Activation Shift from Medial to Lateral Temporal Cortex Associated with Recency Judgments Following Impoverished Encoding

Recency judgements can be performed on the basis of across-event relational information that directly provides temporal order among past events. Non-relational item-based information internal to individual past events, such as information retrieved through familiarity, may also contribute to recency judgements. The present functional magnetic resonance imaging study examined neural substrates for item-based processing during recency judgements as an alternative to relational recency judgements. One half of word stimuli were encoded relationally prior to recency judgements, and the relational encoding of the other half was hampered such that the words were processed relatively in an item-based manner. Brain activity in the medial temporal lobe was observed during recency judgements for words studied with relational memory processing, whereas brain activity in the lateral temporal cortex was observed during recency judgements for words studied relatively in an item-based manner. It was revealed further that recognition of individual words per se, which can also be regarded as familiarity/recency judgements but is non-relational in nature, also activated the lateral temporal region. These results indicate multiple routes for recency judgements within the temporal lobe that are recruited depending on how past episodes are represented and retrieved for judgements of their temporal order.

Keywords: episodic, memory, recency, retrieval, semantic, temporal

Introduction

Recency judgements (Yntema and Trask, 1963; Milner, 1971), retrieval of the temporal order of past events, have been investigated intensively in relation to the prefrontal cortex. Lesions to the prefrontal cortex impair recency judgement performance (Shimamura et al., 1990; Milner et al., 1991; Petrides, 1991; Butters et al., 1994), and neuroimaging studies confirmed the prefrontal contribution to recency judgements (Eyler Zorrilla et al., 1996; Cabeza et al., 1997, 2000; Dobbins et al., 2002, 2003; Konishi et al., 2002; Suzuki et al., 2002). On the other hand, the temporal lobe involvement in recency judgements has been less elucidated. Although lesions to the medial temporal lobe have also been reported to impair recency judgements (Kopelman et al., 1997; Mayes et al., 2001), the lesion effects are relatively milder than the profound mnemonic impairments in the traditional medial temporal amnesic syndrome (Scoville and Milner, 1957; Squire et al., 1981; Corkin, 1984; Sagar et al., 1990).

It is noteworthy that recency judgements can be achieved by multiple solutions. One solution may involve relational memory processing implemented in the hippocampal system (Cohen and Eichenbaum, 1993; Squire, 1994; Henke et al., 1999; Davachi and Wagner, 2002; Giovanello et al., 2004; Preston et al., 2004; Prince et al., 2005), wherein temporal relations that have been coded across events are retrieved and the relative recency is decided directly. An alternative solution may involve retrieval of item-based information internal to individual events. For example, relative recency of the events can be determined on the basis of their familiarity that should be felt stronger for more recent events (Mandler, 1980; Cabeza et al., 1997; Aggleton and Brown, 1990; Henson et al., 1999, 2003; Eldridge et al., 2000; Yonelinas, 2002; Davachi et al., 2003; Ranganath et al., 2003; Wheeler and Buckner, 2004; Yonelinas et al., 2005).

Shifting to another solution when one solution is ineffective may account for the milder impairments in recency judgements following lesions to the medial temporal lobe (Squire et al., 1981; Sagar et al., 1990; Kopelman et al., 1997; Mayes et al., 2001).

The present functional magnetic resonance imaging (fMRI) study aimed to explore temporal lobe regions that implement item-based recency judgements that emerge when relational recency judgements are dysfunctional. One half of word stimuli were encoded relationally prior to recency judgements, and relational encoding of the other half was hampered by imposing distracter task performance such that the words were processed relatively in a non-relational manner (Fig. 1). Recency judgements for words encoded relatively in a relational way were intermixed and compared with recency judgements for words encoded relatively in an item-based manner (Experiment 1). Prominent double dissociation within the temporal lobe was found between medial temporal activation during recency judgements for relationally encoded words and lateral temporal activation during recency judgements for words encoded under the hampered, item-based condition. To characterize the lateral temporal activation further, a second experiment (Experiment 2) was conducted that investigated the recovery of individual events per se in a simpler form using word recognition where word encoding was processed in an item-based manner: word stimuli were deep or shallow encoded individually, and recognition of the deep and shallow encoded words were intermixed and compared. The lateral temporal region was activated more during recognition of deeply encoded words than during recognition of shallowly encoded words, suggesting that the lateral temporal activation reflected successful recovery of past episodes.

