Using model-based functional MRI to locate working memory updates and declarative memory retrievals in the fronto-parietal network

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Contributed by John R. Anderson, December 14, 2012 (sent for review August 24, 2012)

In this study, we used model-based functional MRI (fMRI) to locate two functions of the fronto-parietal network: declarative memory retrievals and updating of working memory. Because regions in the fronto-parietal network are by definition coherently active, locating functions within this network is difficult. To overcome this problem, we applied model-based fMRI, an analysis method that uses predictions of a computational model to inform the analysis. We applied model-based fMRI to five previously published datasets with associated computational cognitive models, and subsequently integrated the results in a meta-analysis. The meta-analysis showed that declarative memory retrievals correlated with activity in the inferior frontal gyrus and the anterior cingulate, whereas updating of working memory corresponded to activation in the inferior parietal lobule, as well as to activation around the inferior frontal gyrus and the anterior cingulate.

In this study, we used model-based functional MRI (fMRI) to locate two functions of the so-called "fronto-parietal network." The fronto-parietal network consists of brain areas that are coherently active and assumed to implement cognitive control functions: working memory, attentional selection, and error monitoring (1–5). It typically involves at least the dorsolateral prefrontal cortex, the anterior cingulate, and a region around the intraparietal sulcus. Because the regions in the fronto-parietal network are by definition active at the same time, distinguishing the precise functional characteristics of those regions is difficult with conventional fMRI methods. Model-based fMRI is particularly well suited for dissociating between highly correlated contributions to the blood oxygen level-dependent (BOLD) signal. We used model-based fMRI to locate two functions within the fronto-parietal network: declarative memory retrieval and updating of working memory. These functions are often assumed to be part of the fronto-parietal network, but the hypothesized locations within the network differ among studies (2, 6–11).

Model-based fMRI is a relatively recent approach to analyzing fMRI data. Instead of using the condition structure of the experiment to inform the analysis, as in a conventional fMRI analysis, model-based fMRI uses information derived from a computational model (12, 13). For example, Daw et al. (14) fitted a mathematical reinforcement learning model to the behavior of their study participants and then used parameter values of the model as regressors in the fMRI analysis. This resulted in brain regions that correlated significantly with those parameter values, and thus with certain features of their model. Another recent study showed that model-based fMRI can be used successfully in combination with more high-level information-processing models (15). By regressing the activity of model components (e.g., visual processing, declarative memory retrieval) against neural activity, the neural correlates of the model components can be located.

To identify the neural correlates of declarative memory retrievals and working memory updates, we applied model-based fMRI to five previously published studies. These studies all consist of an fMRI experiment and an associated computational cognitive model in the Adaptive Character of Thought–Rational (ACT-R) cognitive architecture (16). This has two advantages: (*i*) Because the tasks ranged from paired-associate learning to multitasking, we can be reasonably sure that the located regions are task-independent, and (*ii*) because the models were all developed in the same framework, the results of the different model-based analyses reflect the same underlying constructs. Thus, the results can be combined in a meta-analysis, removing idiosyncrasies of the tasks and models.

The ACT-R architecture consists of a set of independent modules that interact through a central production system. For instance, the visual and aural modules process perceptual input, and the manual module is used to interact with the world. ACT-R has a number of central cognitive modules for processing information, two of which are of particular interest for this work:

- Declarative memory is used to store facts. Facts have a certain activation level, which determines how easily and how quickly they can be retrieved. The more frequent and the more recent a fact has been used, the easier and faster it is to use it again (16).
- The problem state module (sometimes referred to as the imaginal module) is used to maintain intermediate representations necessary for performing a task. Its function is similar to the focus of attention in current working memory theories (17), and it can hold only one coherent chunk of information (18). We use the problem state module to locate working memory updates.

The goal of the present work was to identify the neural correlates of these modules—model components—with model-based fMRI. We analyzed five different components: retrieval of declarative facts, working memory updates, visual perception, aural perception, and right-manual actions. Although we are interested mainly in declarative memory and working memory, the perception and action components serve as a proof of concept.

The ACT-R modules have been mapped onto brain regions before (see ref. 19 for a concise introduction); however, these mappings were done a priori, based on the literature on regional functions, and might not be optimal. The current research does not use these a priori mappings, but instead applies model-based fMRI to evaluate in a data-driven way whether the existing mapping is correct. Thus, the current analysis differs from most previous work that has connected ACT-R to fMRI, although we do use a previously developed method to generate BOLD predictions from ACT-R models (19).

