SPATIAL LOCATION OF RESPONSE KEY SELECTS THE NEURAL SYSTEM FOR VISUAL RECOGNITION

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ABSTRACT OF THE THESIS

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Dual system hypothesis suggests that there are two distinct memory systems, the instrumental system and the habit system. Our experiment is trying to demonstrate whether the dual system hypothesis is correct and under what circumstance we use each system. We used a same-different matching task. An observer had to respond rapidly whether a test consonant had just appeared in the study string by pressing one of two response keys, labeled *same* and *different*. When the *same* response was assigned to the right response key, there was no effect of study-string position on target RT, indicating that test item was not compared with the study string. When the *different* response was assigned to the right response key, *same* RT was an increasing function of the left-to-right position of a target in the study string and *different* RT was slower than *same* RT, indicating that during test the study string was serially generated and compared with the test item. fMRI confirmed that caudate and CA1 of hippocampus (habit system) were active when *different* was assigned to the right location and CA3 of hippocampus (instrumental system) was active when *different* was assigned to the left location.

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1. Introduction

Over the past two decades, it has become increasingly evident from animal and human studies that the mammalian brain contains two integrated but distinct systems of learning and memory (Packard, 1999; Packard & McGaugh, 1992; Packard & Teather, 1997; Yin & Knowlton, 2006). The *instrumental system* within the medial temporal region surrounding and including the hippocampus, receives input from the visual system. It also organizes the visual input both spatially into maps and other spatial patterns, and temporally into more or less recently seen visual targets. For the latter function, the instrumental system generates a holistic perception of recency to a repeated visual pattern, or a holistic perception of novelty to a visual pattern that shares few features with previously encoded patterns. On the contrary, the *habit system* within the basal ganglia region surrounding and including the caudate nucleus of the striatum originally evolved to encode and serially generate sequences of actions (Knowlton, Mangels, & Squire, 1996; Packard & McGaugh, 1996). In addition, it serially generates the local features of a previously studied visual pattern in response to a cue (Sinha & Glass, 2017). As mentioned below, evidence for the distinct roles that the two systems play in human cognition has been collected for five kinds of tasks: navigation, sequence learning, visual recognition, prediction, and language comprehension.

Navigation. Studies of human navigation have found that when exploring a new area (wayfinding) the instrumental system constructs a mental map of the area that includes spatial (or global) relations among non-adjacent local features but when traversing a familiar area to a goal (route following) the habit system retrieves a sequence of actions that generate the route, defined by sequence of left or right turns in response to local features, to the goal (Baumann Chan, & Mattingley, 2010; Brown, Ross, Tobyne, &

Stern, 2012; Doeller, King, & Burgess, 2008; Hirshhorn et al., 2012; Konishi et al., 2013; Marchette, Bakker, & Shelton, 2011; Wegman, Tyborowska, & Janzen, 2014; Woolley et al., 2013).

Sequence Learning. The study of sequence learning has revealed that the habit system constructs and generates a sequence of actions to locations in space through the encoding of a sequence of target – response – effect contingencies by the habit system (Ziessler and Nattkemper, 2001). Spatial memory is the engine that organizes target – response – effect contingencies into sequences and drives the learning of a sequence of actions to both visual and non-visual targets (Deroost & Soetens, 2006), including auditory targets (Hartman, Knopman, & Nissen, 1989; Hoffmann, Sebald, & Stöcker, 2001). If an initially randomly generated sequence of targets is repeated, each time the sequence repeats reaction time to respond to each target decreases. However, when the repeated sequence is longer than nine members and /or a participant is distracted by performing another task at the same time, there is little or no recognition or recall of the sequence. The participant has no awareness that they have been responding to a repeated sequence nor any ability to recognize the sequence (Nissen & Bullemer, 1987).

Sequence learning is not impaired in patients with amnesia from hippocampal damage (Nissen & Bullemer, 1987; Nissen, Willingham, & Hartman, 1989; Reber & Squire, 1998). The robustness with respect to hippocampal damage along with the lack of declarative memory together indicate that sequence learning is not produced by the instrumental system.

Sequence learning is impaired in patients with moderate Parkinson's disease (Deroost, Kerckhofs, Coene, Wijnants, & Soetens, 2006; Vandenbossche, et al., 2013), and in patients with Huntington's disease (Knopman & Nissen, 1991), which are both the

result of damage to the basal ganglia. Hence, sequence learning is produced by the habit system.

Visual Recognition. The instrumental system and the habit system provide alternative mechanisms for recognizing individual targets when there is little or no delay between the initial presentation of a study string and subsequent presentation of a test item. The instrumental system makes a recognition judgment on the basis of its perceived recency or novelty, which is generated by the perirhinal cortex (Suzuki & Naya, 2014). The habit system makes a recognition judgment by retrieving the study string from memory, one item at a time, from left to right, when the test item is presented (Checkosky & Baboorian, 1972).

Therefore, both habit and instrumental systems contribute to sequential *same* - *different* judgments for successively presented strings. Sinha and Glass (2017) showed that paradoxical response times (RT) for *same – different* judgments were caused by the distinct, complementary contributions of the habit system and the instrumental system to visual recognition. Participants had to respond as rapidly as possible whether successively presented 4-consonant strings were the *same* or *different*. *Different* RT was an increasing function of the first left-to-right position at which there was a difference between the study string and the test string, indicating serial, left-to-right generation of the study string by the habit system, which terminated when a mismatch between the just-generated study-string consonant and the consonant in the same position of the test string was found. However, *same* RT was faster than *different* RT, indicating that the instrumental system generated a same response on the basis of the *perceived* recency of the entire test string without comparing it to the study string (Bamber, 1969; Proctor & Healy, 1987). Supporting this interpretation, Sinha and Glass (2017) found that *different*

responses were associated with fMRI activation of the caudate and hippocampus and *same* responses were associated with activation of just the hippocampus.

Prediction. A sequence encoded by the habit system may influence conscious decisions about the future by detecting and correcting errors (Seger & Cincotta, 2005). In the prediction task, it often requires a participant to make a prediction of what would occur next. The experimental paradigm always involves a visual cue, a predictive motor response, and a visual outcome, which are collectively sufficient to activate the caudate (Poldrack, Prabhakaran, Seger, & Gabrieli, 1999), indicating habit system involvement. More specifically, consistent with Packard and McGaugh's (1996) seminal animal finding, Poldrack et al. (2001) found that in humans there was initial medial temporal activation at the beginning of the task that was soon replaced by caudate activation. Damage to the basal ganglia as indicated by Huntington's disease (Knowlton, Squire, Paulsen, Swerdlow, & Swenson, 1996) or Parkinson's disease (Shohamy et al., 2004) impaired performance on the human prediction task.

One advantage of the dual-system is that it is robust because often only one system is necessary to perform a task. Myers (2003) found that both individuals with only damage to the caudate (the habit system) and individuals with only damage to the medial temporal area (the instrumental system) still learned the cue – outcome contingencies in the prediction task, though by different strategies consistent with their preserved abilities. Foerde, Knowlton, and Poldrack (2006) found that performing a secondary task in which subjects had to count high tones in an auditory sequence while performing the prediction task reduced declarative knowledge of what they had seen in the task, indicating interference with the instrumental system. However, the accuracy of task performance was unimpaired, indicating a fully functioning habit system.

Language Comprehension. Ullman (2004) reviewed the evidence that during the language comprehension, semantic comprehension of words is associated with medial temporal activation, indicating instrumental system involvement. He also reviewed the evidence that syntactic integration of the words into sequences that form meaningful sentences is associated with basal ganglia activation, indicating habit system involvement.

Overview. Taken together, these results suggest that the dual-system provides humans with two distinct ways of retrieving knowledge of the world; as a target-response-effect sequence of contingent events by the habit system versus the recency or novelty of targets by the instrumental system.

The role of the habit system supported by this review of its known effects is different from an older view in which the habit system was associated solely with procedural learning and implicit effects on performance (Cohen, Poldrack, & Eichenbaum, 1997; Squire, & Zola, 1996). This new view converges with the older view in attributing procedural learning and implicit effects on performance to the habit system. However, it differs from the older view in attributing the recall and the recognition of patterns, both examples of declarative memory, to the computational contributions of both the habit system and the instrumental system.

The initial purpose of this study was to determine how details of a specific recognition task determined which response, *same* or *different*, was controlled by the instrumental system and which was controlled by the habit system. To this end, predictions about the speed with which *same* and *different* decisions were derived from the dual-system model for different versions of a *same – different* task. The dual-system model predicted that in the study string – test string comparison task (Sinha & Glass, 2017) *different* responses were controlled by the habit system and *same* responses were

controlled by the instrumental system. Experiment 1 was a study string – test consonant task for which the dual-system model predicted that both *same* and *different* responses would be controlled by the habit system. However, on the basis of the results of Experiment 1, the purpose of the study broadened to also consider how response assignment, whether the right response key was assigned the *same* or *different* response, determined which response, *same* or *different*, was controlled by the instrumental system and which was controlled by the habit system. In the fourth experiment, predictions about the active brain areas associated with *same* and *different* decisions were derived from the model and tested by fMRI during the visual recognition task.

2. General Experimental Method

The four experiments described below shared a common methodology.

2.1. Materials

There were 360 pairs of study strings test consonants. The study string consisted of four upper-case consonants and the test consonant was upper case. For 180 pairs the consonant was in the study string (hence, a target) and for 180 pairs the consonant was not in the study string (hence, a foil). Targets appeared equally often (45 trials) in each of the four positions of the study string. Except for these constraints, the strings and test consonants were selected through random selection from the pool of consonants without replacement until the pool was empty, at which point it was refilled.

2.2. Procedure

The experiment was programmed in MATLAB and presented on a laptop computer.

As shown in Figure 1, each trial began with a fixation asterisk in the center of the screen for 0.5 seconds. The asterisk was replaced by a study string above the fixation

point for 2 seconds, followed by a blank interval for 0.5 seconds. Finally, the test consonant was shown below the fixation point for 3 seconds. Subjects responded whether or not the test consonant appeared in the study string by pressing one of two keys as rapidly as possible without an error. RT was measured from the onset of the test consonant. The interval between the onset of successive trials was 6 seconds.

Each participant performed at least 15 practice trials before the experiment. A participant had to have a mean RT of less than 800 ms and percent correct higher than 75% in order to move to the experiment. The participant repeated the practice block until performance reached the criteria, which was usually after one, and always after no more than three blocks of practice.

The 360 trials were divided into twelve 30-trial blocks. Between each block, participants could take a break with no time constraint and press the spacebar themselves to continue. There was also a mandatory one-minute break automatically timed by the computer after the subjects finished every 2 blocks.

The entire task lasted about 40 minutes, not including the practice blocks.

In Experiments 1 – 3 response assignment was a between – subject factor. The participants were randomly divided into two equal groups of subjects. One group of subjects pressed the F key with left hand for *same* responses and J key with *right* hand for *different* responses. The other group pressed the J key with right hand for *same* responses and the F key with left hand for *different* responses. In Experiment 4 response assignment was a within – subject factor.

3. Experiment 1

3.1. Predictions

Sinha and Glass (2017) found that when a 4-consonant study string was immediately repeated as the test string the system generated a perceptual recency effect and a rapid *same* response was made. So the instrumental system generated a recency response when an entire visual study item was repeated. This result leaves open the question of whether the instrumental system would generate a recency response when only a single consonant of the study string was the test item.

If recency responses are not generated by the instrumental system for single-letter targets then in order to determine whether the test consonant was in the study string it would be necessary for the habit system to serially generate the study string from left to right when the test item was presented so that each consonant of the study string could be compared in turn with the test consonant. The generation and comparison process would terminate with a *same* response when the generated study consonant matched the test consonant. Otherwise, a *different* response would be made if none of the four comparisons produced a match. So RT would be an increasing function of the serial position of the target in the study string for *same* responses and *different* responses to foils would be about as slow as *same* responses to targets that appeared in the fourth and final position of the study string. Notice that these predicted results are almost the exact opposite of the results found by Sinha and Glass (2017), in which it was *different* RT that was an increasing function of the serial position of the foil in the study string. So, if the predictions derived for Experiment 1 were confirmed, together with the results of Sinha and Glass (2017) they would strongly confirm details of the model by demonstrating that precise, task-specific predictions of the dual-system model could be verified.

Notice that in deriving the predicted RT pattern, it was assumed that when the test item is presented, the habit system generates the previously presented study string one consonant at a time. This is a different hypothesis from the hypothesis that when the test item is presented, the test item is serially compared to each of the study consonants. The hypothesis that serial generation of the study string, not serial comparison of the test item, produces the relationship between serial position and RT has been confirmed (Checkosky & Baboorian, 1972). Holyoak, Glass, and Mah (1976) found the same result for a sentence comparison task.

Alternatively, if recency responses were generated by the instrumental system for single-letter targets then in order to determine whether the test consonant was in the study string it would only be necessary for the instrumental system to assess whether it was recent. *Same* responses would be made to test items that were perceived as recent and *different* responses would be made to test items perceived as novel without reference to the study string. If this were the case, then neither target RT nor foil RT would be a linear function of the position of the test item in the study string.

