise models. It will describe an information-processing model developed within the ACT-R cognitive architecture (Anderson & Lebiere, 1998) for a symbol-manipulation task and how that model was used to predict both latency data and the blood oxygen level-dependent (BOLD) response obtained in an functional magnetic resonance imaging (fMRI) study. By combining the two data sources, we obtained much greater guidance in the development of cognitive models. In particular, we will show that given an association of components of a cognitive architecture with brain regions and given a model fit to latency data, it

is possible to make a priori predictions about the BOLD response in these regions. This model-development methodology is not unique to the ACT-R theory nor are the conclusions. The methodology can be applied to any well-specified architecture and we believe that it would force convergence among different cognitive architectures in terms of the characterizations they give of the cognitive processes involved in the performance of a task. We also suspect that the methodological program, if successful, would help bring some convergence in the brain-imaging literature as to the function of different brain regions.

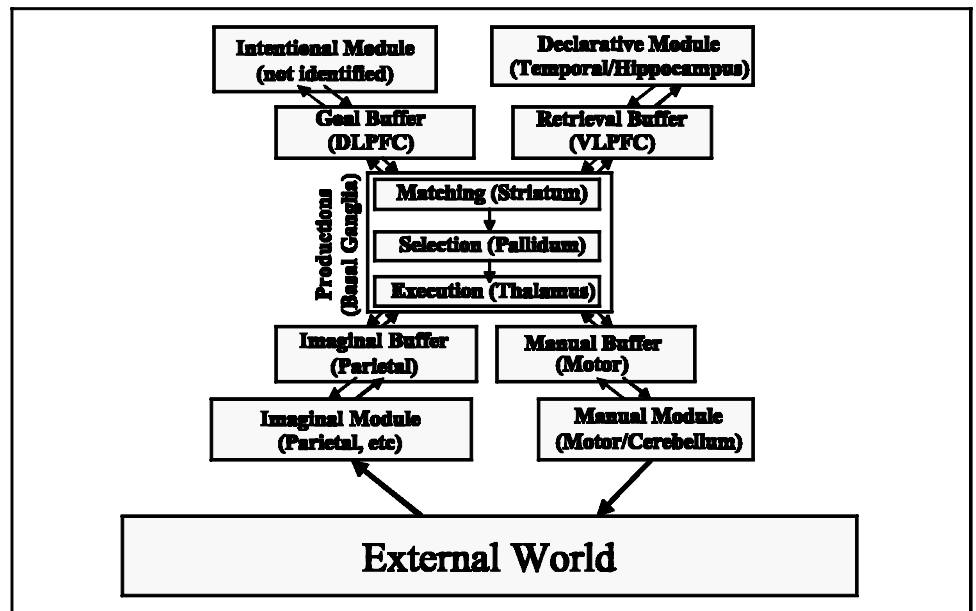
This article will begin with a brief description of the ACT-R architecture and the associations of components of that architecture with brain regions. Then it will describe a new experiment that was motivated to test some predictions that followed from these associations. After describing this experiment and its results, the article will describe a model that we developed for this task and how the development of an accurate model was informed by the results of the imaging study.

The ACT-R 5.0 Architecture and the BOLD Response

Figure 1 illustrates the basic architecture of ACT-R 5.0. There are a set of “modules” devoted to processes like

¹Carnegie Mellon University, ²University of Pittsburgh

Figure 1. The organization of information in ACT-R 5.0.



identifying objects in the visual field, controlling the hands, retrieving information from declarative memory, or keeping track of current goals and intentions. There is a central production system that is not sensitive to most of the activity in these modules but rather can only respond to information that is deposited in the “buffers” of these modules. For instance, people are not aware of all the information in the visual field but only the object they are currently attending to. Similarly, people are not aware of all the information in long-term memory, only the fact currently retrieved. Each module makes this information available as a chunk (an ACT-R declarative structure) in a buffer. As illustrated in Figure 1 the core production system can recognize patterns in these buffers and make changes to these buffers—as for instance, when it makes a request to perform an action in the manual buffer. In the terms of Fodor (1983) the information in these modules is largely encapsulated and they communicate only through the information they make available in their buffers.

This article will be principally focused on three buffers. The first buffer is an imaginal buffer that holds the representations of problems, like mental images of equations, while operations are being performed on these problems. In line with other work (Dehaene, Piazza, Pinel, & Cohen, 2003; Reichle, Carpenter, & Just, 2000) we found evidence for this buffer in the left posterior parietal cortex. The second buffer holds information retrieved from declarative memory and is associated with a portion of the left prefrontal cortex across BA 45 and BA 46 (a similar region has been reported by a number of investigators: Cabeza, Dolcos, Graham, & Nyberg, 2002; Donaldson, Petersen, Ollinger, & Buckner, 2001; Fletcher & Henson, 2001; Wagner, Maril, Bjork & Schacter, 2001; Wagner, Pare-Blagoev, Clark, &

Poldrack, 2001; Lepage, Ghaffar, Nyberg, & Tulving, 2000; Buckner, Kelley, & Peterson, 1999). The third is the manual buffer, which is responsible for programming and execution of hand movements. It is associated with the region of the left motor cortex that controls right-hand movements (Roland, Larsen, Lassen, & Skinhoj, 1980).

Anderson, Qin, Sohn, Stenger, and Carter (2003) performed a study of two algebraic tasks that served to test certain components of the architecture. The first experiment involved solution of real algebraic equations like $3x + 5 = 23$. The second, motivated in part to show that the imaging results did not depend on the involvement of arithmetic, used an artificial string transformation task that preserved many of the formal properties of algebra but did not involve arithmetic. ACT-R models (Anderson, Reder, & Lebiere, 1996, for real algebra; Blessing & Anderson, 1996, for artificial algebra) already existed for these two tasks. These models were updated to correspond to ACT-R 5.0 and to generate predictions about the fMRI signal. As we will describe later, it is possible to generate predictions for the exact form of the BOLD response. We found left parietal, prefrontal, and motor regions whose BOLD responses corresponded to the predictions derived from the ACT-R model. In this article, we will work with three prespecified regions-of-interest (ROIs) based on the ROIs from this earlier study. Each region was 5 voxels wide, 5 voxels long, and 4 voxels deep (approximately $16 \times 16 \times 13$ mm) and was centered at or near the center of the regions found by Anderson et al. To explore the laterality of these effects we also looked at prespecified 100-voxel ROIs in the right hemisphere obtained by just switching the sign of the x coordinate. Thus, our prespecified ROIs are:

1. *Parietal*: centered at $(x = \pm 23, y = -64, z = 34)$ covering Brodmann's areas 39 and 40 at the intraparietal sulcus.
2. *Prefrontal*: centered at $(x = \pm 40, y = 21, z = 21)$ covering Brodmann's areas 45 and 46 around the inferior frontal sulcus.
3. *Motor*: centered at $(x = \pm 37, y = -25, z = 47)$ covering Brodmann's areas 3 and 4 at the central sulcus.

The advantage of working with predefined regions such as these is that we can perform more powerful statistical tests because we do not have to correct for the kind of false positives that can occur in exploratory analyses. We will have specific regions and specific predictions about the responses found in these regions. Indeed, it makes the logic of our statistical tests identical to the logic used on behavioral measures like latency and accuracy. We have just added six additional dependent measures corresponding to these six prespecified regions. Because of this, when we assess our model fits to the BOLD functions we do not have to worry about correcting for confirmatory biases that would occur if we selected regions because they happened to show the effects predicted by the model.

The Current Study

This study has a number of goals besides testing the earlier associations of these brain regions with specific information-processing components. The first was to ascertain better what the BOLD response reflects in terms of the activity of the postulated buffers. Although we assume that these regions hold a representation of the information in the corresponding buffer (prefrontal holds a representation of a retrieved fact, motor a representation of a manual program, parietal a representation of the problem state), our assumption is that the BOLD response reflects the processing required to change the contents of the buffer (i.e., retrieve a new fact to place in the retrieval buffer, produce a program for the manual buffer, transform the problem representation in the imaginal buffer). Thus, it should not matter how long the information is held but rather how much time is spent transforming the information. However, in Anderson et al. (2003) the duration of maintenance was confounded with number of changes. To separate out the effects of active transformations from passive holding, we introduced a delay during which participants had to just hold the information. According to the ACT-R model, regions like the prefrontal and parietal should not be affected by this delay.

A second goal was to assess the degree to which these effects are left lateralized. Our original study that defined the regions involved high school algebra, which one might assume is left lateralized. The research reported here will use a more abstract symbol-manipulation task that might not have the same degree of lateralization. It

will examine the behavior of the right homologues of the regions found in the Anderson et al. (2003) study. In addition, to separate any effect of hand of responding, half of the participants (all right-handed) responded with their left hands and half responded with their right hands.