Materials and Methods

Subjects and fMRI Procedures

Informed consent was obtained from 56 healthy right-handed subjects. Thirty-two subjects (aged 20–31 years, 13 males) participated in Experiment 1, and 24 subjects (aged 20–26 years, 10 males) participated in Experiment 2. MRI scans were conducted using experimental procedures approved by the institutional review board of the University of Tokyo School of Medicine, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113, Japan
of Tokyo School of Medicine. In Experiment 1, three subjects were unable to complete the scan and two subjects performed the task poorly. In Experiment 2, two subjects were unable to complete the scan, and their data were excluded from analysis. Therefore, data from the remaining 27 subjects (aged 20-31 years, 11 males) in Experiment 1 and the 22 subjects (aged 20-26 years, 9 males) in Experiment 2 are reported here. Scanning was conducted using a 1.5 T fMRI system. Scout images were first collected to align the field of view centered on the subject's brain. Then T2-weighted spin-echo images were obtained for anatomical reference (TR = 5.5 s, TE = 30 ms, 75 slices, slice thickness = 2 mm, in-plane resolution = 2 x 2 mm). For functional imaging, gradient echo echo-planar sequences were used (TR = 3 s, TE = 50 ms, flip angle = 90°, 22 slices, cubic voxel of 4 mm and 3 mm for Experiments 1 and 2, respectively). The first four functional images in each run were excluded from the analysis to take into account the equilibrium of longitudinal magnetization.

Behavioral Procedures

Visual stimuli were presented to subjects by projecting them onto a screen. Subjects viewed the screen through prism glasses. A magnet-compatible button press was based on a fiber-optic switch was used to record subjects’ performance.

The recency judgements task in Experiment 1 consisted of two main phases, study and test (Fig. 1). During the study phase, 12 words were presented sequentially. For the first six words, subjects were instructed to intentionally encode them in a relational way for later recency judgements. Each word was presented for 3 s, with an inter-stimulus interval (presentation of a white fixation cross) of 3 s. The encoding of the last six words differed from the relational encoding such that relational encoding would be hampered and later recency judgements would be shifted relatively from relational to item-based one. First, subjects simultaneously performed odd/even judgements on the number of characters that constituted each of the studied words. Second, each word was presented for 3 s (as opposed to 3 s), with an inter-stimulus interval of 1 s. In between the two encoding conditions, the fixation cross turned red for 3 s to signal the encoding condition change. The words were concrete nouns taken from an object stimulus set (Snodgrass and Vanderwart, 1980) and were presented in strings of Japanese characters.

The test phase was administered while functional images were acquired. The interval between the study and test phases was ~1 min. In one recency judgement trial, two words in the studied list were simultaneously presented, one to the right and the other to the left for 3 s with an interval of stimulus onset set at 4 s (that is, 3 s word presentation plus 1 s fixation). The subjects were instructed to choose which word had been studied more recently. The right or left word was chosen by the subjects by pressing a right or left button, respectively, using the same right thumb. There were two types of trials of interest: trials with word pairs from the relational encoding condition (relational trials) and trials with word pairs from the hampered encoding condition (item-based trials). The temporal distance between paired words was 2 words, and word stimuli at the end positions (W1, W6, W7 and W12) were not used in trials of central interest to minimize possible primacy and recency effects. The specific pair was W2-W4 or W3-W5 for relational trials, and W8-W10 or W9-W11 for item-based trials. Any pair out of W1-W7, W1-W12, W6-W7 and W6-W12, was also included as a residual trial type of no interest, in order to keep the subjects' strategy of encoding the twelve words in a totally seamless way, instead of two six-word lists, during the study phase. The four recency judgement trials (two relational and two item-based trials), together with the two residual and two fixation gap trials, were pseudo-randomly counter-balanced in each run. The trial type (relational or item-based) for each word pair was also counterbalanced across subjects by modifying the word orders in the study lists. Twelve runs were administered to the subjects, each with a different word list.