Notice that even if both the instrumental and habit systems influenced the final motor response there would be no way to ascertain this from the accuracy results of a task that emphasized accuracy. It is only when RT is the dependent measure that different predictions can be derived from the different computational processes implied by the two systems.

As reviewed above, the RT results of previous studies indicate that both systems may influence the response to a test item on the same trial. However, an oversight in the previous studies (Bamber, 1969; Proctor & Healy, 1987; Sinha & Glass, 2017) is the failure to analyze the results as a function of response assignment. Therefore, these

analyses leave open the possibility that on some trials the instrumental system controlled the response, on other trials the habit system controlled the response, and the system that controlled the response was determined by the assignment of the *same* and *different* responses to the two response keys.

Studies of split-brain patients begun by Gazzaniga, Bogen, and Sperry (1959) established that the left and right hemisphere were specialized for a variety tasks so that each hemisphere would perform the same task differently. However, intact individuals do not exhibit response conflict between the hemispheres nor between the instrumental and habit systems. One way of avoiding conflict is for the prefrontal cortex to determine whether the instrumental or habit system controls the response before the task begins. There is already considerable evidence that the ventrolateral prefrontal cortex exerts control over the processing of an immediate visual recognition task (Blumenfeld & Raganath, 2007). It is suggested here that the control begins before the study string is presented. One cue that might influence the roles of the systems could be the assignment of the *same* and *different* responses to the left and right response keys. This hypothesis was tested through the assignment of the *same* and *different* responses to each key for half the participants and the inclusion of this factor in the analysis.

As shown in Experiment 1, the study string (e.g. FBHG) was followed by a test consonant (F would be a target and C would be a foil). Half the participants responded *same* with the right key (and *different* with the left key). The other half of the participants responded *different* with the right key (and *same* with the left key).

3.2. Method

As described in the General Method, on each trial, a fixation point appeared in the center of the screen for 0.5 sec, the study string appeared above the location of the

fixation point for 2 sec, a blank field appeared for 0.5 sec, and a single test consonant was shown right below the location of the fixation point for 3 sec.

There were 24 subjects (16 females, 8 males; age rage, 19-35 years) from undergraduate psychology classes offered at Rutgers, including 22 right-handed subjects and 2 left-handed subjects based on their self-report.

3.3 Results and Discussion

We excluded 7% of the observations, including 5% incorrect responses and 2% responses with reaction time outside three standard deviations in the analyses of the RT data. Overall, the participants scored 95% (SD = 3.45) correct, with an average reaction time of about 654 milliseconds (SD = 222). Percent accuracy for each condition is shown in Table 1.

The RT results, shown in Figure 2, were analyzed in a 2 x 5 mixed ANOVA. The two independent variables were (1) the between-subject factor: response-assignment (whether the *same* or *different* response was assigned to the right key), and (2) the within-subject factor: match-location (whether the test consonant appeared in the 1st, 2nd, 3rd, or 4th position of the study string, eliciting a *same* response or did not appear in the study string, eliciting a *different* response).

As is obvious from a comparison of the left and right panels of Figure 2, there was a significant interaction between response-assignment and match-location, $F(4,88) = 10.1$, $p < 0.001$, partial eta squared = 0.315. The right panel shows the results when the *different* response was assigned to the right key. *Same* RT was an increasing function of the target in the study string, indicating serial generation of each consonant of the study string by the habit system prior to its comparison with the test consonant. There were

significant differences among the four positions, $F(3,33) = 29.1$, $p < 0.001$, partial eta squared = 0.726.

However, *different* RT was faster than *same* responses to targets in the fourth position of the study string, when the serial generation and comparison model predicts that *different* responses should only be made after the test consonant is found to be different from the consonant in the fourth position of the study string, so should be no faster than these responses. However, the faster than predicted *different* responses are explained by evidence of speed – accuracy trade off in the task: more errors for the condition producing faster responses.

That *different* RT is faster than *same* RT when the test consonant is in the fourth position of the study string is explained by early termination of the generation of the study string before the fourth study consonant was produced, causing both faster responses and more error, resulting in the speed – accuracy trade-off. As shown in Table 1, the decline in correct *same* responses from 97% for position 3 to 87% for position 4 implies that when the first three study consonants did not match the test consonant, the fourth study consonant was generated by the habit system only three-quarters of the time. One quarter of the time the participant responded *different* without having access to the final study consonant so without knowledge whether it differed from the test consonant. Consequently, 6% of the *different* RTs are guesses after the third study consonant had been generated rather than responses after the fourth consonant had been generated. While 6% is a modest number of guesses, they would have a disproportionate effect on RT if they replaced what would have been the longest *different* RTs when all four study consonants were generated.

The left panel of Figure 2 shows the results when the *same* response was assigned to the right key. There was no significant difference among the four positions, $F(3,33) = 0.97$, $p = 0.42$, partial eta squared = 0.081. Neither *same* RT nor *different* RT was a function of serial position of the test consonant in the study string, ruling out serial generation by the habit system. Rather, the results are consistent with the generation of recency and novelty values for the test items by the visual system and the use of these values to sort the test items into targets and foils by the instrumental system.

The pattern of RT results could not have been more strikingly different if they had been performed by split-brain patients for which a single, surgically isolated hemisphere controlled every response. However, the participants were normal college students and the contrasting results shown in the two panels of Figure 2 are for the same task performed on the same materials. The only difference was the assignment of the *different* response or *same* response to the right hand.

Ultimately, the different patterns of RT results are caused by the different ways the two functional systems perform the *same – different* task. The habit system serial generates the study string and detects differences between the study consonants and the test consonant. So the habit system treats the task as difference – detection task. In the contrast, the instrumental system detects whether the test consonant is accompanied by a recency response indicating that it has just been presented. So the instrumental system treats the task as a repetition – detection task.

Suppose that the hemisphere that has primary responsibility for understanding language, the left hemisphere, interprets the task instructions and organizes the functional response of the brain to carry them out. So the left prefrontal cortex determines which system has control of the response on the basis of the verbal label presented on the side of

body on which the left hemisphere focusses: the one assigned to the right side. Then, when *different* is assigned to the right side, the task is categorized by the left hemisphere as a difference – detection task so the habit system is given control of the response. When *same* is assigned to the right side, the task is categorized by the left prefrontal cortex as a repetition – detection task so the instrumental system is given control of the response.

We understand that this is a novel explanation of a novel result. We shall see that the results of Experiments 3 – 4 both confirm it while ruling out alternative explanations of the effect of response assignment. To begin, notice that the assignment of the *different* response to the right key caused the serial processing of study items producing *same* responses. So the verbal label assigned to a key did not facilitate or inhibit the named response; rather, it elicited a particular functional system for generating a response. Also, Sinha and Glass (2017) performed a causal analysis of the whole – brain data. The analysis revealed a causal effect of the prefrontal cortex on the caudate.

Overall, the results confirm all of the predictions of the dual-system model, providing further evidence for it. Notice that the predictions of the model that have been confirmed were highly task-specific. When the dual-system model predicted that only *different* RT would be a function of serial position in the study string, Sinha and Glass (2017) found that only *different* RT was a function of serial position. When the dual-system model predicted that only *same* RT would be a function of serial position in the study string, the results of Experiment 1 were that only *same* RT was a function of serial position.

4. Experiment 2

4.1. Predictions

In Experiment 1 the test consonant was presented in the center of the visual field so there was no information about its position in the study string. In this case, there was serial, left-to-right, generation of each consonant of the study string and comparison with the test item until a match was found or the string was exhausted (Checkosky & Baboorian, 1972). Consequently, *same* RT was a linear function of serial position and was faster than *different* RT. *Different* responses were made only after most or all of the study string had been generated and a match with the test consonant had not been found.

Suppose that the test consonant was to be compared with only a single position of the study string. Would either the instrumental system or the habit system have direct access to that position, thus avoiding the need for left to right generation?

If direct access were possible then providing position information would eliminate the effect of position on RT for the habit system, revealing a heretofore hidden level of sophistication and complexity in the generation of the study string when the test item was presented.

If direct access were not possible, then a different effect on RT was predicted. In Experiment 1, the generation of the study string continued until a match between the generated consonant or test consonant was found and a *same* response was made, or the entire string was generated and a *different* response was made. Consequently, RT was an increasing function of left-to-right serial position for *same* responses and *different* responses were slower than *same* responses. When the test consonant is only compared with a single position of the study string it is only necessary to generate the study string up to the position of the test consonant and compare that one study consonant with the test consonant. A match would result in a *same* response and a mismatch would result in a *different* response. Therefore, both *same* and *different* RT would be linearly related to

the serial position of the test consonant. Testing this prediction was the purpose of Experiment 2. This result would be further confirmation of the dual-system model.

So, the purpose of Experiment 2 was to determine how position information influenced *same* or *different* RT for the task. In Experiment 2 the test consonant was presented in the exact location of one of the four consonants of the study string by embedding it in a test string in which the other three positions were filled by underscore, e.g. B_ _ _, _B_ _, _ _B_, or _ _ _B, and the test consonant was in the exact position of the study consonant to which it should be compared.

4.2. Method

Following the study string, a test string was presented that included the test consonant and 3 underscores, indicating which position of the study string the test consonant should be compared with. Subjects responded whether the test consonant was present in that position of the study string.

The participants were 16 subjects (9 female, 7 male; age range: 19 – 23 years) from undergraduate psychology classes offered at Rutgers University. They were all self – reported being right-handed.

4.3. Results and Discussion

Overall, participants scored 96% (SD = 3.74) for correctness, with an average reaction time of about 695 milliseconds (SD = 235.12). Accuracy for each condition is shown in Table 1.

The results, shown in Figure 3, were analyzed in a 2 x 4 x 2 mixed ANOVA. The three independent variables were (1) the between-subject factor: response-assignment, (2) the within-subject factor: test-position (1st position, 2nd position, 3rd position, or 4th position), and (3) the within-subject factor: response (*same* response, *different* response).

As is obvious from a comparison of the left and right panels of Figure 3, there was a significant two-way interaction between response-assignment and test-position, $F(3,66) = 7.3$, $p < 0.001$, partial eta squared = 0.248. There was also a three-way interaction between response-assignment, test-position, and response, $F(3,66) = 3.1$, $p = 0.032$, partial eta squared = 0.124.

The right panel shows the results for the eight participants who responded *different* with the right key. Both *same* RT and *different* RT were a function of the serial position of the test position in the study string. For *same* responses, there was a significant difference among the four positions, $F(3,33) = 22.4$, $p < 0.001$, partial eta squared = 0.670. For the *different* responses condition, there was also a significant difference among the four positions, $F(3,33) = 7.3$, $p = 0.003$, partial eta squared = 0.398. Nevertheless, there was a significant interaction between test position and response condition, $F(3,33) = 3.5$, $p = 0.027$, partial eta squared = 0.239. As can be seen in the right panel of Figure 3, the interaction was the result of fast responses to targets compared with the 1st test position of the study string.

The left panel of Figure 3 shows the results for the eight participants who responded *same* with the right key. Neither *same* RT nor *different* RT was a function of serial position of the test consonant in the study string, ruling out serial generation by the habit system. There was not a significant interaction between test-position and response, $F(3,33) = 2.9$, $p = 0.051$, partial eta squared = 0.207. For both *same* responses and *different* responses, there was not a significant difference among the four positions, $F(3,33) = 3.3$, $p = 0.058$, partial eta squared = 0.228 for *same* responses; $F(3,33) = 1.7$, $p = 0.208$, partial eta squared = 0.136 for *different* responses. The results are consistent with the generation of recency and novelty values for the test consonants by the visual

system and the use of these values to sort the test items into targets and foils by the perceptual system.

Taken together the results shown in Figure 3 are entirely consistent with the dual-system model. The habit system used the position information provided by the task to terminate the generation of the study string after the study consonant corresponding to the test consonant was generated. Otherwise, the position information did not influence the processing of either the habit system or the instrumental system. Therefore, neither system can use the position of a previously presented study item to gain direct access to the item. The only process available for retrieving study items from memory appears to be serial generation by the habit system.

Notice that again the predictions of the dual-system model were confirmed at a high level of specificity. In previous experiments, when only *different* or *same* RT was predicted to be a function of serial position in the study list only that response was a function of serial position. In Experiment 2, when both *same* and *different* RT were predicted to be a function of serial position in the study list, both were functions of serial position.

Replicating the results of Experiment 1, assigning the *different* response to the right key elicited a difference-detection process requiring serial generation and comparison of the study consonants. Assigning the *same* response to the right key elicited a repetition detection process involving the generation and detection of visual recency.

5. Experiment 3

5.1. Predictions

In Experiment 1 and Experiment 2, whether the *different* or *same* response was assigned to the right key determined which part of the brain controlled the visual

recognition response. However, these two experiments did not make clear how response assignment determines the decision process. One possible explanation was that assignment of a verbal label, *same* or *different*, to a specific hand might cause the specific hemisphere that controls that hand to control the decision process for the response. Another possible explanation was that assignment of the verbal label to a key in a relative right or relative left position might cause a central, pre-frontal, area to select a specific decision procedure for the response. These are very different explanations, implicating hemispheric versus bilateral control of the response.

The purpose of Experiment 3 was to determine whether the spatial location of the key or the body location of the hand determined the decision process by crossing spatial location of response key with hand in a 2 x 2 design.