Another goal was to more carefully separate retrieval from transformation. In the past studies, they were confounded because number of retrievals increased with number of transformations. Here we wanted to perform a study in which retrieval and transformation were more independently manipulated.

A fourth goal was to minimize the effect of eye movements. The expressions used in the past research were rather large and subtended many degrees of visual angle. In the current experiment, we used a task in which all the critical information could be perceived in the fovea.

The experiment involved two phases. In the first phase (outside the magnet), participants memorized information that they would use in the second phase of the experiment that took place in the magnet. The material to be memorized involved associations between two-letter words and two-digit numbers such as:

$$AT \rightarrow 13 \text{ and } BE \rightarrow 26$$

Then in the second phase of the experiment, participants either saw these two-letter words or two-digit numbers paired with permutations of the letters A, B, C, and D. Table 1 illustrates the various conditions of the experiment. Participants were told that the two-digit codes that they had learned were instructions for transforming the four-letter sequences. Thus, 13 means that the first and third letters should be reversed. Applied to *CDAB* it would produce *ADCB*. Some two-digit codes are "no-ops" such as 26 because one of the digits is greater than 4 and so in this case does not require a transformation. The difference between no-op digit pairs and ones that require an operation is referred to as the *transformation* factor in Table 1 and throughout the article. Participants can either be given the digit pair directly in which case no retrieval is required or be given a word from which they have to retrieve the digit pair. The requirement to perform this retrieval is referred to as the *substitution* factor in Table 1 and throughout the article because it required the participant to substitute the digit for the word.

Table 1. Illustration of the Four Conditions of the Experiment (Assuming AT Is Associated to 13 and BE to 26)

	<i>No Transformation</i>	<i>Yes Transformation</i>
No substitution	Stimulus: CDAB 26 Response: CDAB	Stimulus: CDAB 13 Response: ADCB
Yes substitution	Stimulus: CDAB BE Response: CDAB	Stimulus: CDAB AT Response: ADCB

Figure 2 illustrates the scanning procedure for the experiment. Each trial lasted 24 sec and consisted of 20 1.2-sec scans. During the first 1.2 sec an asterisk appeared. Then the letter string with a number or word instruction below appeared until the participant pressed a thumb key indicating that they were ready to key the answer (the letters A, B, C, and D were mapped to index, big, ring, and small fingers). The time to press the thumb key is our most important behavioral measure reflecting the time to comprehend the instruction and plan the response. When the thumb key was pressed, the letter string disappeared and the participant either would have to wait 4 sec before keying out the answer or could respond immediately. The choice of immediate or delay was randomly determined from trial to trial. When the prompt to respond appeared they had to key out their letters quickly and so had to have the response sequence preplanned.

Thus, the fundamental design of the experiment was a $2 \times 2 \times 2 \times 2 \times 20$ design with choice of response hand a between-participant variable, and the within-participant variables being whether a delay was involved, whether a transformation was involved, whether retrieval of a paired associate was required, and scan (20 values).

Predictions

The following were our predictions for the experiment:

1. The parietal ROI would show a stronger effect of transformation than substitution since transformation requires more substantial changes to the problem representation.
2. The prefrontal ROI would show a stronger effect of substitution than transformation since substitution is associated with greater retrieval requirements.
3. The prefrontal ROI would show no response in the no-substitution, no-transformation condition because no

retrieval is required, but the parietal region would show a substantial effect because it is still necessary to build up a representation of the problem.

4. Neither the prefrontal nor the parietal ROI would show an effect of delay.

5. Neither the prefrontal nor parietal ROI would be affected by the choice of response hand, but the dominant motor ROI should switch hemispheres according to the response hand.

6. Anchored for time of response, the motor region would not show an effect of substitution or transformation.

We did not have a priori predictions as to what region would show an effect of delay.

RESULTS

Behavioral Results

Figure 3A shows the mean latencies of the thumb press (our measure of planning time) as a function of condition and Figure 3B shows the mean times for each of the subsequent key presses separately for delay and no delay. Response hand had no significant effect on any key time. With respect to planning time, participants show significant effects of transformation, $F(1,20) = 78.70$, $p < .0001$; $SEM = .396$, and of substitution, $F(1,20) = 156.60$; $p < .0001$; $SEM = .158$, but no interaction between the two, $F(1,20) = .47$; $SEM = .10$. Note that the time in the substitution, no-transformation condition (4.21 sec) is close to the time in the no-substitution, transformation condition (4.34 sec). Therefore, differences between these conditions in BOLD response are unlikely to be due to total time. With respect to subsequent keying times, participants average well under a half a second per key indicating that they must have planned their responses as instructed. These keying times show an effect of key, indicating a basic

Figure 2. The 24-sec structure of an fMRI trial. It is assumed that the word “we” is associated with 34.

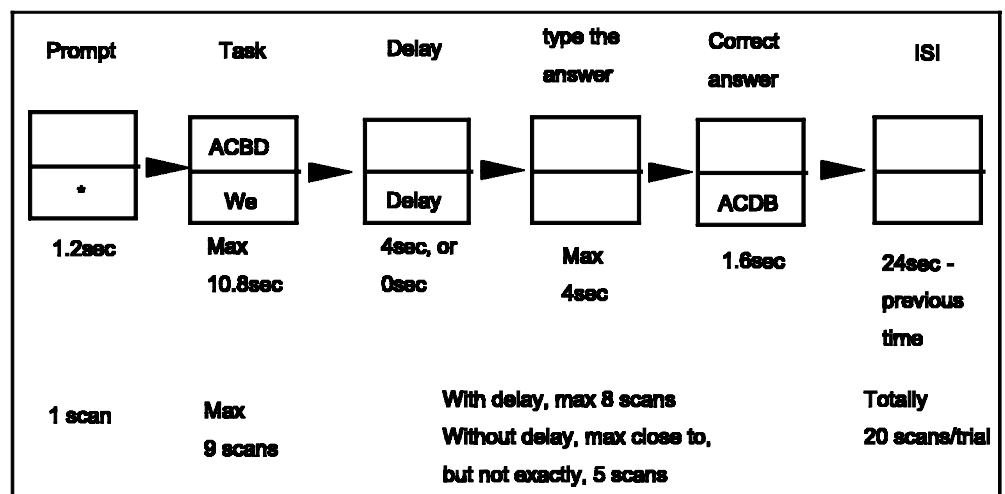
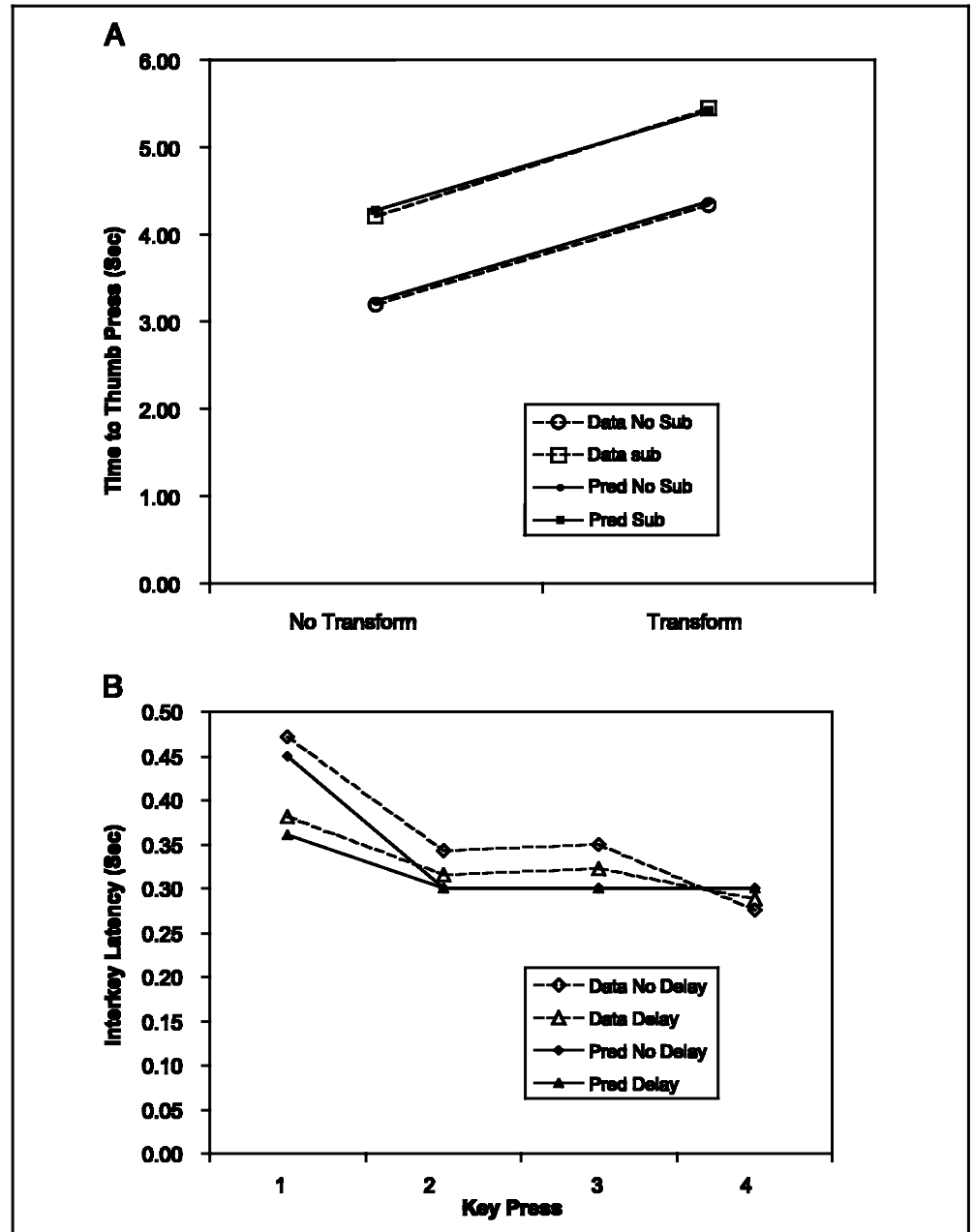