Results

We identified the neural correlates of the model components with model-based fMRI through the following steps: (*i*) record the activity of the model components over the course of the experiments, (The experiments that we reanalyzed are described in *SI Materials and Methods*.) (*ii*) convolve this activity with a

Author contributions: J.P.B. and J.R.A. designed research; J.P.B. performed research; J.P.B. analyzed data; and J.P.B. and J.R.A. wrote the paper.

The authors declare no conflict of interest.

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This article contains supporting information online at www.pnas.org/lookup/suppl/doi:10.1073/pnas.1221572110/-/DCSupplemental.

hemodynamic response function (HRF), and (*iii*) regress the resulting signal against the measured BOLD response. To record the activity of model components, we used the models published in the original articles. (The model presented in (20) was updated to reflect recent findings that the problem state module can only maintain a single chunk of information at a time (18). The updated model can be downloaded from www.jelmerborst.nl/models. A discussion of the effects of the updated model compared with the old model is provided in *SI Materials and Methods*.)

For each individual participant, we ran a model using the same trials as the participant underwent.(Three of the five models are deterministic, whereas the other two models incorporate noise on memory retrievals. However, because the noise is relatively small compared with the effects of lining up key presses between model and data, and because the convolution with the HRF blurs the effects further, we ran the models only once.) For these trials, ACT-R predicts the onset and duration of model component activity. For instance, a paired-associate task will start with encoding a stimulus on the screen, followed by a declarative retrieval. ACT-R predicts how long the encoding persists, and depending on that, when the retrieval starts and how long it takes (the duration of memory retrievals is dependent on the activation of facts in memory; see ref. 16 for a detailed explanation and rationale). Because model activity is regressed directly against the preprocessed BOLD data, correct time mapping between model and data is important (12). To ensure that we were not comparing, for example, response activity in the model with fixation activity in the data, we lined up the start and the response of each trial between model and data with a linear transformation (see ref. 15 for details of this procedure). We then convolved the activity of the model components with an HRF to enable direct comparison with the BOLD response. Note that ACT-R predicts the onset and duration of model component activity, but does not distinguish amplitude between different model components or different actions of a single component. This means that the amplitude of the regressors depends solely on the duration and frequency of model component activity.

Fig. 1 shows an example of model activity over two trials in one of the studies that we reanalyzed, the paired associates study (6). The top graph shows declarative memory retrievals, and the bottom graph updates to the problem state. The two trials represent different conditions in the experiment, which result in different patterns of predicted BOLD activity. It is clear that updating the problem state and declarative memory retrievals are closely related and thus provide highly correlated predictions (especially considering that only the shape of the predictions, and not the amplitude, is of importance for the regression analysis). This is a typical pattern seen in ACT-R models. On the one hand, information that is retrieved from declarative memory is often stored in the problem state module for further processing. On the other hand,

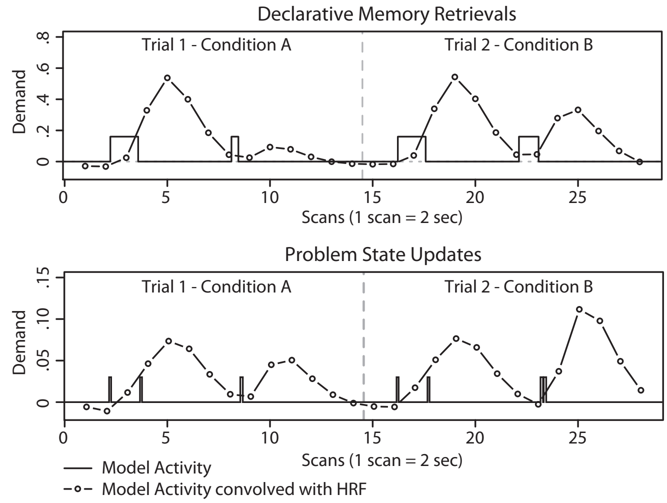

Fig. 1. Example of predicted model activity over two trials of the experiment of Anderson et al.(6).

information stored in the problem state module (e.g., from perception) is often used to initiate declarative retrievals (but see, e.g., ref. 20 for a study that manipulated these functions independently). The strong correlation between these two functions is probably the reason why they both typically activate large parts of the fronto-parietal network.

Table 1 shows the correlations among predicted activities of the model components in the five studies. In general, the predictions correlated moderately within the studies, possibly making it difficult to identify different regions for the different model components. The relatively high correlations are largely caused by the convolution with the HRF; even though model components show different raw activation patterns, the convolution makes the predicted BOLD responses very similar (Fig. 1). Over all studies, the highest correlation was between problem state activity and declarative memory activity. This is in accordance with the assumption that both components are part of the fronto-parietal network, which is by definition coherently active. Although some correlations are high, there was sufficient variation across these experiments to suggest the possibility of separating these functions.