5.2. Method

There were 24 subjects (19 females, 5 males; age range, 18 – 32 years) from undergraduate psychology classes offered at Rutgers University. They all self – reported being right-handed. Experiment 3 was an exact replication of Experiment 1 except that there were four response assignment conditions instead of two. Subjects were divided into four groups of 6 participants each. Two groups used the index finger and the middle finger of the left hand to press the “A” key and the “S” key, respectively, to make responses and two groups used the index finger and the middle finger of the right hand to press the “K” key and the “L” key to make responses.

5.3. Results and Discussion

Overall, the participants scored 96.3% (SD = 2.17) correct, with an average reaction time of about 714 milliseconds (SD = 256.98). The accuracy for each condition is shown in Table 1.

The results, shown in Figure 3, were analyzed in a 2 x 2 x 5 mixed ANOVA. The three independent variables were (1) the between-subject factor: response-hand (left versus right), (2) the between-subject factor: response-key (left versus right), and (3) the within-subject factor: match location (whether the test consonant appeared in the 1st, 2nd, 3rd, or 4th position of the study string, eliciting a *same* response or did not appear in the study string, eliciting a *different* response).

Whether the *same* or *different* response was assigned to the right key determined the pattern of *same* and *different* RT but the use of the left or right hand did not affect the response pattern in any way.

As shown in Figure 4, there was a significant interaction between response-key and match location that mirrored the interaction between response-assignment and match location found in Experiment 1, $F(4,80) = 6.5$, $p < 0.001$, partial eta squared = 0.245.

The right panels show the results when the *different* response was assigned to the right key. *Same* RT was an increasing function of the position of the target in the study string, indicating serial generation of each consonant of the study string by the habit system prior to its comparison with the test consonant. For the group using their left hand (top right), there was a significant difference among the four positions, $F(3,15) = 5.5$, $p = 0.009$, partial eta squared = 0.523. For the group using their right hand (bottom right), there was a significant difference among the four positions, $F(3,15) = 9.9$, $p = 0.001$, partial eta squared = 0.664. These results indicate that when the *different* response was assigned to the right hand, the dorsolateral prefrontal cortex of the left hemisphere, with primary responsibility for comprehending language, interpreted the task as a difference-detection task, which required serial generation of the individual study consonants by the habit system.

In contrast, the left panels of Figure 4 show that when the *same* response was assigned to the right key, the task as interpreted as a repetition-detection task, which activated the detection by the instrumental system of the recency effect generated by the visual system, so where the test item (when a target) had appeared in the study string was not involved in the decision and did not influence *same* RT. For the group using their left hand (top left), there was no significant difference among the four positions for *same* RT, $F(3,15) = 2.2$, $p = 0.125$, partial eta squared = 0.310. *Same* RT was not a function of serial position of the test consonant in the study string, ruling out serial generation by the habit system. Also, for the group using their right hand (bottom left), there was no significant difference among the four positions for *same* RT, $F(3,15) = 0.4$, $p = 0.754$, partial eta squared =0.074.

These results contradict a model in which assigning a task to a hand results in the hemisphere having primary control over that hand also having primary control over the decision process that produces the response. As can be seen in Figure 4 from a comparison of the top right with the bottom right panel and the comparison of the top left with the bottom left panel, response-hand had no effect on RT.

Rather, the results show that the verbal label assigned to the right location determined the response. Presumably, this was because one role that hemispheric dominance did play was that since the left hemisphere is dominant for language, when right and left (location) verbal labels elicit different processes, the verbal label on the right, with the stronger connection to the left hemisphere, will determine the selection of the decision process. This explanation implies that the decision process that controls the response is determined when the response assignments were made at the beginning of the experiment before the task was begun. This implies that the different areas activated by

the *same* versus *different* response assignments to the right hand would show differential activation during the study period before the test consonant was presented. This was one of the predictions tested by a replication of Experiment 1 that included fMRI.

6. Experiment 4

6.1. Predictions

The purpose of Experiment 4 was to record brain activity during the immediate visual recognition task. Experiment 1 was replicated with a within-subjects design and fMRI was recorded while the task was performed. A within-subject design was used to increase the precision of the comparison of neural activity at different brain locations when the task was performed under *same* versus *different* response assignment to the right key.

Sinha and Glass (2017) performed fMRI during the test period of a trial, the time period beginning with the onset of the test item. Also, the ROIs of Sinha and Glass were the subcortical areas of the habit and instrumentals systems, the caudate and hippocampus. Since these analyses were already found to be informative by Sinha and Glass they were repeated in the current study.

In addition, the behavioral results of the first three experiments indicated that two entirely different computational processes determined the responses depending on the response assignment. The different computational processes indicated that the responses were controlled by two entirely different systems of the brain depending on the brain. Specifically, for the right key = *different* response assignment, the habit system controlled the response. For the right key = *same* response assignment, the instrumental system controlled the response. Since response assignment was assigned at the beginning of the experimental session, this hypothesis raised the possibility that either the instrumental

system or the habit system controlled processing during the study period as well as the test period. So fMRI was done and analyzed for the study period as well as the test period in this investigation.

Also, the frontal cortex generally directs cognitive processing and could have different roles during the study and test periods of the test. To investigate this possibility, study period versus test period contrasts were added for the frontal eye fields, BA 8. The frontal eye fields were an obvious ROI because they control visual scanning (Dias & Segraves, 1999) and visual scanning of the study string was an essential component of the task.

The fMRI data was analyzed using a contrast methodology in which the level of activation of various neural structures in one condition is subtracted from the level of activation in another condition in order to determine whether there is a higher level of activation in a specific condition. The contrast methodology was used to test several a priori hypotheses about areas of activation derived from the models of the instrumental and habit systems inferred from the results of previous studies and the behavioral results described above.

First, if the assignment of the *same* response to the right key induced the prefrontal cortex to delegate control of the response to the instrumental system then there should be hippocampus activation, as found by Sinha and Glass (2017) and consistent with the effects of lesions in studies of mammalian memory (Yin and Knowlton, 2006).

Second, if the assignment of the *different* response to the right key induced the prefrontal cortex to delegate control of the response to the habit system then there should be both hippocampus activation and caudate nucleus activation, as found by Sinha and

Glass (2017) and consistent with the effects of lesions in studies of mammalian memory (Yin and Knowlton 2006).

Third, the hippocampal formation (HF) of the mammalian brain is conventionally defined as consisting of entorhinal cortex, dentate gyrus, Areas CA1 and CA3, and subiculum (Eichenbaum & Cohen, 2001). Among these areas, CA3 has been found to be involved in context-free memory, indicating involvement in the instrumental system (Chen, Olsen, Preston, Glover, & Wagner, 2011) and CA1 has been found to be involved in a context-dependent response, indicating involvement in the habit system in both rats (Ji & Maren, 2008) and humans (Dimsdale-Zucker, Ritchey, Ekstrom, Yonelinas, & Ranganath, 2018). Within the framework of the experiments reported here, the recency/novelty reference is context-free but the comparison of the test consonant to the study string is context-dependent. In fact, Sinha and Glass (2017) found that the *same* responses generated by the instrumental system and the *different* responses associated with the habit system were associated with the activation of different areas of the hippocampus. However, they were not able to analyze the activation in sufficient detail to distinguish CA1 from CA3 at that time.

Table 2 shows the subcortical areas of activation predicted by the dual – system model as a function of response – assignment (right = *same* versus right = *different*), key making response, and test item (target versus foil). As shown at the tops of the second and third columns of Table 2, the regions of interest for the contrasts were the caudate and CA1 for the habit system and CA3 of the hippocampus and for the instrumental system.

Five pairs of contrasts were performed that tested the predicted activation patterns shown in Table 2. All five pairs of contrasts tested a prediction of the dual system

hypothesis by performing subtractions between a response assignment predicting instrumental system activity (second column) and a response assignment predicting habit system activity (third column). Four contrasts tested the predicted patterns of activation for the different response assignments for responses to either targets or foils during the test period. One contrast tested the activation pattern predicted by response assignment during the study period.

Each row of Table 2 contains a contrast pair. The first column of the table indicates whether the test period supplied the data for the contrast pair or study/test contrasts were made. For each contrast pair (A, B), the second column of the table shows A for the A > B contrast and the third column shows B for the B > A contrast. Furthermore, the second column of the table shows the contrast that predicted CA3 activation of the hippocampus and the third column of the table shows the contrast that predicted caudate activation and CA1 activation of the hippocampus. The fourth column of the table identifies the figure showing the results of the pair of contrasts.

Additional analyses investigated the functional relationships among cortical and subcortical areas of the habit system during the study and test periods. Causal modelling was used to identify the relationships among the active neural structures during the test period.

6.2. Method

Participants. In this experiment, to maximize sensitivity and statistical power we used a within-subject design. Each subject performed the *same-different* task twice, a week apart; once using the right key to respond *same* and once using the right key to respond *different*. Therefore, we estimated the sample size for this fMRI study using a

method that is suitable for repeated measurements (Zandbelt et al., 2008). The sample size was estimated by:

$$n = \left(\frac{\sqrt{2}\sigma_w}{d}\right)^2 \times \left(t_{1-\alpha/2,df} + t_{1-\beta,df}\right)^2 \qquad (1)$$

where σ_w is the within-subject standard deviation in the task-related signal change. We estimated the within-subject standard deviation in the BOLD signal changes using the contrast between test versus study, and calculated the mean signal change in caudate, which was the main region of interest (ROI) associated with our task. The measure d is the absolute difference in the outcome measure between the two conditions, and $t_{1-\alpha/2,df}$ and $t_{1-\beta,df}$ are the corresponding values from the Student's *t*-distribution.

We ran 4 subjects as our pilot study, in order to estimate the sample size for this fMRI study. The results showed that the within-subject standard deviation in the BOLD signal changes was 0.08% in caudate. The difference in the mean BOLD signal change in caudate between the two sessions with different response assignment conditions was 0.15%. Hence, the effect size was 1.875 (i.e. d/σ_w = 0.15/0.08=1.875%). And we used a significance level of 0.05 and a power level of 0.80. With these parameter values, from equation (1) we resulted in a sample size of 8, meaning that 8 subjects were sufficient to detect the effect on the fMRI signal change in caudate using a ROI-based analysis in our within-subject design.

Therefore, we recruited 8 right-handed Rutgers University undergraduates as subjects (5 female, 3 male; age rage, 20-28 years) for this fMRI study. All the participants were right-handed, as indicated by the laterality index from 85.00 to 100.00 and decile from 6nd right to 10th right on the adapted Edinburgh Handedness Questionnaire from Oldfield (1971).

Experiment 4 was a replication of Experiment 1 except that each subject participated in two sessions a week apart, one in which the *different* response was assigned to the right key and one in which the *same* response was assigned to the right key. Four of the subjects responded *different* with their right key in the first session and four responded *same* with their right key in the first session.

At the beginning of each session, subjects were first asked to complete a practice test of 30 trials before entering the scanner, ensuring they understood the instructions and the procedure. Experiment 4 was identical to Experiment 1 except for two changes to accommodate it to the scanners

The experiment conducted in the scanner included 296 trials for 8 blocks instead of the 360 trials in 12 blocks. Remaining still in a scanner is tiring and reducing the length of the experiment reduced the likelihood of fatigue effects at the end. There was a mandatory 10-second break controlled by computer after each block in the scanner instead of allowing the participant to control the duration of the break, as in Experiment 1. Equalizing each break made the segmentation and analysis of the fMRI data easier and computer control of the break reduced interference from non-response movements by participants. There was an on – screen countdown from 10 to 1, indicating the time left to begin the next block. The computer automatically started the next block after the break.

Subjects performed the task while being scanned in a 3T Siemens TRIO scanner at the Rutgers University brain imaging center (RUBIC). Subjects responded by pressing buttons on an MR-compatible two-button box held comfortably by both hands somewhere along the midline of the body.

fMRI acquisition. Imaging was performed on a 3T Siemens TRIO scanner with a 32-channel head coil at the Rutgers University Brain Imaging Center (RUBIC).

Participants were scanned in the supine position and foam cushioning was used to stabilize head position and minimize head movement.

The stimuli were presented using PsychoPy (Peirce, 2007) software under the Windows 10 operating system projected onto a back-projection screen placed at the rear of the scanner bore. An MRI compatible two-button box was used for responses. Functional scanning was synchronized with the beginning of the experimental trials through a trigger pulse sent by the magnet to the PsychoPy software.

T1-weighted axial anatomical scans with 3D SPGR (TR = 1900 ms, TE =2.52 ms, field-of-view (FOV) = 256 mm, flip angle = 9°, slice thickness 1 mm, 176 slices per slab) were obtained prior to the experimental trial sequence. These anatomical scans were used to register the functional imaging data. Functional imaging was done using an echo planar gradient echo imaging sequence and axial orientation, including 928 volumes in time series per subject per session. These scans were obtained using the following parameters: TR = 2000 ms, TE = 25 ms, FOV = 192 mm, flip angle = 77°, slice thickness 3 mm, 33 axial slices covering the whole brain.

fMRI analysis of dual – system model. The fMRI data were analyzed using the FSL suite of programs (Jenkinson, Beckmann, Behrens, Woolrich & Smith 2012; Woolrich et al., 2009; Smith et al., 2004). BET (brain extraction tool) was used for skull stripping and removing non-brain tissues from both functional (BOLD) and anatomical images for each subject. Functional data were preprocessed using FSL default options: motion correction was applied using rigid body transformations (Jenkinson, Bannister, Brady & Smith, 2002); Gaussian spatial smoothing was applied with a full-width half-maximum of 5 mm; high-pass temporal filtering was applied using a Gaussian-weighted running lines filter, with a cut-off of 100 sec.