Figure 3. (A) Mean latencies for a thumb press as a function of whether a transformation or a substitution was required. (B) Mean interkey times for the subsequent four keys as a function of whether there is a delay or not. The solid lines indicate the predictions of ACT-R and the dotted lines indicate the data.



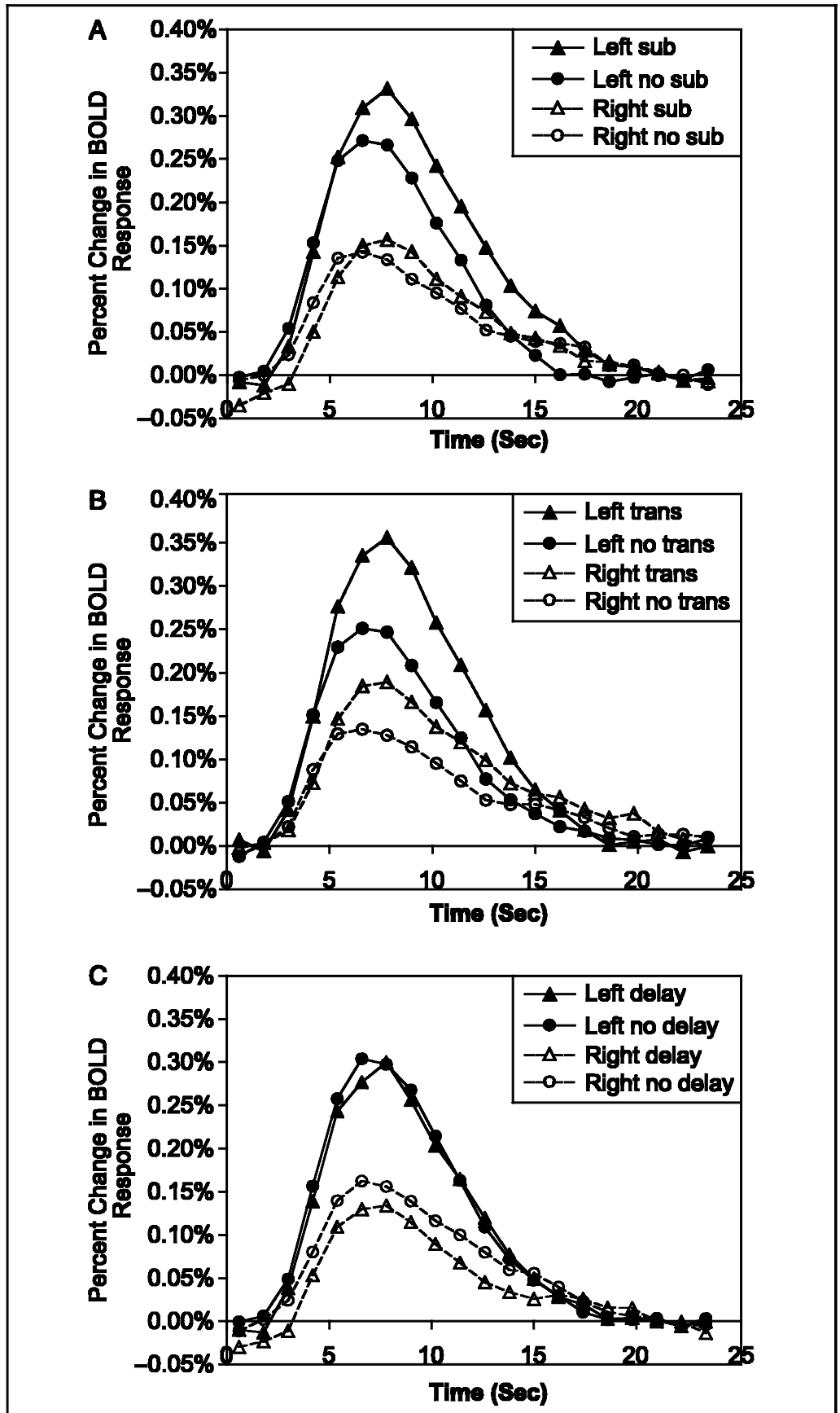
speedup, $F(3,60) = 54.47$, $p < .0001$; $SEM = .012$, as they progress through the keying sequence. In the model, times are slower for key 1 (first key of the answer after the thumb key) because participants must wait for the answer prompt to respond. The ACT-R predictions in the Figure 3B are a priori predictions based on the times for its perceptual-motor components. There is also a significant effect of delay, $F(1,20) = 15.97$; $p < .001$; $SEM = .021$, and a significant delay by key interaction, $F(3,60) = 11.84$; $p < .0001$; $SEM = .006$. The model is faster for the first key of the answer with a delay because it can use the delay between the thumb key and the answer prompt to prepare to respond. There is also a significant effect of substitution, $F(1,20) = 19.83$; $p < .001$, $SEM = .0031$, and a significant delay by substitution

interaction, $F(1,20) = 11.92$; $p < .01$; $SEM = .002$. Participants are 6 msec slower to key in the substitution condition when there is delay and 28 msec when there is not. These effects are miniscule compared to the over 1 sec effect of substitution on planning time.

The Posterior Parietal Regions

Figure 4 reports the effects of substitution, transformation, and delay on the BOLD response in the left and right parietal regions. These curves take as baseline the average of Scans 1 and 2 (before the response begins to rise) and Scan 20 (by which time it has returned to baseline). Each point is defined as the percent rise above this baseline. We performed an analysis of the degree to

Figure 4. Effect of main factors on the BOLD response in the left and right parietal regions: (A) substitution; (B) transformation; (C) delay.



which the curves defined by Scans 3–19 rose above the baseline, which we measured as the area under the curve. There was no difference between left and right responding participants, $F(1,20) = .06$, $SEM = 24.77\%$, or between delay and no delay, $F(1,20) = .43$, $SEM = 1.00\%$. However, the left side responds significantly more than the right, $F(1,20) = 8.34$, $p < .01$, $SEM = 6.15\%$; the responses rise more when there is a transformation than not, $F(1,20) = 26.67$; $p < .0001$; $SEM = .89\%$; and more when there is a substitution than not, $F(1,20) = 24.90$, $p < .0001$, $SEM = .89\%$. There was one significant interaction and one marginally significant interaction—hemisphere by substitution, $F(1,20) = 9.31$, $p < .01$, $SEM = .46\%$, and hemisphere by transformation, $F(1,20) = 4.29$, $p = .05$, $SEM = .43\%$. Both of these interactions reflect the fact, apparent in Figure 4, that the effects are stronger in the left hemisphere. However, note that while the left hemisphere reflects both effects, there is only an effect of transformation and not an effect of substitution in the right hemisphere.

The fact that there was no effect of hand or of delay confirms the predictions about this region. The BOLD response in this region seems to reflect changes to the

problem representation and not the duration that this representation must be held. Once the solution has been obtained it is not affected by downstream factors like delay or response hand. We also had predicted that this region would show a larger effect of transformation than substitution. Comparing Figure 4A and B, one sees that at peak transformation has a larger effect than substitution, but the substitution effect maintains itself longer, resulting in an equivalent difference in area between the substitution and no-substitution curves in Figure 4A and between the transformation and no-transformation curves in Figure 4B. A test looking at the differences in the heights of the two curves between scans 5 and 10, where they peak, does find the difference between transformation and no transformation significantly greater than the difference between substitution and no substitution, $t(21) = 2.54$, $p < .01$.