After explaining the general task rules to the subjects, a story-making strategy was instructed to enhance relational processing during encoding. The subjects were instructed to make up their own story by relating sequentially presented words that had otherwise no context among them, and were also informed that this encoding strategy was a powerful one to solve later recency judgements. A translation of the instruction was like this:

The temporal order judgement might be a bit tough for you, but it will be much easier if you try hard when you learn the words. You will not perform well by trying hard to judge the temporal order, but trying hard to learn the words is much more important. A most powerful way to do so is to make up your own stories from the string of words, and trying hard to learn the words means trying hard to make up your own story. Then you will judge the temporal order much more easily.

Although such stories are usually too ambiguous to tell, a hypothetical example of the story would be: 'Looking out of the window, a cat was eating an onion, and then I answered the phone and heard a tiger playing ball. . .\' The subjects were asked if they were successful in making up such stories in practice sessions.

To prevent the subjects from rehearsing the words between the study and test phases, a modified Wisconsin card sorting test (WCST) (Konishi et al., 2003) was performed for ~30 s as a distracter task. The modified WCST contained verbal demands such as the maintenance of current dimensions and the reception of verbal instruction of next dimensions, and is considered to be suitable as a distracter (Petersen and Petersen, 1959). The subjects were familiarized with the above procedures in the study-distracter-test sequence prior to scanning sessions.

In Experiment 2, a recognition task was used to examine neural substrates for item-based processing. Recognition can be regarded as recency discrimination between items presented during the study phase and items presented prior to it, but the related processes should be item-based. The recognition task similarly had the study and test phases. During the study phase, 24 words were sequentially presented. For the first 12 words, the subjects were instructed to perform semantic judgements on each of the words individually, pressing the right button when the word indicated a living thing or food, and pressing the left button when the word indicated neither option. In the deep encoding, each word was presented for 2.5 s, with an inter-stimulus interval (presentation of a white fixation cross) of 0.5 s. On the other hand, encoding of the last 12 words was shallow. Subjects performed odd/even judgements on the number of characters that constituted the words. Each word was presented for 0.5 s, with an inter-stimulus interval of 0.5 s. In between the two encoding conditions, the fixation cross turned red for 3 s to signal the encoding condition change.

The test phase was administered while functional images were acquired, and the interval between the study and test phases was ~1 min, similarly to the Experiment 1. In one recognition trial, one word in the studied list and a new word were simultaneously presented, one
to the right and the other to the left for 1.5 s with a stimulus onset asynchrony of 2.0 s (that is, 1.5 s word plus 0.5 s fixation). The subjects were instructed to choose which word had been studied previously. The trials of interest were trials with old words from the deep encoding condition (deep trials) and trials with old words from the shallow encoding condition (shallow trials). The twenty forced-choice recognition trials (10 deep and 10 shallow trials), together with 10 fixation gap trials, were pseudo-randomly counterbalanced in each run. The first and the last words in the first and the last twelve-word lists were not used to minimize the possible primacy and recency effects. The trial type (deep or shallow) for each word pair was also counterbalanced across subjects by modifying the word orders in the study lists. Four runs were administered to the subjects, each with a different word list.

**Data Analysis**

Data were analyzed using SPM99 (http://www.filion.ucl.ac.uk/spm/). Functional images were realigned, slice timing corrected, normalized to the default template with interpolation to a $2 \times 2 \times 2$ mm space, and spatially smoothed. Then event timing was coded into a general linear model (GLM) (Worsley and Friston, 1995). In Experiment 1, the two types of events of central interest, correct relational trials and correct item-based trials, together with other types of trials and error trials, were coded using the canonical hemodynamic response function, time-locked to the onset of these trials. In Experiment 2, the two trials of interest were correct deep and shallow trials.