General linear modeling (GLM) based analysis was performed on the functional data using FEAT (FMRI Expert Analysis) software tool. For the group of 8 subjects, each was scanned under two different conditions, right-*same* (*same* response assigned to right key, *different* response assigned to left key) versus right-*different* (*different* response assigned to right key, *same* response assigned to left key).

The five pairs of contrasts shown in Table 2 were performed. They are described in row order from top to bottom.

For the first row of Table 2, the first level regressors were (a) *same* responses to targets with the right key and (b) *same* responses to targets with the left key. Both regressors spanned the (entire) duration of the 3 sec interval during which the test string (probe) was presented and convolved using a gamma hemodynamic response function. Hence, the analyses were confined to the comparison period during which a *same* response was made by the participant using either left key or right key (and did not include the encoding of the study item or the delay period). The resulting contrast images were then submitted to a second level group analysis.

We used a two-sample paired t-test, in which we excluded each participant's mean effect and only estimated the brain activation for both right key = *same* > left key = *same* and left key = *same* > right key = *same* contrasts. FLAME (FMRIB's Local Analysis of Mixed Effects) stage 1 mixed-effects model was used with a (corrected) cluster significance threshold of P=0.05 (Worsley, 2001).

The second contrast between right = *different* and left = *different*, the third contrast between left = *same* and left = *different*, and fourth contrast between right = *same* and right = *different* were performed using the same methodology as for the first contrast.

Unlike the first four contrasts, which contrasted the effects of response-assignment during the test period, the fifth contrast contrasted the effects of response assignment during study. The fifth contrast was right = *same*, left = *different* versus left = *same*, right = *different* response assignments during study. The first level regressor was study: when participants encoded the study string presented on the screen without making any response during study. The regressor spanned the (entire) duration of the 2 sec interval during which the study string was presented and convolved using a gamma hemodynamic response function.

For the group level analysis, we used a two-sample paired t-test as well, excluding each subject's mean effect and only estimating the right = *same*, left = *different* versus left = *same*, right = *different* paired differences for the brain activation during study phase. FLAME (FMRIB's Local Analysis of Mixed Effects) stage 1 mixed-effects model was used with a (corrected) cluster significance threshold of P=0.05 (Worsley, 2001).

fMRI analysis of habit system. Sinha and Glass (2017) found that activation in the caudate increased and activation in the hippocampus decreased as a function of the position of the mismatching study – test pair of consonants when the test string was presented. This functional analysis of the relationship between activation in the caudate and the position in the study string of the item determining the correct response was replicated in this investigation. A correlation analysis was conducted between activation in BA 8 and the position of the test item in the study string using a contrast in which activation during the study period was subtracted from the activation during the test period.

To further investigate the locus of the control of visual scanning of the study string and the locus of control of serial retrieval of the study string during test, for ROI

BA 8 (frontal eye fields) a contrast between activation during the study period and activation during the test period was conducted. Further evidence was provided by a contrast between right = *same* versus left = *same*, right = *different* response assignments during the study period, and a contrast between right = *same* versus right = *different* response assignments during test period.

Finally, a causal connectivity analysis of the components of the habit system and prefrontal cortex was performed.

6.3. Results and Discussion

Behavioral data. For the analysis, we excluded the incorrect responses and responses with reaction time outside three standard deviations. Overall, the participants scored 95% (SD = 2.69) correct with an average reaction time of 676 milliseconds (SD = 249). The accuracy in each condition is shown in Table 1.

The RT results, shown in Figure 5, were analyzed in a 2 x 5 within-subject ANOVA. The two independent variables were response-assignment and match-location.

As is obvious from a comparison of the left and right panels of Figure 5, there was a significant interaction between response-assignment and match-location, $F(4,28) = 8.2$, $p < 0.001$, partial eta squared = 0.541. The right panel shows the results when the *different* response was assigned to the right key. *Same* RT increased as a function of the position of the target in the study string, indicating serial generation of each consonant of the study string by the habit system prior to its comparison with the test consonant. There were significant differences among the four positions, $F(3,21) = 9.8$, $p < 0.001$, partial eta squared = 0.582.

The left panel in Figure 5 shows that when the *same* response was assigned to the right key there were no significant differences among the four positions of the target,

$F(3,21) = 1.2$, $p = 0.350$, partial eta squared = 0.142, indicating *same* RT was not a function of serial position of the test consonant in the study string. As is obvious from a comparison between Figure 2 and Figure 5, the results of the between-subjects design of Experiment 1 were replicated with the within-subject design of Experiment 4.

fMRI activation during testing confirms instrumental system versus habit system activation as a function of response assignment. Preparatory to performing the contrasts testing the predictions of the dual system hypothesis, we subdivided hippocampus into subfields and determined which subfields were activated in different conditions, using tools of segmenting hippocampal subfields in FreeSurfer 6.0 (Iglesias et al., 2015). As shown in Figure 6, the subfields that were identified were the parasubiculum, presubiculum, subiculum, CA1, CA2/3, CA4, GC-DG (granule cell layer of dentate gyrus), HATA, fimbria, molecular layer, hippocampal fissure, and tail.

To perform an unbiased analysis, first a whole-brain analysis of activation was performed and then those specific areas predicted to be activated by our a priori hypotheses were examined. We examined relative activation specifically in the instrumental and habit systems for the behavioral contrasts shown in Figures 2 – 5.

Table 3 contains the precise location values for the contrasts shown in Figures 7 and 8. First, the contrast of left = *same* versus right = *same* response assignments was performed (row 1 of Table 2). For the left = *same* response assignment, during the test period activation in CA1 of the right hippocampus (Figure 7, Top Right) and in the left and right caudate were found (Figure 7, Bottom Right), demonstrating habit system involvement. For the right = *same* response assignment during test, activation in CA3 in the right hippocampus was identified (Figure 7, Top Left) but no activation was found in the caudate (Figure 7, Bottom Left), demonstrating instrumental system involvement.

For *different* responses during test (row 2 of Table 2), under right = *different* response assignment, during the test period activation in CA1 in the right hippocampus (Figure 8, Top Right).and in the left and right caudate (Figure 8, Bottom Right) were found, demonstrating habit system involvement. For the left = *different* assignment during test, activation in CA3 in the right hippocampus was identified (Figure 8, Top Left) but no activation was found in the caudate (Figure 8, Bottom Left), demonstrating instrumental system involvement.

In addition to contrasts that compared neural activity when the right versus left key was used to make the *same* response, shown on the first and second rows of Table 2, contrasts were made that compared activity when the *same* versus *different* responses were performed using the same key. Table 4 contains the precise location values for the contrasts shown in Figures 9 and 10.

For the left key (row 4 of Table 2), for the left = *same* response assignment, during the test period activation CA1 in the right hippocampus (Figure 9, Top Right) and activation in the left and right caudate were found (Figure 9, Bottom Right), demonstrating habit system involvement. For the left = *same* response assignment, during the period test activation CA3 in the right hippocampus was found (Figure 9, Top Left) but no activation was found in the caudate (Figure 9, Bottom Left), demonstrating instrumental system involvement.

For the right key (row 4 of Table 2), for the right = *different* response assignment, during the test period activation in CA1 in the right hippocampus (Figure 10, Top Right) and in the left and right caudate were identified (Figure 10, Bottom Right), demonstrating habit system involvement. For right = *same* response assignment, during the test period activation in CA3 in the right hippocampus was identified (Figure 10, Top Left) but no

activation was found in the caudate (Figure 10, Bottom Left), demonstrating instrumental system involvement.

To summarize, all analyses demonstrated that the right key = *different* response assignment caused caudate and hippocampal CA 1 activation in the habit system and right key = *same* response assignment caused hippocampal CA 3 activation in the instrumental system.

fMRI activation during study further confirms instrumental system versus habit system activation as a function of response – assignment. There are two possible interpretations of the pattern of active areas observed during the test phase of a trial. One interpretation is these are the areas that become active when the test consonant appears in order to determine whether it was in the study string. If this hypothesis were true, then the pattern of activation on each trial during the study period before the test consonant appeared would not be the same as the pattern that was observed after the test consonant was presented.

The other interpretation is the areas active during the test period first became active at the beginning of the experimental session when the response assignment was made. They reveal the system, instrumental or habit, selected by the prefrontal cortex to perform the *same – different* task on the basis of the verbal label assigned to the right-key response. If this hypothesis were true then the pattern of activation on each trial during the study period before the test consonant appeared would be the same as the pattern that was observed after the test consonant was presented.

To test these predictions, we did the contrast for right = *same* (and left = *different*) versus right = *different* (and left = *same*) response assignments during study. Table 5 contains the precise location values for the contrasts shown in Figures 11. For the right =

different response assignment, during study activation was found in CA1 in the right hippocampus (Figure 11, Top Right) and in the left and right caudate (Figure 11, Bottom Right), demonstrating habit system involvement. For the right = *same* response assignment, during study activation was found in CA3 in the right hippocampus (Figure 11, Top Left) bunt not the caudate (Figure 11, Bottom Left), demonstrating instrumental system involvement.

To summarize, the results shown in Figure 11 are consistent with the hypothesis that the control of the task by the instrumental or habit system begins at the onset of the study string rather than at the onset of the test item.

Correlation between position of target in study string during test and fMRI caudate activation confirms serial retrieval of study string during test. We further analyzed correct *same* judgments during the test period under the right = *different* response assignment to determine if there was a linear trend between activation in the habit system and the position of test item (when it was a target) in the study string. For each position in the study string, the activation during the study period was subtracted from the activation during the test period for each trial. The linear trend analysis included four levels of positions (1, 2, 3 and 4). A positive linear trend was detected in the habit system for the left and right caudate and CA1 of hippocampus, $r = .37$, $p < .04$, indicating the continued comparison of the study string with the test item until a match was found.

In addition to replicating the results of Sinha and Glass (2017), the linear trend in activation during test as a function of target position in the study string also clarified the source of the activation observed during the study. We have attributed the activation observed during the study periods as ongoing activation as the result of the operation of either the instrumental system or the habit system. An alternative explanation is that the

activation observed during the study period of trial n is actually the residue of the activity caused by the processing of a test item during the test period of trial n – 1. If this were the cause then the same linear trend in activation observed for the test period of trial n – 1 would be observed for the study period of trial n. So subtracting the activation for the study period of trial n from the activation for the test period of trial n – 1 would produce a contrast showing no areas of activation. However, when
we subtracted activation in the study period of trial n from the test period of trial n the same linear trend in caudate and hippocampal CA 1 activation as a function of target position in the study string on trial n – 1 was observed, $r = .35$, $p = .053$.

These results are not consistent with the hypothesis that study period activation is the residue of the previous test period activation because if this were the case then the same linear increase in activation as a function of target study position would be observed for both periods. Rather, the results indicate that when the habit system is active, when the test item appears, there is a subsequent increase in habit system activation while the study string is being retrieved until a match with the test item is found and the retrieval process is terminated.

fMRI activation of the frontal eye fields during study and test reveals different control areas for scanning and retrieval of a string. Finally, recall that the frontal eye fields control visual scanning (Dias & Segraves, 1999). Study – test contrasts of the activation of the frontal eye fields were performed to investigate whether these contrasts would reveal evidence of visual scanning of the study string and its serial retrieval during test. Table 6 contains the precise location values for the contrasts shown in Figure 12 for the frontal eye fields. We looked for clusters in BA 8 where activity for the right = *different* response assignment during study was higher than that for right =

different response assignment during test. Clusters in both left and right BA 8B were identified (Figure 12, Top Right). Then we looked for clusters in the prefrontal cortex where activity for right = *different* response assignment during test was higher than that for right = *different* response assignment during study. Clusters in both left and right BA 8A were identified (Figure 12, Bottom Right).

Given that frontal eye fields, BA 8 in humans, were already known to control visual scanning in mammals, the activation of BA 8B during study confirms that the study string was scanned from left to right during study but is not surprising. However, the activation of BA 8A during test is a new finding that reveals a new function of the frontal eye fields. During the test period, only a single test consonant was presented, at the fixation point, so there was nothing to scan. Rather, the task required serially retrieving the study string from memory, one consonant at a time. The activity of BA 8A indicates that it plays a role in serially retrieving a recently scanned string.

The only other result in the research literature indicating that the frontal eye fields are involved in the retrieval of just-presented visual information was for monkeys. When the monkey frontal eye fields were inactivated with muscimol, the first ability to disappear was performance in a memory-guided saccade task where the monkey was briefly remember (200-800 msec) the location of a flashed visual target before the cue to make a saccade to that target (Dias & Segraves, 1999).

Also, the fact that BA 8B but not BA 8A was active during study confirms that the activation observed during study was not the residue of the activation during the test period of the previous trial.