The Prefrontal Regions

Figure 5A shows the results for the left prefrontal region, collapsing over delay. Our prediction was that this region would show no rise in the condition of no

Figure 5. The BOLD responses for the left prefrontal region: (A) each condition with its own baseline; (B) the no-transformation, no-substitution condition serving as the baseline.

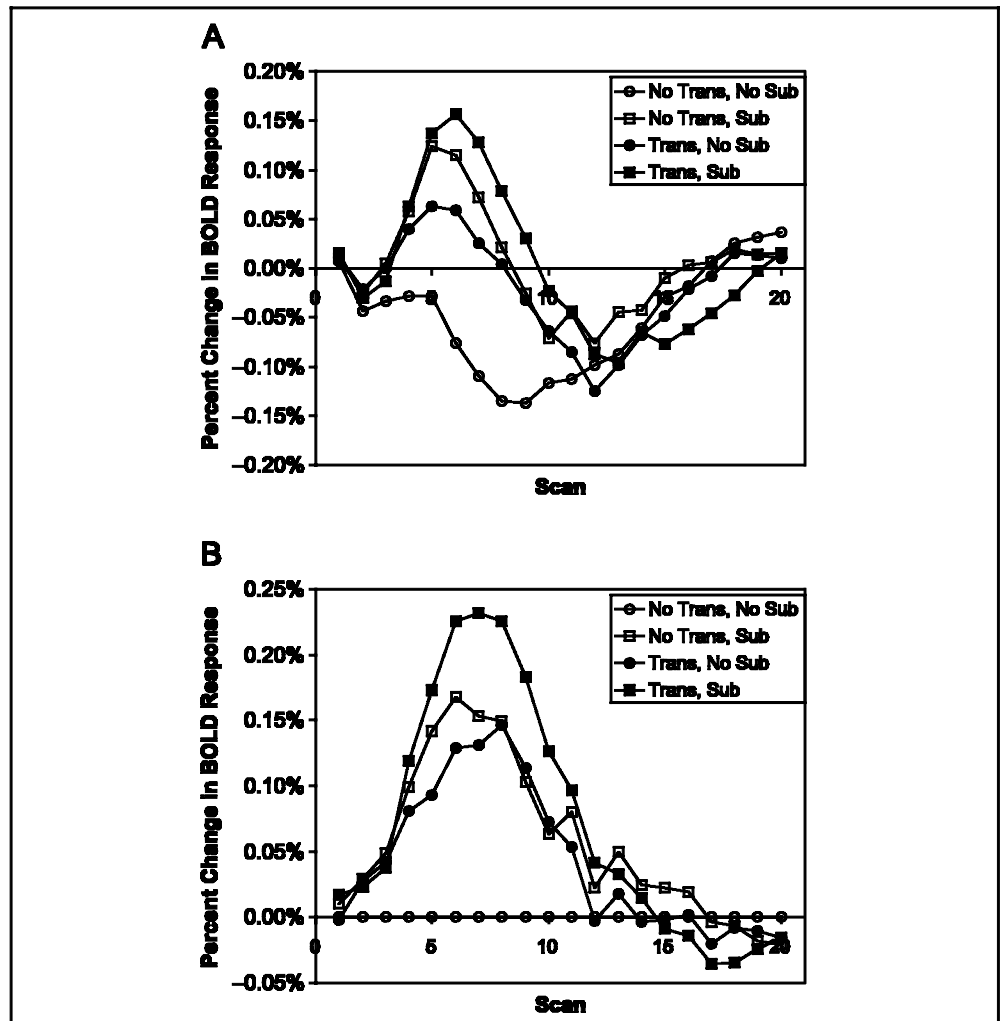
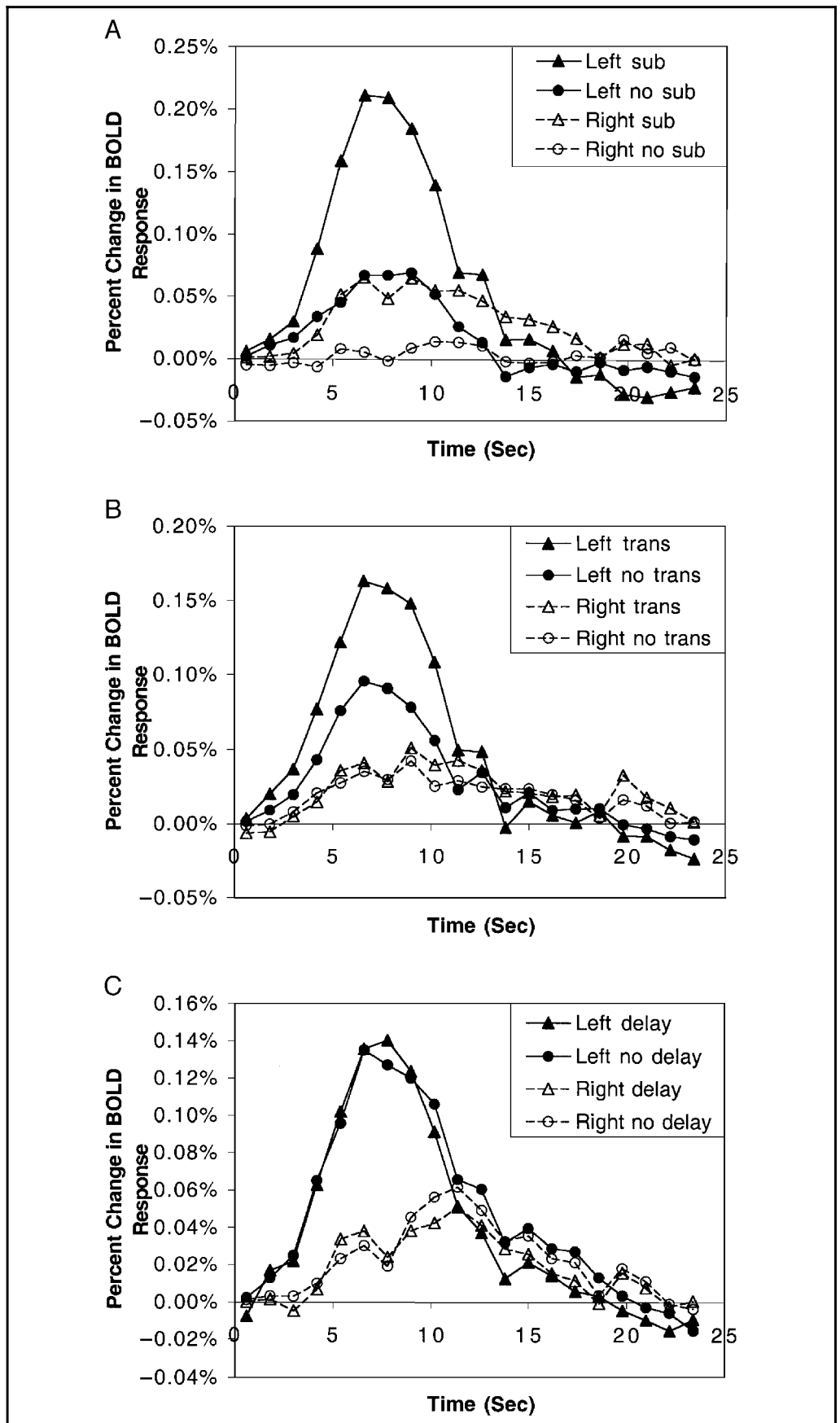


Figure 6. Effect of main factors on the BOLD response in the left and right prefrontal: (A) substitution; (B) transformation; (C) delay.



substitution and no transformation. It would seem that our predictions have been exceeded in that there is a dip in this condition that seems to begin after the other curves have peaked. The other curves also seem to dip at below baseline. Anderson et al. (2003) found some suggestion for negativity in the prefrontal response but nothing so strong as this. Actually, only half of the participants show this negative effect (5 left-responding and 6 right-responding). For purposes of model fitting we have chosen to adopt the no-substitution, no-transformation condition as reflecting baseline (zero) and to plot differences from this. This is the way Figure 5b plots the data and it shows that there are systematic differences among the other conditions relative to this baseline. Subsequent analyses will work with transformed BOLD responses as in Figure 5b. We think the negativity in Figure 5a reflects some other process that occurs after the offset of the trial and view Figure 5b as reflecting the real process of interest. The statistical tests reported below have identical results for the transformed and pretransformed data. The purpose of the transformation was to extract the critical component for later model fitting.