Manual Results for All Five Studies. To illustrate our analysis, Fig. 2 presents results of the model-based fMRI analyses of the manual component in the five studies. Regions that correlate significantly with the predicted manual activity are shown [$P < 0.05$, uncorrected (see *Materials and Methods* for a discussion of significance thresholds)]. All studies show a significant region in

Table 1. Correlations between predicted activity of the model components in the five studies

Model components	Paired associates	Visual and aural fan	Algebra	Information processing	Multitasking	Average
Declarative memory–problem state	0.50	0.88	0.89	0.91	0.78	0.79
Declarative memory–visual	−0.32	0.50	0.83	0.52	0.41	0.39
Declarative memory–manual	−0.30	0.79	0.63	0.83	0.39	0.47
Declarative memory–aural	—	0.54	—	0.60	—	0.57
Problem state–visual	0.12	0.58	0.99	0.49	0.46	0.53
Problem state–manual	0.43	0.88	0.85	0.87	0.39	0.68
Problem state–aural	—	0.60	—	0.77	0.13	0.50
Visual–manual	0.68	0.46	0.91	0.44	0.93	0.68
Visual–aural	—	−0.28	—	0.41	0.29	0.14
Manual–aural	—	0.50	—	0.67	0.28	0.48

Correlations were calculated over the entire experiments, at time points at which at least one of the two model components predicted nonzero activity. The multitasking study does not a have an aural–declarative memory correlation, because these functions were not analyzed on the same trials (24).

the left motor cortex ($z = +52$), which overlaps in four of the five studies with the previously identified ACT-R region (indicated by the left white square in Fig. 2) (19). All studies also show additional significant correlations throughout the brain. This is not unexpected, given that other functions may correlate with motor processing, given the task demands of specific experiments. Although these other areas sometimes correlate more significantly than the motor areas (e.g., the visual cortex in the multitasking study), the meta-analysis should pull out areas that correlate consistently over the five studies.

Meta-Analysis. Fig. 3 shows the results of the meta-analyses, and Table 2 characterizes the identified clusters. The statistical maps were thresholded based on the results of the manual model component. We decreased the minimum P value and increased the minimal cluster size until we found a single cluster for the manual component. This cluster was located in the left motor cortex, which should correspond to right manual actions, indicating that the analysis can give reasonable results. We used the same thresholds for the other model components as well.

The aural component correlated significantly with an area around the superior temporal gyrus, which is known to be involved in speech processing (21). Visual processing of the models revealed the strongest effects in the left and right middle occipital gyri, extending into the inferior parietal lobules. These areas are typically involved in visual spatial attention (22). Manual processing of the model correlated with the BOLD response in the precentral gyrus, as expected, and extended into the postcentral gyrus and the inferior parietal lobule.

Both problem state updates and declarative memory retrievals correlated significantly with areas of the fronto-parietal network. Problem state updates were reflected by the inferior parietal lobule, a prefrontal region around the inferior frontal gyrus, and the anterior cingulate, whereas memory retrievals correlated significantly with activity around the inferior frontal gyrus and the anterior cingulate. The prefrontal region for both functions extended from the insula, via the inferior and middle frontal gyri, to the premotor cortex.

To further dissociate between those functions, we investigated the voxels in which the problem state regressor explained significantly more variance than the declarative memory regressor, and vice versa. (For this analysis, we first normalized the regressors to a mean of 0 and an SD of 1; otherwise, the amplitude of the regressors would have influenced the analysis.) Fig. 4 shows the results of these analyses within the regions that were identified with the standard meta-analysis (compare Fig. 3). Table 3 provides details of the located clusters. In Fig. 4, orange areas indicate regions in which the declarative memory regressor explained more variance than the problem state regressor, and blue areas indicate the opposite.

Taken together, our analyses show that the parietal regions respond exclusively to problem state updates. The anterior cingulate reflects a mix of problem state updates and memory retrieval activity, but responds more strongly to working memory updates. The prefrontal region is mixed as well. The area around the inferior frontal gyrus corresponding to memory retrievals is larger than the area contributing to problem state updates, and in part of this area the declarative memory regressor explains significantly more variance than the problem state regressor ($z = +16$). However, most of the area seems to reflect problem state activity in addition to retrieval activity.