Images of parameter estimates for the signal response magnitudes (i.e. the difference between the baseline and the peak of an estimated transient signal time course) were analyzed in the second-level group analysis using a random effect model. Peak coordinate locations in activation maps were generated using a threshold of 19 or more contiguous significant voxels above $t < 0.001$ ($z > 3.5$) (each voxel: $2 \times 2 \times 2$ mm$^3$) (Konishi et al., 2001). This statistical threshold was set based on an empirical approach whereby the same statistical procedure were applied to a control data set in which no activation should occur (see also Buckner et al. 1998). For this analysis, independent control data from 12 subjects (two functional runs each) were acquired during which the subjects fixated on a small visual cross-hair during the entire duration of the run. Thus, any detected peaks of activation in this control data set would reflect false positives, and the thresholds were set to minimize false positive activations. Critical activations highlighted in the figures (i.e. the lateral and medial temporal regions) cleared $t < 0.05$ corrected for multiple comparison after small volume correction (i.e. restriction of regions of interest for improved statistical power) was employed based on the estimated volume of gray matter in the temporal cortex (100 cm$^3$) (Petrides et al., 2003; Van Essen et al., 2005).

**Results**

The mean correct performances in RELATIONAL and ITEM-BASED trials in Experiment 1 were 91.4 ± 1.2% (mean ± SEM) and 78.1 ± 1.7%, respectively, and the difference was statistically significant [$t (26) = 7.1$, $P < 0.001$]. On the other hand, the mean reaction times in correct relational and item-based trials were 2047 ± 58 and 2081 ± 56 ms, respectively, and the difference was not statistically significant [$P > 0.05$].

Brain activity associated with the difference between relational and item-based trials was revealed by a group analysis using a random effect model as shown in Figure 2. Prominent differential signals in relational trials were observed in the hippocampus ($-30, -30, -8$) ($z = 4.3$). On the other hand, prominent differential signals in item-based trials were observed in the anterior part of the right middle temporal gyrus near Brodmann area 21 at $(50, 6, -30)$ ($z = 4.2$). Figure 2 also shows the double dissociation pattern of the medial and lateral temporal activations by tracing their time courses. A complete list of the activations in both the contrasts is shown in Table 1.

In Experiment 2, the mean correct performances in deep and shallow trials were 95.0 ± 0.9 and 80.0 ± 2.0%, respectively, and the difference was statistically significant [$t (21) = 8.3$, $P < 0.001$]. On the other hand, the mean reaction times in correct deep and shallow trials were 1095 ± 21 and 1191 ± 23 ms, respectively, and the difference was statistically significant [$t (21) = 6.9$, $P < 0.001$].

The contrast deep minus shallow revealed multiple activations including the lateral temporal activation at (56, 4, -34) ($z = 4.3$), as shown in Figure 3. No significant activation was detected in the opposite contrast, indicating that, unlike in the case of the recency judgement paradigm in Experiment 1, the behavioral manipulation during the study phase in Experiment 2 did not alter the quality of retrieval processes during the recognition task. The lateral temporal activations in Experiments 1 and 2 are close, separated by <8 mm, comparable to the spatial smoothing size of this study. The differential activation was significant in Experiment 1 [$t (26) = 2.9$, $P < 0.01$] based on the peak coordinates of Experiment 2 (56, 4, -34), and the differential activation was also significant in Experiment 2 [$t (21) = 3.4$, $P < 0.005$] based on the peak coordinates of Experiment 1.
(50, 6, –30), indicating the lateral temporal activation is common to the two experiments.