Figure 6 displays the main effects of each factor using the recalculated BOLD responses for the left and right prefrontal regions. Again, we performed an analysis of the degree to which the curve defined by Scans 3–19 rose above the baseline or the area under the curve. There was no difference between left and right responding participants, $F(1,20) = 1.08$, $SEM = 10.17\%$, or between delay and no delay, $F(1,20) = 0.40$, $SEM = 3.48\%$. The left side responds more than the right and this is marginally significant, $F(1,20) = 3.53$, $p < .10$, $SEM = 2.88\%$. The effect of substitution is significant,

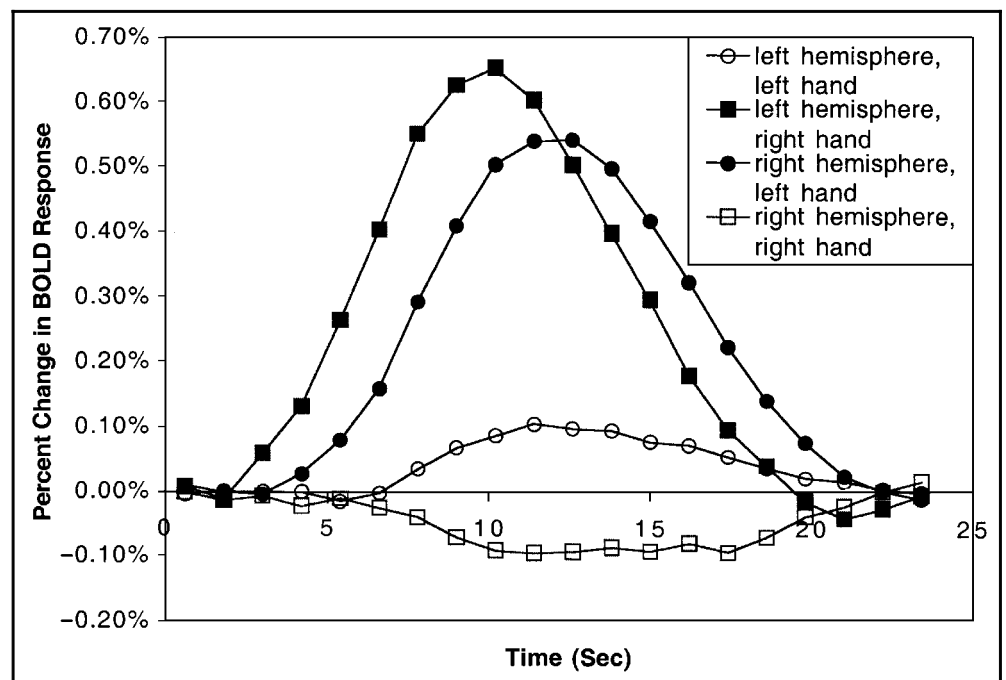
$F(1,20) = 8.98$, $p < .01$, $SEM = 3.20\%$, but not the effect of transformation, $F(1,20) = 1.35$, $SEM = 1.04\%$, as predicted. However, there is a significant region by transformation interaction, $F(1,20) = 6.09$, $p < .05$, $SEM = 0.36\%$, reflecting the fact that the left but not the right seems to respond to transformation. The interaction between region and substitution is marginally significant, $F(1,20) = 3.96$, $p < .1$, $SEM = 0.70\%$. These interactions may just reflect the greater sensitivity of the left prefrontal region to manipulations. There are no other significant interactions. The prediction of a greater effect of substitution than transformation seems confirmed. A contrast comparing the substitution, no-transformation condition with the transformation, no-substitution condition is significant, $t(21) = 2.29$, $p < .05$.

The Motor Regions

Figure 7 displays the average response of the left and right motor regions for the left and right responding participants. As would be expected, those participants who respond with their right hand show a large effect in the left motor cortex and those participants who respond with their left hand show a large effect in their right motor cortex. There is a suggestion of an interaction in the other hemisphere such that the BOLD response rises a little in the left hemisphere for participants responding with their left hands, while it drops a little in the right hemisphere for participants responding with their right hands.

The graphs to this point are stimulus-locked in that they begin with the onset of the stimulus. However, in the case of the motor regions it would be more infor-

Figure 7. Stimulus-locked BOLD responses in the left and right motor regions for participants responding with the left and right hands.



mative to do a response-locked analysis where time zero was set to be when participants emitted their response. Figure 8 shows the data plotted this way with 5 scans before the response scan and the 14 scans after. The baseline for these graphs are taken as the first three scans. The BOLD response is beginning to rise even on the scan before the response, indicating some preparatory motor behavior.

We performed an analysis of the degree to which the curve defined by scans -2 to 14 rose above the baseline defined by scans -5 to -3 . For purposes of analysis and display in Figure 8, we classified the left hemisphere for the right-responding participants as the major hemisphere and the right as the minor; this labeling was reversed for the left-responding participants. There was no difference between left and right-responding participants, $F(1,20) = .93$, $SEM = 29.24\%$, but there was large difference between the major and minor hemispheres, $F(1,20) = 101.46$, $p < .0001$, $SEM = 16.98\%$. There was also an interaction between response hand and hemisphere, $F(1,20) = 5.52$, $p < .05$, $SEM = 16.98\%$, reflecting the fact that the two minor hemispheres react oppositely as noted with respect to Figure 7. As predicted there is no significant effect of transformation, $F(1,20) = 1.77$, $SEM = 2.43\%$, or substitution, $F(1,20) = 0.14$, $SEM = 14.33\%$. There is, however, a strong effect of delay, $F(1,20) = 22.38$, $p < .0001$, $SEM = 3.99\%$, which was not predicted. There is also a significant interaction between delay and region, $F(1,20) = 99.22$, $p < .0001$, $SEM = 3.08\%$, which reflects that delay only has an effect on the major hemisphere. There are no other significant interactions.

Confirmatory Analyses: Summary

By way of summary, whereas the prefrontal and parietal responses are strongly left lateralized, there are weaker responses in the homologous right-hemisphere regions. As predicted the prefrontal region was more sensitive to substitution, reflecting its role as a retrieval region. The parietal region is more sensitive to transformation than substitution in its peak response, but not in its total area. Interestingly, in both cases the right hemisphere only responded to the hypothesized more important factor (transformation in the case of the parietal region and substitution in the case of the prefrontal region), while the left hemisphere responded to both, but more strongly to the more important factor. Both prefrontal and parietal regions respond to actual information-processing engagement and not just time, and so neither was sensitive to delay. Unexpectedly, the motor region did respond to delay, suggesting that people were rehearsing their motor responses over the delay. In addition, the fact that the motor region started to rise before the overt response indicates anticipatory motor preparation before the thumb press. We used this behavior of the motor region to tune our model for this task.