Recall that only the computational process used by the habit system required left to right scanning of the study string and then its serial retrieval during test. Therefore, we

also conducted a contrast between right = *same* response assignment and right = *different* response assignment during study period for eye field activation to determine its relationship to the habit system. Table 7 contains the precise location values for the contrasts shown in Figure 13 for the frontal eye fields. For right = *different* response assignment during study, activation was found in both left and right BA 8B (Figure 13, Right). For right = *same* response assignment during study, no activation was found in BA 8B (Figure 13, Left). Together, these results identify BA 8B as part of the habit system but not the instrumental system.

We performed the same contrast between right = *same* response assignment and right = *different* response assignment during test period. Table 8 contains the precise location values for the contrasts shown in Figure 13 for the frontal eye fields. For the right = *different* response assignment, during test active clusters in both left and right BA 8A were identified (Figure 14, Right). For the right = *same* response assignment, during test no active cluster was identified in BA 8A (Figure 14, Left). Together, these results identify BA 8A as part of the habit system but not the instrumental system.

Correlation between position of target in study string during test and fMRI BA 8A activation. We further analyzed correct *same* judgments during the test period under the right = *different* response assignment to determine if there was a correlation between activation in BA 8A and the position of the test item (when it was a target) in the study string. For each position in the study string, the activation during the study period was subtracted from the activation during the test period for each trial. The linear trend analysis included four levels of positions (1, 2, 3 and 4). A positive linear trend was detected in the left and right BA 8A, $r = .46$, $p < .01$, indicating an increase in activation until a match was detected. When we subtracted activation in the study period of trial n

from the test period of trial n the same linear trend in BA 8A activation as a function of target position in the study string on trial n – 1 was observed, $r = .43$, $p = <.02$.

The fMRI activation of the entire dorsal frontal cortex during study and test is shown in Table 9.

Connectivity analysis. We conducted a connectivity analysis on the timeseries data from the ROIs using graphical causal modeling with IMaGES (the Independent Multiple sample Greedy Equivalence Search) and LOFS (Linear non-gaussian Orientation, Fixed Structure) algorithms (Ramsey, Hanson, & Glymour, 2011; Ramsey et al., 2010) implemented using the TETRAD IV (version 5.0.0–1; http://www.phil.cmu.edu/projects/tetrad) software, in order to estimate the causal relationships among the structures that increased in activation for responses under right-*different* response assignment.

First, according to the GLM analyses before, responses under right-different responses assignment during test were associated with activation of BA 8A, the caudate, and CA 1 of the hippocampus. Furthermore, the probable causal relationship between BA 8A and subcortical structures of the habit system indicated that other frontal structures might have causal relationships with subcortical structures of the habit system and each other that would be revealed by connectivity analysis. As shown in Table 9, to select ROIs for the connectivity analysis, first four contrasts were performed for the frontal cortex, right = different versus right = same response assignment was crossed with the study period versus the test period. As Table 9, five frontal areas were active during the test period. These areas were included in the connectivity analysis.

Therefore, according to the ROI analyses above (Table 9), responses under right-*different* response assignment during test were associated with activation of the caudate,

right CA 1 in hippocampus and SMA, pre-SMA, BA 46, BA 8A and anterior PMd in dorsal frontal cortex. Masks for each of the seven regions of interest (ROI) were constructed. The time series from each ROI was extracted and then used as input to the IMaGES algorithm (Ramsey et al., 2010). Hence, each ROI was a node in the network whose connectivity we examined. The IMaGES algorithm searched for connections between the nodes (ROIs) and produced a graph.

After IMaGES identified a graph for the set of regions, the graph was fed to the LOFS algorithm (Ramsey et al., 2011). LOFS determined the orientation (direction) of each connection. The results of the IMaGES and LOFS analyses are presented in Figure 15. The graph consists of nodes representing the ROIs and arrows that connect some of those nodes, depicting causal relationships between them. We found functional links including:

BA 46 → BA 8A.

BA 46 → CA1 → Caudate.

preSMA→ Caudate.

These functional links may indicate activation or inhibition; this information is not captured by the analysis. An arrow from region A to region B simply implies that changes in activation in the region A cause changes in activation in the region B.

The connectivity analysis confirmed that BA 8A, the caudate, and CA 1 of the hippocampus are parts of a functional system, but the role of BA 46 was a surprise. Its role should the focus of a future research effort.

7. General Discussion

This study produced several new results.

There is Not Direct Access through a Location to the Previous Target at that Location

In immediate visual recognition, as shown in Experiment 2, an observer was not able to use the position of the test consonant to gain direct access to the study consonant that had appeared in the position of the test consonant. So there is not direct access through the location to what was previously presented at a specific location of the visual field.

Despite Speed – Accuracy Trade-Off, the Dual System was Confirmed

The dual system hypothesis was confirmed. Precise predictions about whether target RT or foil RT or both would be a function of study string position were confirmed for the two variants of the *same – different* task that were studied in four different experiments. In Experiment 2 the results were in perfect conformance with the predictions. In Experiments 1, 3, and 4 the results were conformance with the predictions except for one data point, for the *different* response, which was faster than predicted. However, a review of Table 1 indicates that the faster than predicted *different* responses were the result of trading speed for accuracy by responding *different* befor a complete study string had been retrieved.

The model assumed that the habit system serially compared the test consonant with each study consonant until either a match was or all four comparisons were made. Consequently, a *different* response, after all four comparisons had been made, should have been no faster than for a *same* response to a target that had appeared in the fourth position of the study string. In fact, it was faster. However, the faster RT for the *different* response to foils was associated with a higher error rate for responses to targets. An error

to a target is made when a *different* response is made instead of a *same* response. So the higher rate for *same* responses than for *different* responses is clear evidence that the faster RT was the result of a speed – accuracy tradeoff strategy employed by participants in which participants often terminated the left-to-right comparison process between the test item and the study string after the first three study items with a *different* response, resulting in faster *different* RT for foils but also a higher error rate for targets.

By replacing what would have been the slowest *different* responses with much faster partial or complete guesses, they traded off a small increase in error rate for responses to targets for a large reduction in mean RT for foils. A 4 x 2 x 2 analysis of variance of the error rate results shown in Table 1 in which the factors were Experiment, Response Assignment and Response (*same* to targets or *different* to foils) revealed that there was a main effect of response, $F(1,8) = 0.883$, $p < 0.001$, partial eta squared = 0.883. Mean accuracy for responses to targets was 93.9% (95% C. I. = 0.930, 0.948) and mean accuracy for responses to foils was 97.0% (95% C. I. = 0.962, 0.977). So as predicted, the error rate was higher for the responses to targets.

The Frontal Eye Fields Retrieve Visual Targets

BA 8A was causally related through BA 46 to the caudate and CA 1 of the hippocampus in the retrieval of the study string and its comparison to the test consonant (Figure 15).

A Linear Model of Human Information Processing is Wrong

The model inferred from the results of these experiments has novel features with important theoretical and methodological implications. A linear information processing

model of the test period, in which a perceptual stage is followed by a decision stage, which is followed by a response stage, is not consistent with either the effect of response assignment or the similar fMRIs observed for the study and test periods. Within the linear information processing model, response selection occurs after the perceptual and decision stages and so cannot affect the stages that come before it. Processing during the study period is assumed to be the same regardless of the response assignment because no response is actually performed during the study period.

In fact, response assignment determined which of two different neural systems was active during the study period. The neural system active during the study period was again active during the test period. Consequently, response assignment determined the perceptual and decision stages during the processing of the test item because the response assignment determined which of two different neural systems, using two entirely different computational procedures, performed the visual recognition task.

In the model inferred from the results of these experiments, at the beginning of an experimental session, the left prefrontal cortex interprets the *same – different* task on the basis of the label assigned to the right key, which is the key with the stronger pathways to the left hemisphere. If the *same* response is assigned to the right key, then the left prefrontal cortex interprets the task as a *same* judgment. So the instrumental system, which generates recency judgments, which are context-free *same* judgments is selected, presumably by inhibiting the habit system. If the instrumental system is selected then during the study period, activation from the study consonants is directed to CA3 of the hippocampus, which interprets the level of the visual system's response to a test item as an indicator of recency or novelty. During the test period, activation from the test consonant is directed to CA3. If the test consonant was a study consonant, then the

neurons associated with it have been habituated and the weak response is interpreted as recency. If the test consonant was not a study consonant, then the neurons associated with it have not been habituated and the strong response is interpreted as novelty.

Otherwise, if the *different* response is assigned to the right key then the left prefrontal cortex interprets the task as a *different* judgment. So the habit system, which ultimately compares the test consonant with the study string is selected, presumably by inhibiting the instrumental system. If the habit system is selected then during the study period, the caudate selects each study consonant in turn by inhibiting processing of the preceding consonants of the study string. The study string is encoded in CA1 of the hippocampus. During the test period, the caudate serially generates the string encoded during the study period. If the test consonant is generated, then a study – test match is found so a *same* judgment is made.

The processing of the study string is as distinctive as the subsequent processing of the test consonant. The causal chain begins with the assignment of verbal labels to response keys at the beginning of the session. At that point one of two neural systems is chosen to take the lead in performing the task. Neither of the two possible systems is some simple system in which a target automatically triggers a response. Rather, both systems provided the neural machinery for learning a skill that could be performed on demand. The skill involved intentionally encoding the study string in a particular way during the study period, either within or apart from the context of the study string, enabling a specific decision strategy during the test period.

A great advantage of this version of the dual-system model is that it is specific enough to be testable in numerous ways. Among possible areas of inquiry are the

comparison of temporal versus spatial sequences, the comparison of auditory versus visual recognition, and the comparison of similarity with identity judgments.

Immediate Visual Recognition may be Performed by two Entirely Different Neural Systems Making Use of Different Computational Processes

Finally, the finding that two entirely different brain systems make immediate visual recognition judgments has profound theoretical and methodological implications that should not be overlooked. The evidence that a simple immediate visual recognition task is performed by two entirely different neural computational systems in the brain is more comprehensive and compelling than the well-known, classic, finding that the right and left hemispheres process visual and verbal stimuli independently in split brain individuals (Gazzaniga, et al., 1962). Furthermore, the different systems revealed in intact individuals are of more theoretical and practical importance because they are the basis of normal cognition. It cannot be the case that two entirely different systems evolved for a single, artificial, experimental task. Rather, the results of this task have revealed a fundamental feature of functional neural organization that is certain to have wide applications across many kinds of tasks. In fact, the results here suggest a reconsideration of the results of Gazzaniga, et al. (1962). Until now, these results have been interpreted as demonstrating the different competencies of corresponding areas of the left and right hemispheres to perform the same task. The results reported here suggest the earlier results of Gazzaniga et al. (1962) may also have been the result of each hemisphere employing an entirely different neural system to perform the same task.

From a theoretical perspective, in the future one must consider the contributions of these two distinct computational systems to recognition and recall. The possibility of

two such systems has been recognized previously (Atkinson, & Juola, 1973; 1974; Diana, Reder, Arndt, J., & Park, 2006) with the effect of the instrumental system called a *know* judgment and the effect of the habit system called a *remember* judgment. These results demonstrate for the first time the two distinct neural systems that generate *remember* versus *know* judgments.

From a methodological perspective, the results indicate that in future experiments it is important to select a task and task parameters that make it possible to isolate the effects of the different computational systems.

In retrospect, the behavioral results of other studies (Glass, 1993; Kristofferson, 1972a; 1972b) appear to have shown that another task factor also isolates a single system within the dual-system model. This is the similarity among study strings presented on successive trials and the intervals among the strings. When study strings that consist of the same items in different orders are presented on successive trials, habituation of neurons in the perceptual system accumulates over successive trials so that targets and foils come to have uniform recency values, so must be discriminated through serial comparison with the study list, so RT is a monotonic function of the number of study items that must be retrieved for a decision. As the interval between trials increases on which similar study strings are presented, there is more time for test items to become dis-habituated. So responses based on recency increase and responses based on serial comparison between the study string and test item decrease (Glass, 1993; Kristofferson, 1972a; 1972b) so RT is not a linear function of the number of study string. This was found in studies of animal memory as well as in studies of human memory (Wright, Santiago, Sands, Kendrick, & Cook, 1985). Future studies that use fMRI and behavioral measures and that combine response assignment and trial – interval in a single design

should be able to isolate activation in the habit system and instrumental system even more precisely.

More generally, the results here suggest that whenever a two-alternative, choice RT experiment is done in the future, response assignment should not only be counterbalanced but included as a factor in the analysis of the results. Also, there is probably a pool of data from past studies in which response assignment was counterbalanced but not analyzed. The results here suggest that a re-analysis including response assignment as a factor may well provide new insight into the data.