Discussion

Although the predicted activation traces of the model components were highly correlated, they turned out to be sufficiently different to identify separate regions for the different model components. The results of the aural, visual, and manual components were consistent with the literature on those functions, suggesting that the model-based fMRI analysis is able to identify neural correlates corresponding to the model components. Both the problem state and declarative memory components correlated significantly with multiple regions of the frontoparietal network. These analyses suggest that working memory updates are reflected by activity in a large area around the intraparietal sulcus

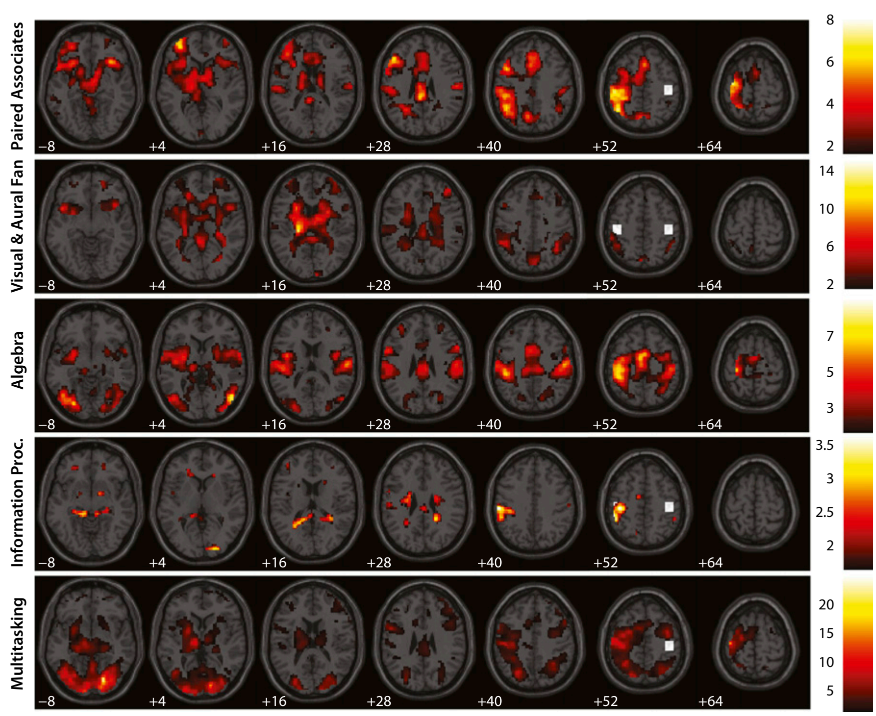

Fig. 2. Results of the model-based fMRI analysis of the manual module for the five studies. Statistical maps were thresholded at $P < 0.05$, uncorrected. White squares indicate previously defined ACT-R regions.

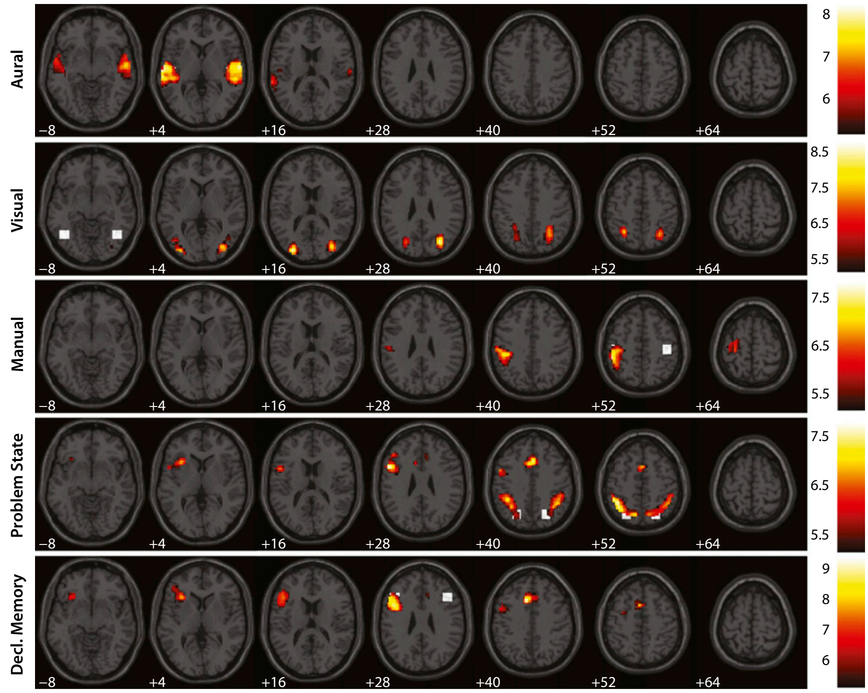

Fig. 3. Results of the meta-analyses. Statistical maps were thresholded at $P < 1 \times 10^{-7}$ (uncorrected) and at least 250 contiguous voxels. White squares indicate previously defined ACT-R regions.

in both hemispheres. In addition, working memory updates correlated with the anterior cingulate and with the left inferior frontal gyrus. Declarative memory retrievals showed a strong correlation with activity in a large area around the inferior frontal gyrus, and with the anterior cingulate. Although part of the prefrontal region is a better indicator of declarative memory retrievals than of working memory updates, most of the region seems to respond to both functions.