Fit of the ACT-R Model to the BOLD Responses

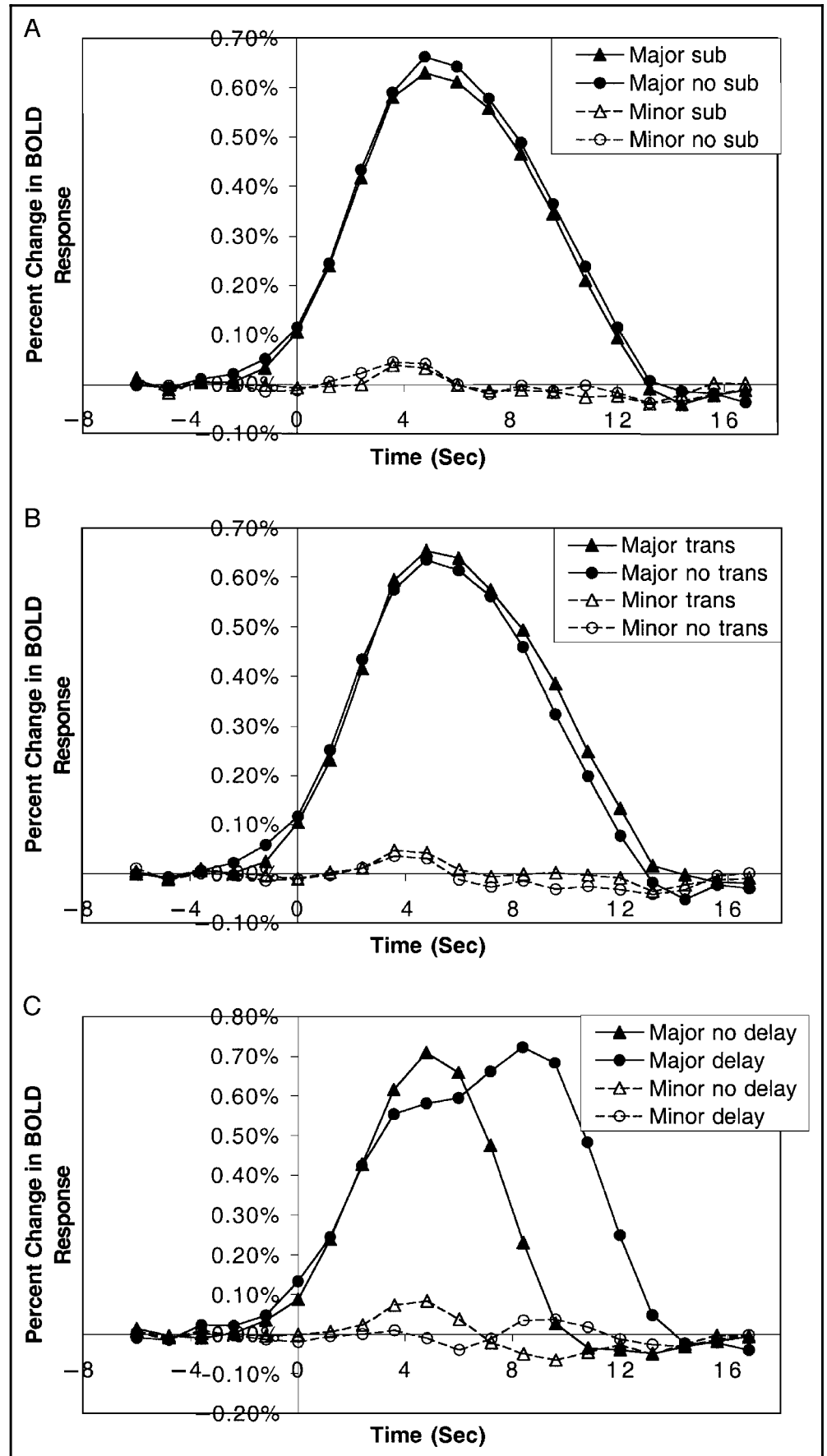
Figure 9 illustrates the behavior of the ACT-R model in the most complex condition of the experiment, which involves substitution, transformation, and delay. Initially, a representation of the string is built up in the imaginal buffer. Then the word command (AT) is encoded and its number representation is retrieved from declarative memory. This number, 14, is added to the imaginal representation and then the letters in the critical positions (in the example, D in first position and B in fourth position) are committed to temporary memory to guide the transformation of the string in declarative memory. Then the motor program for transmitting the string is encoded or rehearsed, a thumb key is pressed, the motor program is rehearsed during the delay, and then the four fingers pressed at the end of the delay. This differs from the ACT-R model we initially proposed before the imaging study, as that model did not include motor rehearsal before the thumb press or during the delay. Guided by the BOLD response in the motor region we assumed the four keys were being rehearsed before the thumb press and an average of five keys were rehearsed in the interval. The addition of these motor rehearsals is an example of how imaging can inform model development.

Besides these rehearsals two parameters were estimated for the model in advance of trying to fit the BOLD responses. The retrieval of the paired associate was estimated at .79 sec and the encoding and retrieval of the critical letters at .54 sec. These parameters were estimated to fit the behavioral data in Figure 3A. None of the other process times were estimated but all come from prior values in the ACT-R architecture. In particular, the imaginal transformations take .2 sec and each manual step (rehearsal or key press) takes .3 sec. The .3 sec for the manual step come from the well-established motor module in ACT-R (which is derived from Meyer & Kieras's 1997a, 1997b EPIC theory). The .2 sec for the imaginal transformations comes from a generalization of the parameters in ACT-R's visual module for encoding an object. This value was used in Anderson et al. (2003). With the processes in Figure 9 and their durations set, it is possible to predict BOLD responses for the three prespecified regions.

Predicting the BOLD Response

Anderson et al. (2003) proposed that whenever an activity takes place to change the content of one of the ACT-R buffers, there is an increased hemodynamic demand and it is this hemodynamic demand that drives the BOLD response in the corresponding cortical region. We developed a precise proposal for how the length of activity of a buffer mapped onto the predicted BOLD response in fMRI. A number of researchers (e.g., Cohen, 1997; Dale & Buckner, 1997; Boyton, Engel,

Figure 8. Effect of main factors on the BOLD response (response-locked) in the left and right motor regions: (A) substitution; (B) transformation; (C) delay.



Glover, & Heeger, 1996) have proposed that the BOLD response to an event varies according to the following function of time, t , since the event:

$$B(t) = t^a e^{-t}$$

where estimates of the exponent a have varied between 2 and 10. This is essentially a gamma function that will reach maximum a time units after the event. We proposed that while a buffer is active it is constantly producing a change that will result in a BOLD response according to the above function. The observed fMRI response is integrated over the time that the buffer is active. Therefore, the observed BOLD response will vary with time as

$$CB(t) = M \int_0^t i(x) B\left(\frac{t-x}{s}\right) dx$$

where M is the magnitude scale for response, s is the latency scale, and $i(x)$ is 1 if the buffer is occupied at time x and 0 otherwise. Note that because of the latency scale factor, the prediction is that the BOLD response will reach maximum at roughly $t = a \times s$ sec.

The peak of the BOLD function reflects roughly when the buffer was active but is offset because of the lag in the hemodynamic response. The height of the BOLD response reflects the duration of the event since the integration makes the height of the function approximately proportional to duration over short intervals. While this relationship is only approximate for the height of the function, the total area under the curve will be precisely proportional to the total time that the buffer is active. If a buffer is active for a total period of time T , the area under the BOLD response will be $M \times s \times \Gamma(a+1) \times T$ where Γ is the gamma function (in the case of integer a , note that $\Gamma(a+1) = a!$).

Thus, we can use the length of duration of the buffer activities in Figure 9 to generate exact predictions for the BOLD responses in each of the prespecified ROIs for each of the experimental conditions. In making these predictions we have to estimate three parameters that determine the exact shape of the BOLD response: the latency scale (s), the exponent (a), and the magnitude (M). These parameters are estimated to minimize the squared deviations between the observed and predicted BOLD functions. While these parameters determine the exact shape of the BOLD response, they do not change the prediction that the area under the BOLD function is proportional to the time the buffer is active. Thus, given a commitment to timing of activity in a buffer across conditions of the experiment, the model is committed to predictions about the relative areas under the BOLD functions for the different conditions in the corresponding brain region. As the timing is set to fit the behavioral data, predictions for the relative BOLD function areas become parameter-free predictions of the theory.

Some strong assumptions underlie the application of this methodology. One is that the BOLD response is

exactly described by a gamma function. Another is that the effect of repeated use of a buffer is additive. A third is that the only thing reflected in the activity of a particular region is the behavior of the assumed buffer. We will return to discussing issues involving each of these assumptions at the end of the article.

Note that this analysis does not reflect a frequent assumption in the literature (e.g., Just, Carpenter, & Varma, 1999) that a stronger BOLD signal reflects a higher rate of metabolic expenditure. Rather, the assumption is that it reflects a longer duration of increased metabolic expenditure. The two assumptions are relatively indistinguishable in the BOLD functions they produce, but the time assumption more naturally maps onto an information-processing model that assumes stages taking different durations of activity. Since these processes are going to take longer, they will generate higher BOLD functions without making any extra assumptions about different rates of metabolic expenditure.