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Table 1.
Response Accuracy for All Four Experiments

		Targets (*Same* Correct)					Foils (*Different* Correct)					All
		Pos 1	Pos 2	Pos 3	Pos 4	All Pos	Pos 1	Pos 2	Pos 3	Pos 4	All Pos	
Exp 1	Right Key = *Different* Response	0.96	0.93	0.96	0.87	0.93					0.97	0.94
	Right Key = *Same* Response	0.9	0.91	0.94	0.94	0.92					0.96	0.95
Exp 2	Right Key = *Different* Response	0.98	0.94	0.94	0.92	0.94	0.98	0.97	0.95	0.95	0.96	0.95
	Right Key = *Same* Response	0.94	0.91	0.96	0.93	0.93	0.99	0.99	0.98	0.97	0.98	0.96
Exp 3	Left Hand, Right Key = *Different*	0.97	0.95	0.97	0.95	0.96					0.99	0.97
	Left Hand, Right Key = *Same*	0.93	0.92	0.98	0.94	0.94					0.96	0.95
	Right Hand, Right Key = *Different*	0.94	0.96	0.97	0.93	0.95					0.98	0.96
	Right Hand, Right Key = *Same*	0.93	0.94	0.97	0.96	0.95					0.98	0.96
Exp4	Right = *Different* Response	0.94	0.94	0.95	0.91	0.93					0.97	0.95
	Right = *Same* Response	0.90	0.94	0.96	0.94	0.94					0.96	0.95

Table 2.

Activated Areas Predicted by Dual System Hypothesis for fMRI Contrasts as a Function of Response – Assignment and Test Item (Target or Foil)

Period	Instrumental System: CA3 Area of Hippocampus Right Key = *Same* Response Assignment	Habit System: CA1 Area of Hippocampus Caudate Nucleus Right Key = *Different* Response Assignment	Figures showing Result
Test	Right Key = *Same* (Targets)	Left Key = *Same* (Targets)	Figure 7
Test	Left Key = *Different* (Foils)	Right Key = *Different* (Foils)	Figure 8
Test	Left Key = *Different* (Foils)	Left Key = *Same* (Targets)	Figure 9
Test	Right Key = *Same* (Targets)	Right Key = *Different* (Targets)	Figure 10
Study	Right Key = *Same*, Left Key = *Different*	Right Key = *Different*, Left Key = *Same*	Figure 11

Table 3.
Instrumental and Habit system analysis for Right Key vs. Left Key Response During Test

Response Assignment					MNI coordinates of max (mm)			Number of Voxels	Intensity (Maximum)
	Right Key = *Different*	Right Key = *Same*			x	y	z		
Same Judgment	Left Key	Right Key	Contrast	Habit System					
			Left > Right	L Caudate	-16	-22	24	414	2.447
				R Caudate	18	-26	22	473	2.596
				R CA 1	36	-10	-16	91	2.144
			Contrast	Instrumental System					
			Left < Right	R CA 3	24	-16	-16	86	2.834
Different Judgment	Right Key	Left Key	Contrast	Habit System					
			Right > Left	L Caudate	-16	-22	24	394	2.664
				R Caudate	18	-26	22	462	2.398
				R CA 1	40	-12	-24	87	1.833
			Contrast	Instrumental System					
			Right < Left	R CA 3	28	-16	-16	90	2.907

Table 4.
Instrumental and Habit system analysis for *Same* vs. *Different* Responses During Test

Response Assignment					MNI coordinates of max (mm)			Number of Voxels	Intensity (Maximum)
	Right Key = *Different*	Right Key = *Same*			x	y	z		
Left Hand	*Same* Judgment	*Different* Judgment	Contrast	Habit System					
			Same > *Different*	L Caudate	-14	22	4	342	2.558
				R Caudate	12	14	4	378	2.633
				R CA 1	36	-12	-16	92	2.285
			Contrast	Instrumental System					
			Same < *Different*	R CA 3	26	-16	-16	90	2.765
Right Hand	*Different* Judgment	*Same* Judgment	Contrast	Habit System					
			Different > *Same*	L Caudate	-16	-22	24	252	2.693
				R Caudate	18	-26	22	307	2.472
				R CA 1	36	-10	-18	86	1.718
			Contrast	Instrumental System					
			Different < *Same*	R CA 3	28	-16	-16	91	2.854

Table 5.
Instrumental and Habit system analysis for Right Key = *Same* vs. Right Key = *Different* during Study

Response Assignment				MNI coordinates of max (mm)			Number of Voxels	Intensity (Maximum)
Right Key = *Different*	Right Key = *Same*			x	y	z		
Right Key = *Different*, Left Key = *Same* (Right*Diff*)	Right Key = *Same*, Left Key = *Different* (Right*Same*)	Contrast	Habit System					
		Right*Diff* > Right*Same*	L Caudate	-12	-8	16	274	2.021
			R Caudate	18	-4	24	306	2.697
			R CA 1	38	-14	-18	71	2.273
		Contrast	Instrumental System					
		Right*Diff* < Right*Same*	R CA 3	28	-14	-12	53	2.194

Table 6.
Prefrontal cortex analysis for Study vs. Test during Right Key = *Same* and Right Key = *Different*

Response Assignment			MNI coordinates of max (mm)			Number of Voxels	Intensity (Maximum)
			x	y	z		
Right Key = *Different*	Contrast	Habit System					
	Study > Test	L BA 8B	-26	22	50	978	1.933
		R BA 8B	24	32	48	547	2.306
	Contrast	Instrumental System					
	Study < Test	L BA 8A	-34	2	42	499	3.191
		R BA 8A	32	2	54	582	3.91
Right Key = *Same*	Contrast	Habit System					
	Study > Test	L BA 8B	-16	38	38	928	1.791
		R BA 8B	16	38	34	364	2.062
	Contrast	Instrumental System					
	Study < Test	L BA 8A	-30	6	48	468	2.461
		R BA 8A	40	16	48	506	3.176

Table 7. Prefrontal cortex analysis for Right Key = *Same* vs. Right Key = *Different* during Study

Response Assignment				MNI coordinates of max (mm)			Number of Voxels	Intensity (Maximum)
Right Key = *Different*	Right Key = *Same*	Contrast		x	y	z		
Right Key = *Different* (Right*Diff*)	Right Key = *Same* (Right*Same*)	Right*Diff* > Right*Same*	L BA 8B	-30	32	42	256	2.266
			R BA 8B	34	22	42	364	2.249
		Right*Diff* < Right*Same*	L BA 8B	No clusters found				
			R BA 8B	No clusters found				

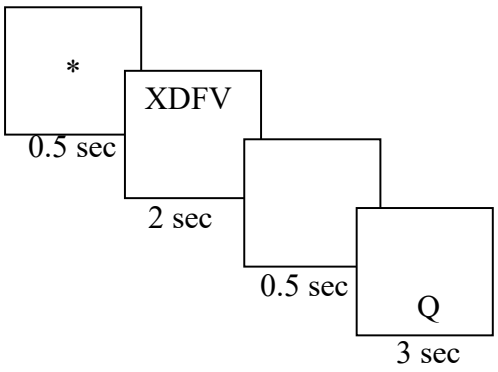
Table 8. Prefrontal cortex analysis for Right Key = *Same* vs. Right Key = *Different* during Test

Response Assignment				MNI coordinates of max (mm)			Number of Voxels	Intensity (Maximum)
Right Key = *Different*	Right Key = *Same*	Contrast		x	y	z		
Right Key = *Different* (Right*Diff*)	Right Key = *Same* (Right*Same*)	Right*Diff* > Right*Same*	L BA 8A	36	2	56	510	2.431
			R BA 8A	-38	2	54	416	2.144
		Right*Diff* < Right*Same*	L BA 8A	No clusters found				
			R BA 8A	No clusters found				

Table 9. Dorsal frontal cortex analysis for Study vs. Test during Right Key = *Same* and Right Key = *Different*

			MNI coordinates of max (mm)			Number of Voxels	Intensity (Maximum)
			x	y	z		
Right Key = *Different*	Study > Test	BA 9	-14	58	16	788	2.336
		BA 8B	24	32	48	1525	2.306
		BA 10	-2	64	0	1027	2.882
	Test > Study	BA 46	40	46	14	1802	3.283
		BA 8A	32	2	54	1081	3.910
		SMA	4	20	46	1833	3.481
		preSMA	6	20	48	923	2.970
		Ant PMd	28	-2	54	2121	3.599
Right Key = *Same*	Study > Test	BA 9	6	60	32	856	2.493
		BA 8B	16	38	34	1292	2.062
		BA 10	-4	66	4	980	3.025
	Test > Study	BA 46	-28	48	18	1812	3.696
		BA 8A	40	16	48	974	3.176
		SMA	14	-6	72	1041	3.085
		preSMA	-6	20	60	1104	2.717
		Ant PMd	24	12	60	1248	2.462

(a)



(b)

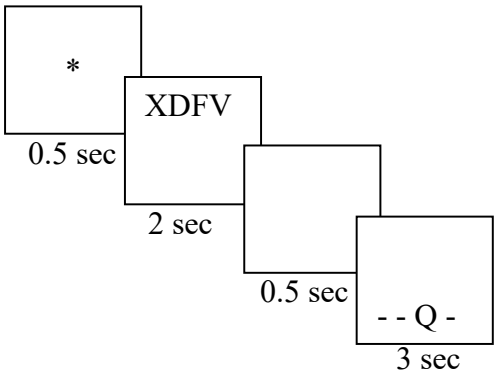


Figure 1. (a) Study – test sequence for Experiments 1, 3, and 4. (b) Study- test sequence for Experiment 2.

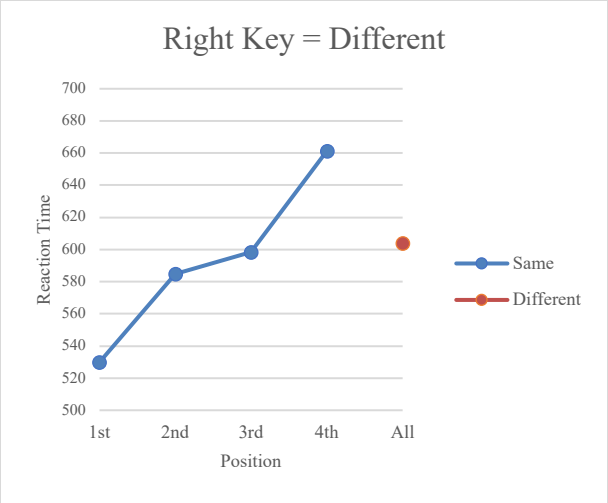


Figure 2. Results of Experiment 1. Right panel shows results serial processing for twelve participants who responded *different* with the right hand. Left panel shows no serial processing for twelve subjects who responded *same* with right hand.

Figure 3. Results of Experiment 2. Right panel shows results for eight participants who responded *different* with right hand. Left panel shows results for eight participants who responded *same* with the right hand.

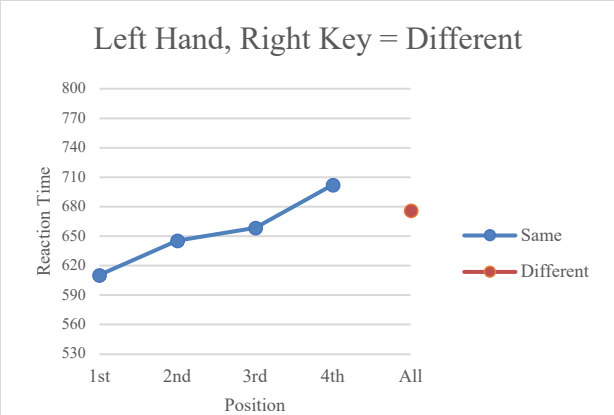


Figure 4. The results of Experiment 3. The right column shows the results for the right key. The left column shows the results for the left key. The spatial position, not the hand, of the response, determines the pattern of *same* and *different* RT.

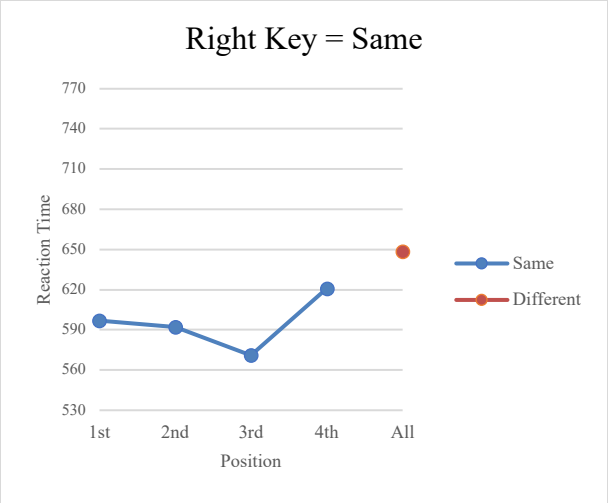


Figure 5. Results of Experiment 4. Right panel shows results serial processing when subjects responded *different* with the right hand. Left panel shows no serial processing when subjects responded *same* with right hand.