Fronto-Parietal Network. The fronto-parietal network is assumed to implement cognitive control, through working memory, attentional selection, and error monitoring (2–5). The current model-based analysis of five very different tasks, ranging from paired-associate learning to multitasking, suggests that the fronto-parietal network is indeed involved in working memory updates and declarative memory retrievals. Nonetheless, there is a region of the intraparietal sulcus that exclusively reflects working memory updates and a region of the left prefrontal cortex that exclusively reflects retrieval. Using these two "exclusive" regions would enable maximal dissociation of the two cognitive functions.

The parietal region of the fronto-parietal network was previously linked to "start-cue" activity, instantiating information

Table 2. Results of the meta-analysis, per connected cluster

Region	BAs	Coordinates *x, y, z*	Maximum *z*-value	Average *z*-value	Size in voxels
Aural					
Right superior temporal gyrus	21, 22, 38, 41, 42	60, −13, −2	8.22	6.48	844
Left superior temporal gyrus	13, 21, 22, 41, 42	−63, −19, 1	8.28	6.45	799
Visual					
Right middle occipital gyrus	7, 19, 39	30, −73, 25	8.69	6.48	709
Left middle occipital gyrus	7, 19	−30, −88, 13	8.82	6.36	516
Manual					
Left postcentral gyrus, inferior parietal lobe, precentral gyrus	2, 3, 4, 6, 40	−48, −28, 49	7.86	6.10	760
Problem state updates					
Left inferior parietal lobule, superior parietal lobule	7, 40	−36, −55, 49	7.60	6.11	623
Right inferior parietal lobule, superior parietal lobule	7, 40	42, −52, 43	7.44	6.02	511
Left inferior frontal gyrus, insula, middle frontal gyrus, precentral gyrus	6, 9, 13, 44	−54, 11, 31	7.82	6.01	510
Left/right anterior cingulate cortex	32	3, 20, 40	7.53	6.12	273
Declarative memory retrieval					
Left inferior frontal gyrus, middle frontal gyrus, insula, precentral gyrus	6, 9, 13, 45, 46, 47	−30, 23, −2	9.20	6.64	832
Left/right anterior cingulate cortex, medial frontal gyrus	6, 8, 32	−6, 20, 43	9.45	6.59	283

Coordinates indicate the maximum voxel in the cluster. All areas that exceed the significance threshold are listed; Brodmann area (BA) numbers are given for BAs in which at least 15 voxels lie within the significant area.

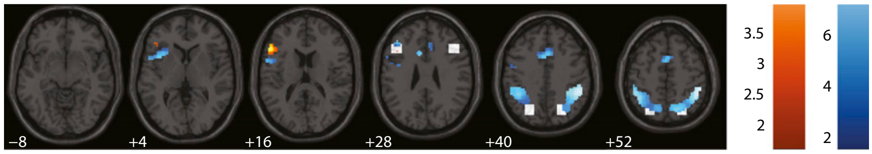

Fig. 4. Results of the additional dissociation analysis. Orange-red areas indicate where the declarative memory regressor explained more variance than the problem state regressor; blue areas indicate the opposite. The results were thresholded at $P < 0.05$, uncorrected.

for the current task (3, 23). Although this is subtly different from updating working memory, it seems to be closely related. In addition, the inferior parietal lobule and the intraparietal sulcus have been repeatedly implicated in working memory research (6–11, 24, 25). The function of the prefrontal region in the fronto-parietal network is less clear; whereas Dosenbach et al. (3, 23) reported start-cue, sustained task activation, and error-related activity in this region, our present data suggest that it is involved in memory retrievals as well as updating of working memory. This is consistent with the literature on memory, which reports activity in this prefrontal region in response to episodic memory retrievals (26–29), working memory activity (11, 30), or both (31–33).