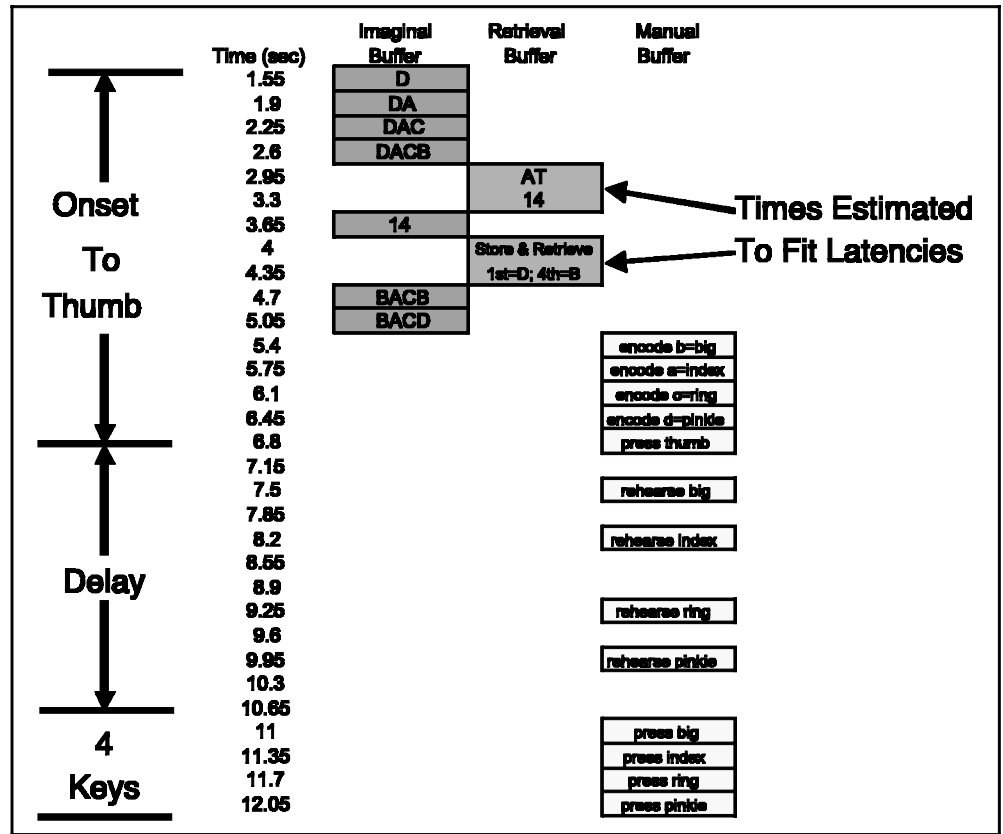
The mathematics in this analysis is basically the same as what underlies the frequent image-analysis technique of correlating the BOLD signal with the temporal profile created by convolving the trial structure with a hypothetical hemodynamic function. Among the differences/elaborations are the following:

1. The temporal structure generated by an ACT-R model (or any information-processing model) is more fine grained, generated from the internal operations of different components of the cognitive architecture.
2. Each condition has a natural baseline defined by the beginning of the trial before the BOLD response has begun to rise and the end of the trial after the BOLD response has come down; hence, there is no need to subtract out some neutral control condition.
3. There is the additional assumption that the magnitude of the response reflects the duration of activation of that component. Combined with point (2) the theory becomes subject to strong parametric tests.
4. There is an association of different regions of the brain with different components of the cognitive architecture.
5. One can estimate the parameters a and s of the BOLD function for a specific region rather than having to fit a single assumed BOLD function to all regions.

With this mapping of activity of information-processing components onto BOLD functions one can derive predictions from a cognitive model and test how well they fit the data. Table 2 summarizes the various fits, which we describe below.

Figure 10A illustrates the ability of the imaginal buffer to predict the behavior of the left posterior parietal region. The overall quality of fit is good, as indicated by a correlation of .990 and a chi-square of 90.59 with 157 degrees of freedom (160 observations minus 3 parameters).¹ Figure 10A collapses over delay because this did not have an effect on the behavior of this region, but

Figure 9. The approximate time line for the buffer activity in the ACT-R model.



the fit is calculated to the data before collapsing. The heights of the curves reflect the numbers of visual operations performed. In the case of no substitution or transformation, four operations are required to encode the letter string. An additional operation is required to encode the result of transforming the word when substitution is required and two additional operations are required to transform the equation in the case of transformation. As predicted the transformation, no-substitution curve is higher than the no-transformation, substitution condition.

Figure 10B illustrates the ability of the retrieval buffer to predict the behavior of the left prefrontal region. As noted earlier, we have made the no-substitution, no-transformation the baseline and so we are only predicting the other conditions. Again, because there is no effect of delay Figure 10B averaged over that factor. The overall fit is reasonable as indicated by a correlation of .939 and a chi-square of 68.21 with 117 degrees of freedom (120 observations minus 3 parameters). The model successfully predicts that the substitution, no-transformation condition will be higher than the no-substitution, transformation condition. However, there is a suggestion of a deviation in the data. Specifically, the model is underpredicting the height of these two curves (substitution, no transformation and no substitution, transformation) and overpredicting the height of the substitution, transformation curve. Thus, even though the behavioral data (Figure 3A) display additivity, the

BOLD responses may not. The actual deviation from additivity is only marginally significant, $t(21) = 1.86, p < .10$, in a test of whether the area under the substitution, no-transformation curve and the area under the no-substitution, transformation curve add to the area under the substitution, transformation curve.

Figure 10C illustrates the ability of the manual buffer to predict the behavior of the major motor region—left motor cortex for right-responding participants and right motor cortex for left-responding participants. This analysis is response-locked and Figure 10C collapses over

Table 2. Summary of Fits to Various Brain Regions

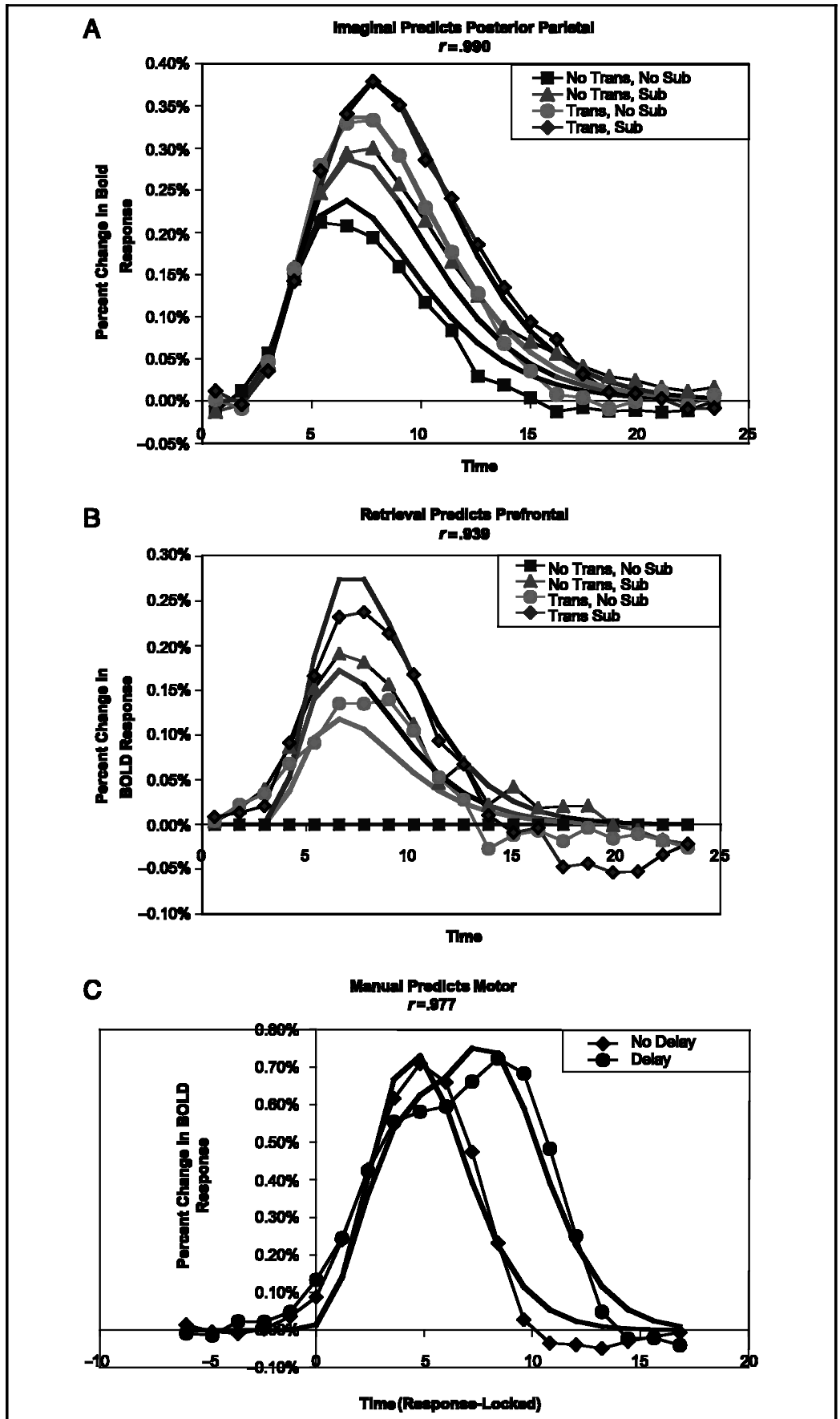
	<i>Parietal</i>	<i>Prefrontal</i>	<i>Motor</i>
Scale (sec)	1.837	1.554	0.862
Exponent (<i>a</i>)	2.412	2.217	5.160
Magnitude*: $M \Gamma(a+1)$	2.219	1.319	1.502
Chi-square**	90.60	68.22	328.42
Correlation***	.986	.913	.971

*This is a more meaningful measure since the height of the function is determined by the exponent as well as *M*.