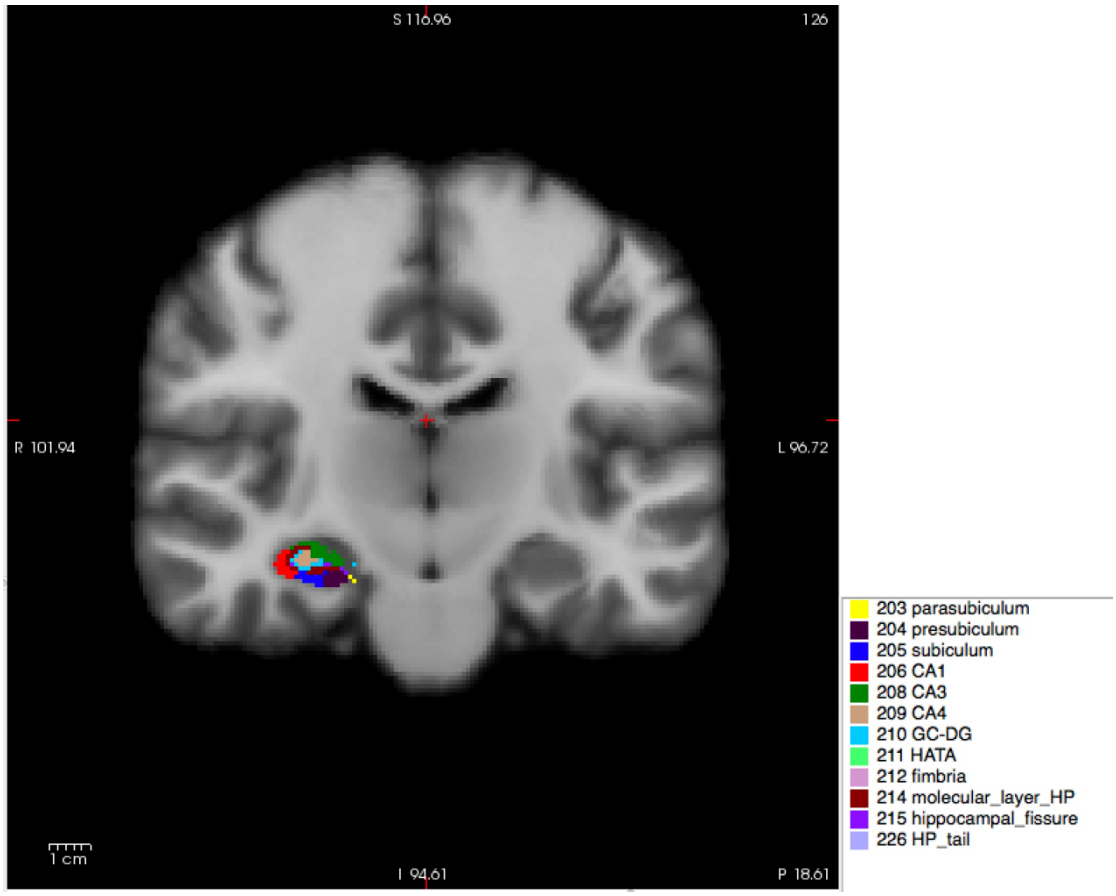


Figure 6. Segmentation of hippocampal subfields

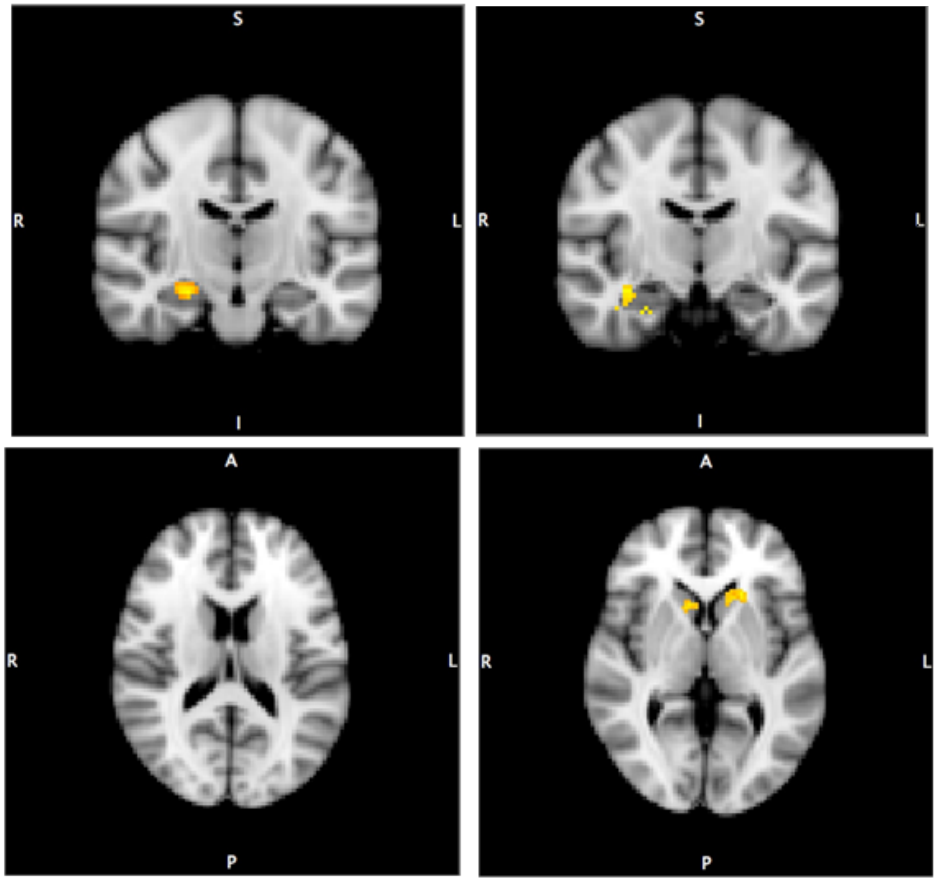


Figure 7. Contrasts for left = *same* versus right = *same*. When the *same* response was assigned to the left key, there was increased activation in CA1 within the right hippocampus (Top Right) and in both left and right caudate (Bottom Right). When the *same* response was assigned to the right key, there was increased activation in CA3 within the right hippocampus (Top Left) but there was not increased activation in the caudate (Bottom Left).

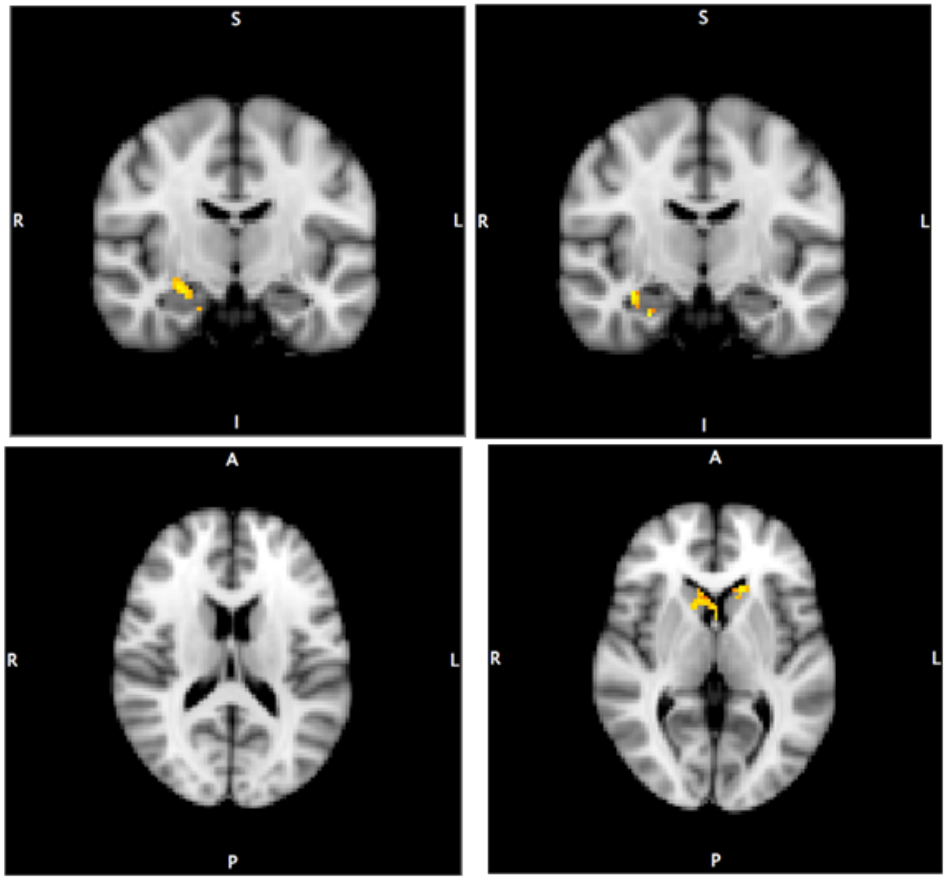


Figure 8. Contrasts of right = *different* versus left = *different*. When the *different* response was assigned to the right key, there was increased activation in CA1 in the right hippocampus (Top Right) and in both left and right caudate (Bottom Right). When the *different* response was assigned to the left key, there was increased activation in CA3 in the right hippocampus (Top Left) but there was not increased activation in the caudate (Bottom Left).

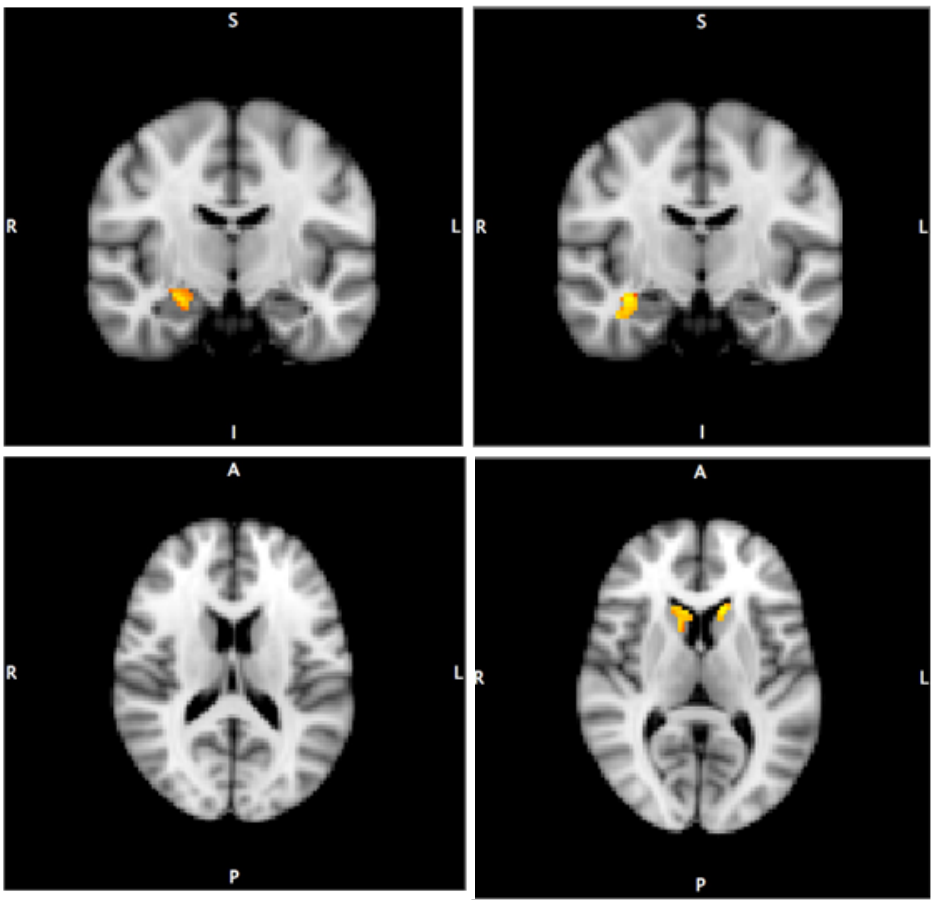


Figure 9. Contrasts for left = *same* versus left = *different*. When the *different* response was assigned to the left key there was increased activation in CA1 within the right hippocampus (Top Right) and in both left and right caudate (Bottom Right). When the *same* response was assigned to the left key there was increased activation in CA3 within the right hippocampus (Top Left) but there was not increased activation in the caudate (Bottom Left).