In addition to the parietal and prefrontal regions, both memory retrievals and working memory updating were also significantly correlated with activity in the anterior cingulate cortex (ACC). The ACC, part of the fronto-parietal network, is reportedly involved in task preparation (2) and task onset, sustained activity during a task, and error activity (23). In the general literature, the ACC is often hypothesized to be a conflict monitoring system (34), whereas the ACT-R theory assumes that it maintains control states that guide behavior during a task (16). Our present results imply that the ACC is closely involved in controlling memory retrievals and working memory updating. This seems to be broadly consistent with previous accounts; task onset and control state activity often lead to updates of working memory (sometimes by retrieving information), and errors and conflict trials should typically lead to better-controlled memory retrievals. However, it might be interesting to include conflict monitoring and control state regressors in future model-based analyses, to determine the precise function of the ACC in the fronto-parietal network.

Model-Based fMRI. Our present results were obtained with model-based fMRI. Instead of using demand functions that are either on or off during complete trials, as in conventional fMRI analyses, model-based fMRI uses predictions from computational models to create more detailed demand functions. In ACT-R models, these demand functions reflect when and how often a certain model component is used over the course of the experiment. Although convolution with the HRF smoothed out much of the detail of the predictions, the differences were still large enough to result in different regions for the model components. The combination of computational models with model-based fMRI is a potentially powerful approach to locating brain functions. Computational models provide detailed characterization of what occurs during an experiment, and using model-based fMRI allows for identification of the simulated functions.

The disadvantage of model-based fMRI is that it depends on the correctness of the models. If the assumptions underlying a model are incorrect, then the results will either not reach significance or indicate an incorrect region. By using a meta-analysis of five different studies, we made sure that our results were consistent over five very different tasks.

Comparison with Previously Identified ACT-R Regions. The modules of the ACT-R architecture were previously mapped onto brain regions, based on a reading of the literature (16, 19). This previous mapping is indicated by white squares in Fig. 3. The areas identified in the present study are located in the same location as the original mappings, except for the visual module. The visual module was previously assumed to correspond to activity in the fusiform gyrus, but actually seems to respond better to activity in the middle occipital gyrus, at least for the five tasks that we analyzed. The middle occipital gyrus is typically involved in visual-spatial attention (22, 35). Given that the visual regressor that we used corresponds to attending objects, this seems to be a sensible match.

Our present results can serve as the basis for more precise regions-of-interest (ROIs) that indicate the activity of model components. These ROIs can then be used to validate new ACT-R models, by comparing predictions of model components in the new models to activity in the ROIs, as has been done with the previous mapping (19). This will provide an additional method of validating cognitive models, along with response times and accuracy.

Materials and Methods

Meta-Analysis. fMRI preprocessing is discussed in *SI Materials and Methods*. To combine the results of the five studies, we used Stouffer's z-transform (36, 37),

$$Z_{meta} = \sum_{i=1}^{k} \frac{\Phi^{-1}(1 - P_i)}{\sqrt{k}},$$

where P_i is the resulting P value of study i, k is the number of studies, and Φ^{-1} is the inverse normal distribution function.

Table 3. Results of the additional dissociation analysis per connected cluster

Region	BA	Coordinates *x, y, z*	Maximum *z*-value	Average *z*-value	Size in voxels
Problem state updates > declarative memory retrievals					
Left inferior parietal lobule, superior parietal lobule	7, 40	−51, −37, 49	5.62	3.40	509
Right inferior parietal lobule, superior parietal lobule	7, 40	48, −40, 52	7.26	4.74	511
Left inferior frontal gyrus, insula	13, 44	−39, 11, 1	4.78	2.78	207
Left/right anterior cingulate cortex	32	−6, 14, 31	4.71	3.02	206
Left middle frontal gyrus	—	−42, 32, 34	5.05	3.17	25
Declarative memory retrievals > problem state updates					
Left inferior frontal gyrus, middle frontal gyrus	45	−51, 26, 13	4.00	2.55	111

Coordinates indicate the maximum voxel in the cluster. All areas that exceed the significance threshold are listed; Brodmann area (BA) numbers are given for BAs in which at least 15 voxels lie within the significant area.

Significance Thresholds. One issue in our analyses was the selection of proper significance thresholds. Fig. 2 illustrates the analysis, which led to an uncorrected $P < 0.05$ threshold, clearly showing how the results differed among studies. Given that the raw *t*-values were used for the meta-analysis, this threshold did not influence the final results.

The meta-analysis (Fig. 3) resulted in large numbers of highly significant voxels. Because we were interested in finding regions that correlated most closely with our model components (because they are most likely to implement the functions of the model components), we needed to set a high threshold. Because we know ground truth for the right-manual component (the left motor cortex), we used this component to calibrate our threshold. We increased the threshold until we were left with a single cluster (uncorrected $P < 1 \times 10^{-7}$ and at least 250 contiguous voxels). This cluster indeed included the left motor cortex, and the threshold also resulted in reasonable regions for the other components.