**157 degrees of freedom except for the prefrontal, which has 117 since the no-transformation, no-substitution condition was defined as the zero baseline.

***Correlation with all 160 observations (rather than with the collapsed data in Figure 10).

Figure 10. Predicted and observed BOLD functions: (A) posterior parietal ROI, (B) prefrontal ROI, and (C) motor ROI. Solid lines are the predictions of the ACT-R model.



the factors of substitution and transformation, which did not have significant effects. It assumes that there are nine events in the manual buffer in the no-delay condition (four encoding/rehearsals of key presses and five finger presses), while there are five additional rehearsal events in the delay condition. As noted earlier, the assumption of motor rehearsal was not part of our original model but was suggested by the data. While the overall fit of the model is good as indicated by the correlation ($r = .977$) the chi-square measure (328.42 with 157 degrees of freedom) indicates that there are significant points of discrepancy. Looking at the curves, it can be seen where these are. First, the model does not rise above zero as quickly as the data. This is particularly apparent on the scan on which the response is emitted—the participants' BOLD response has risen .10%, while the model is still almost at zero. On the other end, the empirical BOLD response goes down more rapidly and slightly undershoots zero, where the model predicts a more gradual approach to zero. These deviations suggest that use of the gamma function to model the shape of the BOLD response may not be exactly correct.

This is the only BOLD function whose form reveals something of the timing of the buffer actions—in particular, in the delay condition. The initial planning of the motor response produces the initial rise (and is the reason why in the model there is some rise even on the response scan). The rehearsal over the 4 sec maintains the height of the BOLD function. The final execution of the response produces the second rise before the function goes back down to zero.

DISCUSSION

The basic premise in this research is that we can map the duration of various components of an architecture like ACT-R onto the BOLD response obtained in various regions. The relative success in this article supports this premise. However, it is worth noting some assumptions on which this effort depends and any signs that these assumptions might have been somewhat stressed in this modeling application.

1. It depends on the assumption that the BOLD response reflects just the duration a component is occupied and not the intensity of occupation. This uniform-intensity assumption seemed to have worked appropriately in most cases.

2. It also depends on the assumption that the BOLD response is additive across multiple events. Again this has proven to be a relatively successful assumption but there was a suggestion that the BOLD response to substitution-plus-transformation in the prefrontal ROI was less than the sum of the responses to substitution and transformation individually. While some people have found that the BOLD response is additive (e.g.,

Dale & Buckner, 1997; Boyton et al., 1996), others have not (e.g., Glover, 1999).

3. A third assumption is that the BOLD response in a particular area reflects, at least for the current task, only a single postulated cognitive function. As a general assertion this seems an improbable assumption, but it might be true in specific tasks. The place where we seemed to have the most problem with this assumption in the current task is in the prefrontal ROI where there seemed a postresponse negativity overlaid on the stimulus-locked positive response to retrieval demands. In this case, we had a neutral condition to serve as a baseline that we could subtract from the other BOLD responses. As a methodological point, it might be worthwhile to try to maintain a condition that deletes all the cognitive processes but retains simple stimulus and motor components. Such control conditions are typical of fMRI designs and this experience suggests that the current approach has not eliminated the utility of such a baseline.

4. The approach depends on the assumption that the gamma function correctly characterizes the BOLD response. We are able to parameterize the gamma function differently for different regions to accommodate regional differences. However, this approach still assumes it is exactly a gamma function everywhere. On the other hand, there was evidence for deviations from the assumed form in certain regions, such as a small negativity at the end of the function. Others (e.g., Glover, 1999) have reported a small negative component to the BOLD response and proposed modeling the BOLD response as the difference of two gamma functions. This would greatly complicate the modeling, but it is an approach that might be necessary.

This methodology should be judged not as absolutely correct or wrong but rather as more or less fruitful. We think it has proven relatively fruitful. However, one needs to remain mindful of the potential pitfalls in using the methodology.

Given that the methodology was relatively successful, this article does illustrate the interaction that is possible between cognitive modeling and neuroimaging. Past research provided a priori hypotheses about the function of specific brain regions interpreted in ACT-R information-processing terms. The results of this study have been to largely confirm these assumptions, but not without consequence for the modeling enterprise. In particular, the behavior of the motor region (surely the most obvious of our associations) told us that covert motor rehearsal was occurring. This led us to incorporate such rehearsal into our information-processing model. With that elaborated model in hand we could go back and better understand the behavior of different brain regions.

Finally, we would like to reiterate and elaborate the major assumption behind the prediction of the BOLD response in the ACT-R model. We assume that the

magnitude of the BOLD response reflects the duration of time to change the representations in the buffers. We do not assume that it reflects the duration of time that these representations reside in the buffers. At least with respect to the retrieval buffer (prefrontal) and the imaginal buffer (parietal) our assumptions seem supported. It might seem strange that there is no metabolic cost associated with maintaining information and, actually, our model fitting does not require this assumption. We are fitting rise of the BOLD response from base line. If we assume that these regions have some asymptotic activation levels to maintain information then we would expect to see no rise from baseline just with maintenance; that is a constant activity. What we see is the extra effort associated with the changing of the information being represented. Thus, the key assumption is that transitions in information representation require special effort and it is this effort that our BOLD measure taps (change from baseline).

METHODS

Task and Procedure

The trial structure is illustrated in Figure 2. A trial began with a prompt, which was an asterisk. After 1.2 sec, a four-letter string was presented above a two-digit number or a two-letter word. Participants were instructed to extract the instruction represented by that number or word and apply it to transforming the string. Participants were instructed to solve the problem mentally and press the thumb key when they were ready to key in the final solution, upon which the problem in the first rectangle disappeared. The thumb press provided a measure of the planning time. If the plan time exceeded 10.8 sec, the trial was scored as incorrect. After the thumb press, they either had to enter the answer or wait 4 sec. If there was a delay, the word “DELAY” appeared in the rectangle for the response and participants could only begin responding when the word disappeared. Once they began entering their answer, they had no more than 1.0 sec to press a key for each of four symbols in the answer. This rapid responding was designed to prevent participants from postponing transformations until they gave their response. The letters A, B, C, and D were mapped to their index, big, ring, and little fingers in the response glove. After the participants typed the answer, the correct answer appeared for 1.6 sec. Then the screen was blank for the remaining portion of the 24-sec trial.

Prescan Practice

On the day before the scan day, there was a prescan session in which participants memorized 12 pairs of word-to-number correspondences (participants practiced until they could produce three consecutive trials without any errors), practiced finger-to-key mappings, and practiced actual problem solving. There were just two blocks (16 trials per block) of practice at the actual

problem solving. This was just enough to familiarize participants with the procedure before going into the scanner.

Parametric Design

Four binary factors were manipulated. First, half of the participants responded with their right hands and half responded with their left hands. The other factors were varied within participants. Half of the trials involved a 4 sec delay and half did not. Half of the trials presented two-letter words and half presented two-digit numbers as instructions. Half of the trials required a transformation of the letter string and half did not. These factors were totally crossed to create 16 conditions. The various within-participant conditions occurred in random order. Participants were tested in 6.5-min blocks, in which two repetitions of each of the eight within-participant conditions were tested in random order for a sequence of 16 trials.

Event-Related fMRI Scan

Event-related fMRI data were collected by using a single-shot spiral acquisition on a GE 3T scanner, 1200 msec TR, 18 msec TE, 70° flip angle, 20 cm FOV, 21 axial slices per scan with 3.2-mm thickness, 64 × 64 matrix (3.125 × 3.125 mm per pixel), with the AC-PC on the second slice from the bottom. Images acquired were analyzed using the NIS (Neuroimaging Software) system (<http://kraepelin.wpic.pitt.edu/nis/index.html>). Images first were realigned using 12-parameter AIR (Woods, Grafton, Holmes, Cherry, & Mazziotta, 1998) and then cross-registered to a common reference brain by minimizing signal intensity difference after which functional images were set to a standard mean intensity, smoothed (6 mm FWHM 3-D Gaussian kernel) and pooled across participants to improve signal-to-noise ratio.

Participants

Participants were 22 right-handed, members of the Carnegie Mellon University community (9 women). Their ages ranged from 18 to 24 years, with an average of 21.1. Half of the participants responded with their right hands and half responded with their left hands.

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Reprint requests should be sent to John R. Anderson, Department of Psychology, Carnegie Mellon University, Pittsburgh, PA 15213, or via e-mail: ja@cmu.edu.

The data reported in this experiment have been deposited in the fMRI Data Center (<http://www.fmridc.org>). The accession number is 2-2003-114B4.

Note

1. In calculating these chi-squares, we divide the summed deviations by the variance of the means calculated from the condition by subject interaction.

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