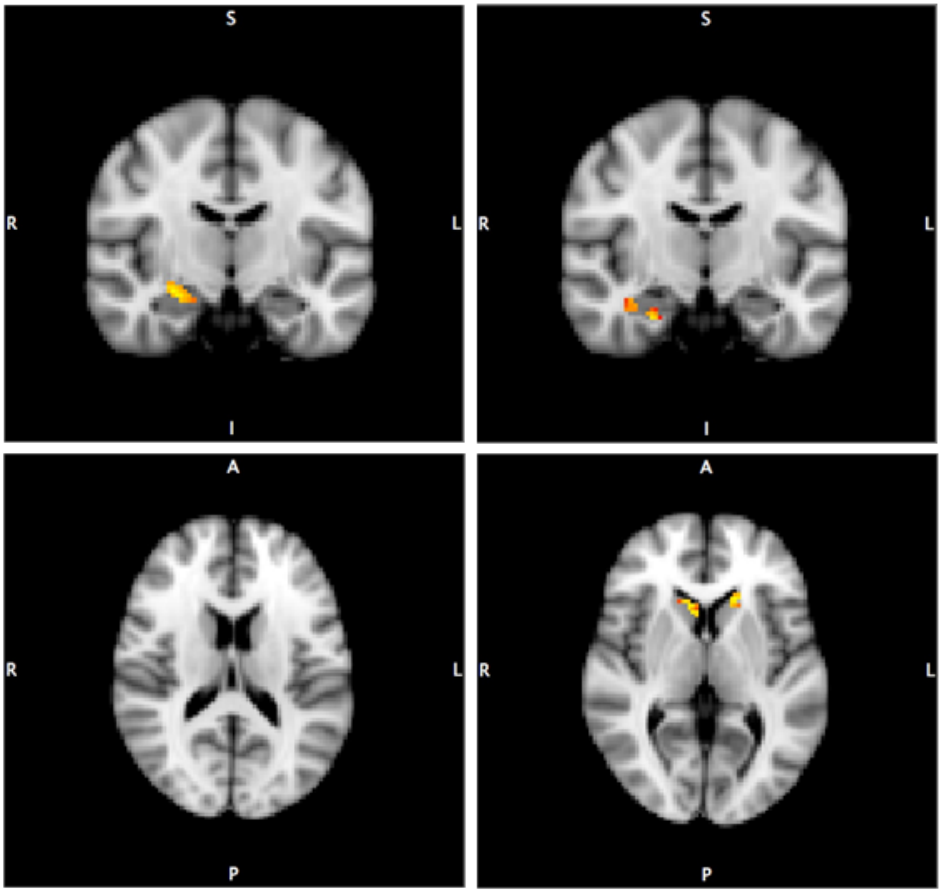


Figure 10. Contrasts for right = *different* versus right = *same*. When the *different* response was assigned to the right key there was increased activation in clusters in CA1 within the right hippocampus (Top Right) and in both left and right caudate (Bottom Right). When the *same* response was assigned to the right key there was increased activation in clusters in CA3 within the right hippocampus (Top Left) but there was not increased activation in the caudate (Bottom Left).

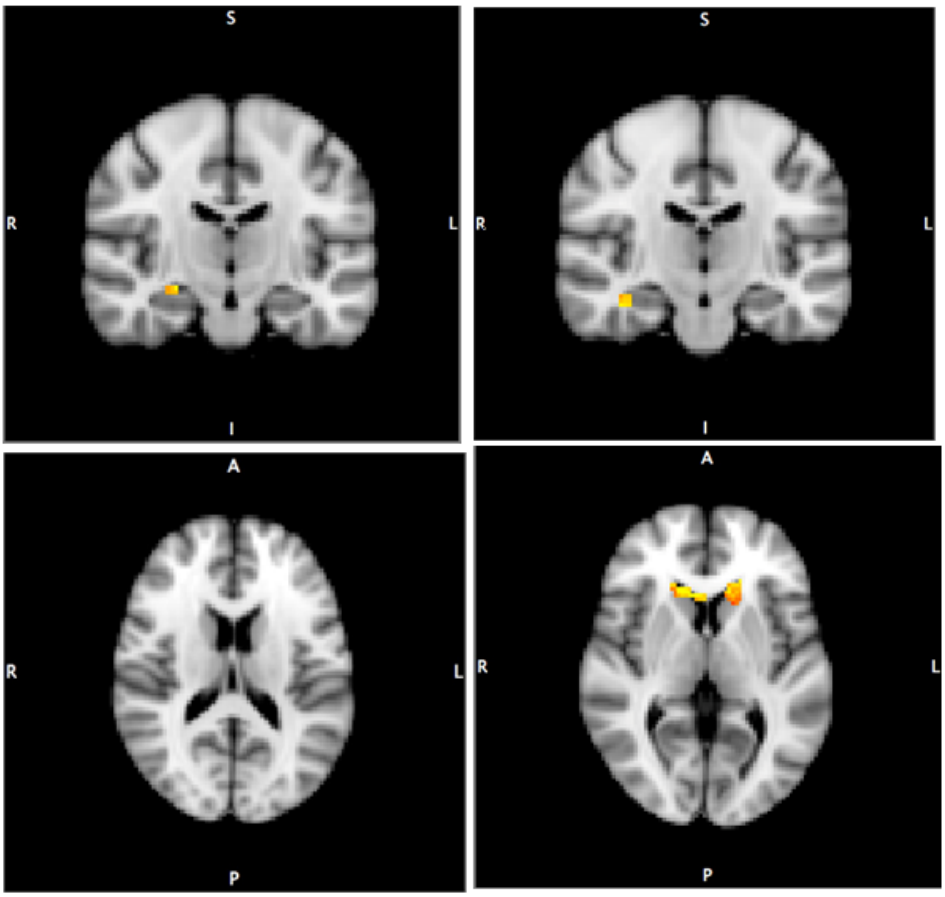


Figure 11. Contrasts for right = *different* during study versus right = *same* during study. When the *different* response was assigned to the right key, for the study period there was increased activation in CA1 within the right hippocampus (Top Right) and in both left and right caudate (Bottom Right). When the *same* response was assigned to the right key, for study period there was increased activation in CA3 within the right hippocampus (Top Left) but there was not increased activation in the caudate (Bottom Left).

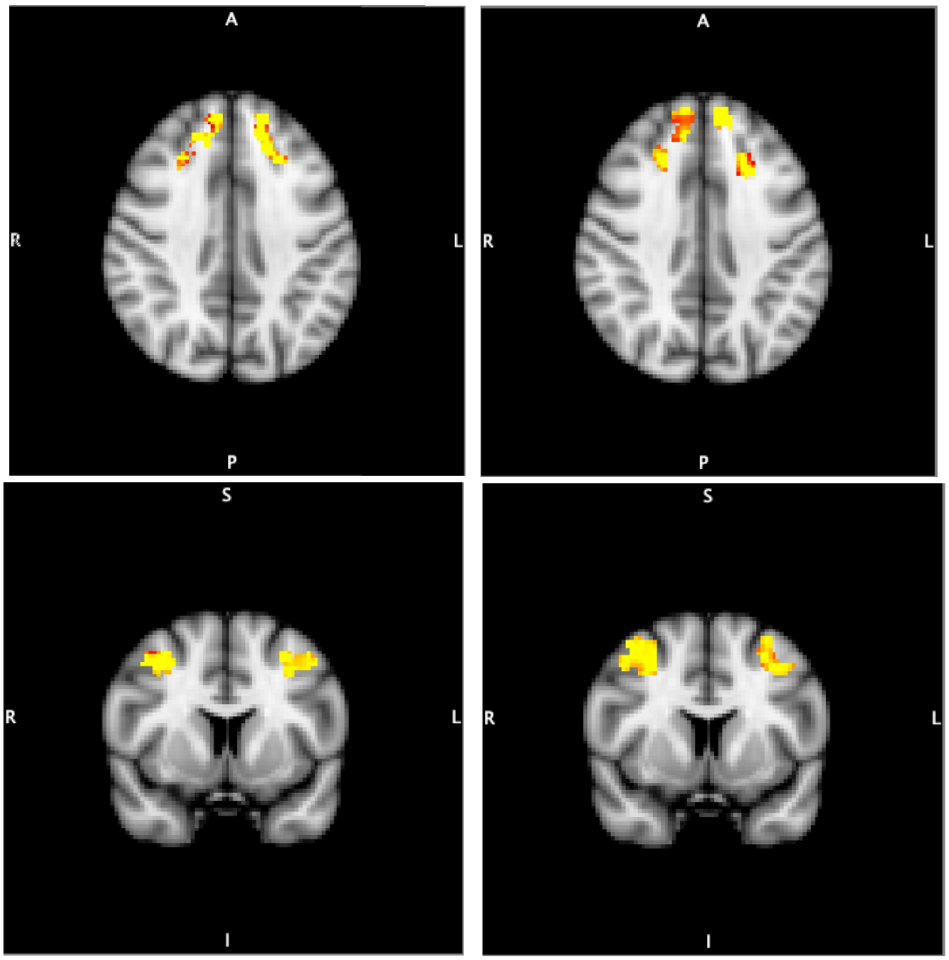


Figure 12. (a) Contrasts for right = *different* during study versus right = *different* during test. (b) Contrasts for right = *same* during study versus right = *same* during test. When the *different* response was assigned to the right key, for the study period there was increased activation in clusters in both left and right Brodmann area 8B (Top Right) in dorsal frontal cortex. For the test period there was increased activation in clusters in both left and right Brodmann area 8A (Bottom Right) in dorsal frontal cortex. When the *same* response was assigned to the right key, for study period there was increased activation in clusters in both left and right Brodmann area 8B (Top Left) in dorsal frontal cortex. For the test period there was increased activation in clusters in both left and right Brodmann area 8A (Bottom Left) in dorsal frontal cortex.

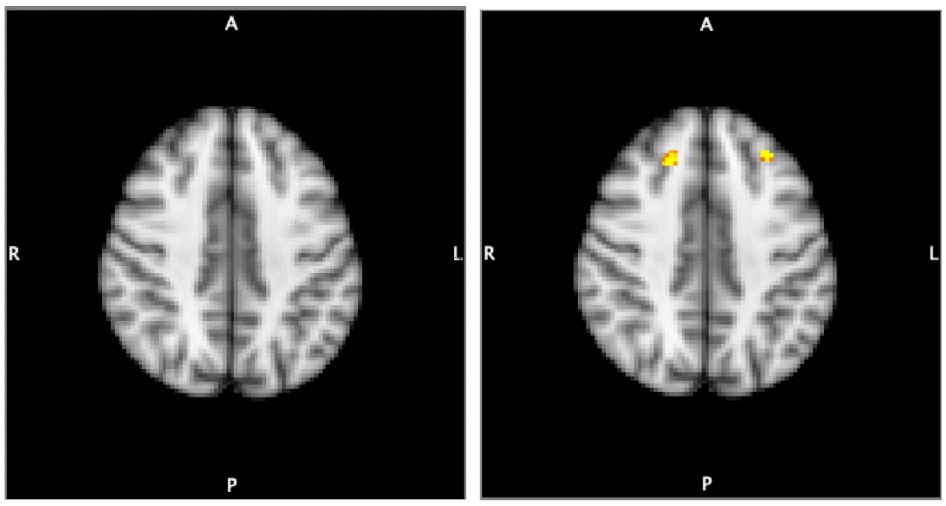


Figure 13. Contrasts for right = *different* versus right = *same* during study in BA 8A. When the *different* response was assigned to the right key there was increased activation in clusters in BA 8B (Right). But when the *same* response was assigned to the right key, no cluster was identified in BA 8B (Left).

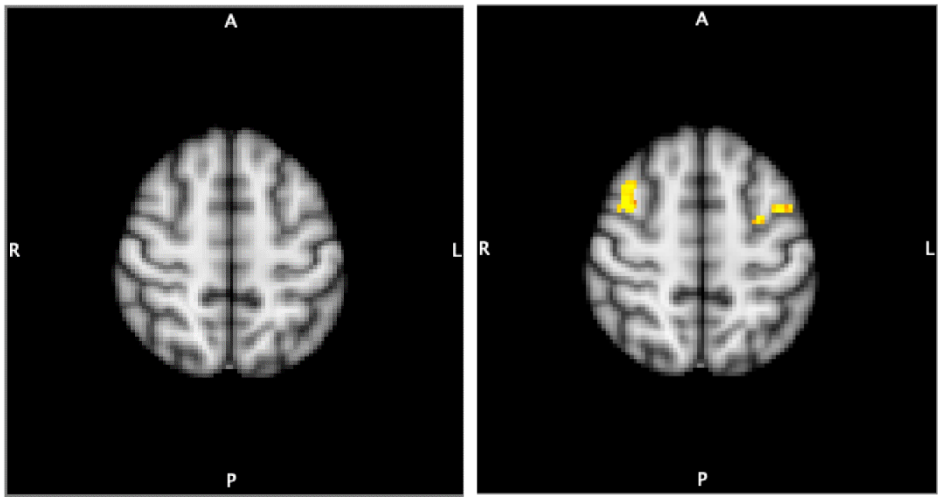


Figure 14. Contrasts for right = *different* versus right = *same* during test in BA 8A. When the *different* response was assigned to the right key there was increased activation in clusters in BA 8A (Right). But when the *same* response was assigned to the right key, no cluster was identified in BA 8A (Left).

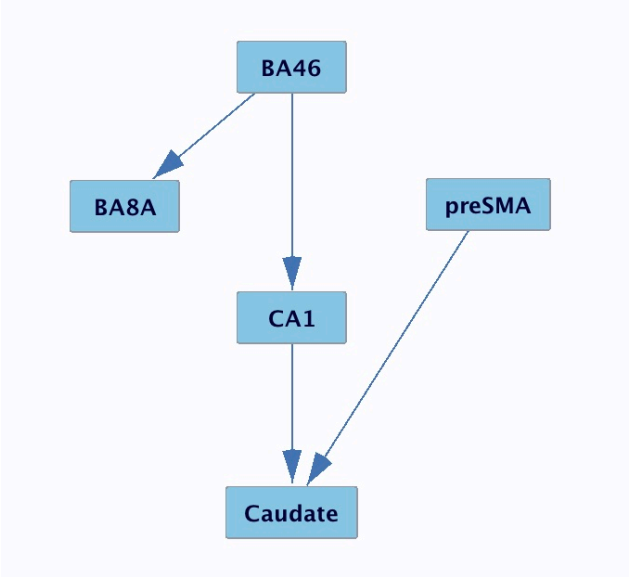


Figure 15. Directed acyclic graph showing inter-regional connectivity for responses under right-*different* response assignment.