One might wonder what happens when this threshold is increased or decreased. If we increase the threshold, we end up with the most significant areas shown in Fig. 3. These are the main areas that we reported, indicating that these results are robust. If we lower the threshold, we find the following additional regions. For the manual component, we find evidence for involvement of the middle cingulate gyrus and visual regions. For the aural component, we see two very small regions in the cerebellum. For the visual component, we start to see activity in the middle and inferior frontal gyri, and activity throughout the brain when we lower the threshold further. Finally, for the problem state and declarative memory components, we find the whole fronto-parietal network at a lower threshold. We believe that at least a number of these regions are spurious. For example, the visual regions that one gets for the manual component are based on two of the studies (algebra and multitasking), and reflect the high correlation between the visual and manual regressors in those studies (Table 1). Calibrating the results based on the manual component seems to deal with these spurious areas and results in a set of reasonable regions. Especially considering that we are interested in finding the best-fitting regions—which are most likely to implement the model functions—we believe that the method is successful.

For the additional dissociation analysis (Fig. 4), we used $P < 0.05$ (uncorrected) as the threshold, with the added requirement that we only searched within the previously identified regions from the standard meta-analysis. Because we are looking within previously identified regions, and because we use this analysis to detail the main analysis, we believe that such a relatively low threshold is warranted.

ACKNOWLEDGMENTS. We thank Jon M. Fincham, Yulin Qin, Myeong-Ho Sohn, and Andrea Stocco for their help with locating and interpreting the old datasets. This research was supported by National Institute of Mental Health Grant MH068243.

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Supporting Information

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SI Materials and Methods

Studies. We used model-based functional MRI (fMRI) to identify the neural correlates of model components in the five studies described herein. We analyzed declarative memory retrievals, problem state updates, manual (right hand) actions, and visual perception in all of the studies. We also evaluated aural perception in the fan, information-processing, and multitasking studies.

Paired associates. In the first study, experiment 2 of Anderson et al. (1), participants had to learn and recall paired associates. Both retrieval difficulty and problem state requirements were manipulated. Retrieval difficulty was manipulated by varying the time between studying a paired associate and having to recall it, with a longer delay between study and recall leading to longer retrieval times. Problem state requirements were manipulated by varying how the paired associates were presented. In one condition, the paired associates were simply shown in the study phase (e.g., "band–2"). In the test phase, 'band' was presented, and participants had to respond "2." In the other condition, participants had to generate the paired associates themselves. In the study phase, "b–nd–id = adhesive strip" was presented. In the recall phase, participants were presented with "band." They had to respond with the position of the letter they had provided at study (i.e., "2"). In the Adaptive Character of Thought–Rational (ACT-R) model, the second condition involved more updates to the problem state.

Visual and aural fan. The second study, experiment 2 of Sohn et al. (2), was a fan experiment in which participants had to learn paired associates with different fan. Here "fan" refers to the number of facts to which items are associated in memory. The higher the fan, the longer it takes to retrieve an item from memory (see ref. 3 for for a review of the fan effect). In the study phase of the experiment, participants studied items with a fan of 1, 2, or 3. In the test phase, they had to judge whether presented items were among the studied items or not, which takes longer for higher fan items. In addition, items could be presented either visually or aurally; thus, this experiment manipulated retrieval duration and modality of input. Problem state requirements were assumed to be the same in all conditions; the problem state module was used to represent the presented items before a retrieval was initiated.

Algebra. Stocco and Anderson (4) investigated the neural correlates of algebraic problem solving. Their study participants were asked to solve an equation such as $8 \times x - 2 = 36 - 6$ in three steps: eliminate the addend on the left side of the equation ($8 \times x = 32$), unwind the unknown ($x = 4$), and provide the correct result. Two factors were manipulated in the experiment: whether equations contained numbers or parameters ($a \times x - a = a \times b - a$), and whether the equations were updated internally or externally. In the external condition, the results of each intermediate step were presented on the screen. In the internal condition, the initial equation was shown on the screen until the participant gave the final response. Thus, in the internal condition, the participant was required to maintain intermediate solutions in working memory, leading to the prediction of greater problem state activity than in the external condition. With respect to declarative memory retrievals, it was assumed that in the numeric condition, number facts were retrieved, whereas in the parametric condition this was not the case.

Information processing. The fourth study was a relatively complex information-processing task that was designed to elicit differential activity in eight ACT-R modules (5). Before the experiment in the scanner, the participant was asked to memorize associations between two-letter words and two-digit numbers, such as "AT–23." In the scanner, the participant was presented with three names, for example, "Tom–Dick–Fred." These names were followed by an instruction in the form of either a two-letter word or a two-digit number. If a word was presented, the participant had to recall the associated number. The number (either presented or recalled) indicated which names should be switched. For example, if the number was "23," the participant was to respond "Tom–Fred–Dick." Instructions could also be "impossible," such as "14." Because there is no fourth name, in this case the participant was to repeat the names in the order in which they were presented. In addition to these manipulations, the names could be presented either visually or aurally, whereas responses had to be given either with the right hand or by speaking the names.

In this task, declarative memory retrievals were manipulated by presenting numbers vs. two-letter words, because in the latter case the associated numbers had to be retrieved from memory. Problem state requirements depended on whether a transformation had to be made to the names, with a transformation leading to more problem state activity.

Multitasking. Our final study was multitask in which participants had to continuously switch between solving 10-column subtraction problems and entering 10-letter words (6). The subtraction task and the text-entry task both had two conditions: a hard condition that required maintaining a problem state from one response to the next and an easy condition that did not. For the subtraction task, this was implemented as carrying between columns (hard) or not (easy): "64–36" vs. "64–32." In the easy condition of the text-entry task, the participant had to enter letters that were presented one-by-one on the screen (see "A," type "A," solve subtraction column; see "B," type "B," etc.), whereas in the hard condition they had to enter 10-letter words without feedback (see "INFORMATION" at the start of a trial, type "I," solve a subtraction column, type "N," etc.). The participant could not see what he or she had entered in either condition. Because participants had to switch between the subtraction and text-entry tasks after every letter and number, they had to maintain whether a carry was in progress and what the to-be-entered word was while performing the other task. As a third task, participants also had to listen to short stories in half of the trials, and answer questions about these stories.

The hard conditions of the subtraction and text-entry tasks required more problem state updates than the easy conditions. In addition, when both tasks were hard, the problem state was swapped out via declarative memory, because only a single chunk of information can be maintained in the problem state module at a time. Thus, when both tasks were hard, problem-state activity was even higher. Declarative memory retrievals increased with the difficulty of the subtraction task, given that more difficult subtraction problems require more and more difficult retrievals (e.g., "64–32" requires retrieving "4–2 and "6–3," whereas "64–36" requires retrieving, for instance, "4–6," "14–6," and "5–3"). In addition, when both tasks were hard, the contents of the problem state were swapped out via declarative memory, further increasing the number of retrievals (see ref. 7 for details of the model). This study was analyzed previously with model-based fMRI (8).

fMRI Preprocessing. All fMRI data were analyzed using SPM8 (Wellcome Trust Centre for Neuroimaging). This included realigning the functional images, coregistering them with the structural images, normalizing the images to Montreal Neurological Institute space, and smoothing them with an 8-mm FWHM Gaussian kernel. For each study, we entered the predicted demand functions of the model components into a general linear model. [Except for the multitasking study, for which the model components were entered into separate generalized linear models, as was done in the original analysis of that dataset. Given the experimental setup of the multitasking study, the analysis could not otherwise distinguish between the aural and declarative memory components (see ref. 6 for details).] Note that each model component was added as a separate regressor into SPM8. This means that they were not orthogonalized, and thus that they explain only their own unique variance. In addition, motion parameters from the realignment step were used as regressors. For each model component and each voxel, we then obtained a *t*-value, indicating whether the model component explained significant variance in that voxel. We transformed these *t*-maps to maps containing the corresponding *P* values, which were used for the meta-analysis.

Updated Model for Information Processing. We updated our previous model (5) to reflect recent findings that the problem state module can maintain only a single chunk of information at a time (7). In addition, we removed motor rehearsals during a delay in the task, because they did not seem to be warranted by the data. One might wonder how these changes influenced the results of the model-based analysis. The results of the old model were comparable to those of the updated model for the aural, visual, retrieval, and problem state components. This is because the same experimental factors still influence the same model components, even though the precise time course differs between the two models. Convolution with the slow HRF means that the final regressors—and the results—were very similar. The manual component of the old model shows activation in the motor cortex as well as throughout the fronto-parietal network, unlike the updated model. However, our meta-analysis would have ensured that this extra activation would not have reached the final results, given that it was not present for the other studies. Thus, although the updated model might be theoretically better, it did not influence our final results.

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