Figure 4 shows the signal magnitude for deep and shallow trials determined based on the regions detected in Experiment 1. The signal difference in the lateral temporal region was significant \( t(21) = 3.4, P < 0.005 \). On the other hand, the medial temporal region was not differentially activated \( (P > 0.05) \), although a more anterior part of the hippocampus showed heightened activity in deep versus shallow \( t(21) = 2.4, P < 0.05 \), consistent with previous studies demonstrating hippocampal involvement in recollection. The functional dissociation of the medial and lateral temporal regions was also significant, as revealed by the region-by-trial type interaction of two-way analysis of variance \( F(1, 21) = 11.4, P < 0.005 \).

**Discussion**

The present study examined the neural substrates for item-based recency judgements by comparing trials requiring relational recency judgements with trials requiring hampered, item-based recency judgements (Experiment 1). The relational trials differentially activated the medial temporal region, whereas the item-based trials differentially activated the lateral temporal region, suggesting a change in the type of retrieved information: during item-based trials the relational processes were recruited to a lesser degree, and the item-based processes were enhanced instead. On the other hand, no such double dissociation pattern was observed in Experiment 2, suggesting that retrieved information did not change during the word recognition, and it was confirmed further that recognition of individual words per se, which can also be regarded as familiarity/recency judgements but is non-relational in nature, also activated this lateral temporal region. These results suggest that the lateral temporal region implements item-based recency judgements that emerged themselves when relational processing was dysfunctional.

The medial temporal region was differentially activated in the contrast relational versus item-based recency judgement trials in Experiment 1. The medial temporal activation is consistent with the demands in the relational trials for the relational processing thought to be implemented in the hippocampal system (Cohen and Eichenbaum, 1993; Squire, 1994; Henke et al., 1999; Davachi and Wagner, 2002; Giovanello et al., 2004; Preston et al., 2004; Prince et al., 2005). It is nonetheless possible that the medial temporal activation also reflects recollection of past episodes (Aggleton and Brown, 1999; Eldridge et al., 2000; Yonelinas, 2002; Yonelinas et al., 2005). On the other hand, the lateral temporal region was differentially activated during item-based recency judgement trials for the words studied relatively in a non-relational manner. Although the correct performance in item-based trials were significantly lower than that in relational trials, it is unlikely that the activation reflects retrieval control processes that are recruited during effortful retrieval (Thompson-Schill et al., 1997; Sohn et al., 2003; Wheeler and Buckner, 2003), or some nonspecific components such as guessing; the correct performance in deep recognition trials in Experiment 2 was higher than that in shallow trials, but deep trials yielded the differential activation in the same lateral temporal region. Thus the results of these two experiments indicate that the lateral temporal region reflects successful recovery of information related to individual words. Therefore, although the present task designs include confound between encoding and time (i.e. relational and deep conditions were always presented before item-based and shallow conditions), the medial and lateral temporal activations would not be explained by the confound alone. A similar caveat could be addressed regarding different durations of presentation items in Experiment 1 and 2. The activation in the medial temporal region was shifted to the lateral temporal region following the task manipulation to the encoding condition. Thus the activation shift during recency judgement may likely...
reflect different re-instantiation of the encoding differences. It is to be noted, however, that an alternative possibility exists that the requirement to use different kinds of information during the test phase may also result in the activation shift. Interestingly, the item-based trials in Experiment 1 elicited an increase in the brain activity relative to the fixation baseline in the lateral temporal region, whereas the shallow trials in Experiment 2 elicited a decrease in the brain activity relative to the fixation baseline. The results of the comparison with the fixation trials in the two experiments illustrate the different ongoing processes in the fixation trials intervened by task trials requiring different cognitive demands that are distinct from the physiological resting state (Gusnard and Raichle, 2001).

The item-based retrieval processes may well involve an episodic memory system that implements recollection and familiarity (Mandler, 1980; Cabeza et al., 1997; Aggleton and Brown, 1999; Henson et al., 1999, 2003; Eldridge et al., 2000; Yonelinas, 2002; Davachi et al., 2003; Ranganath et al., 2003; Wheeler et al., 2004; Yonelinas et al., 2005): recollected contextual information related to individual events (but not related to other events directly) could be used to infer the relative temporal order among other events. Familiarity of individual events should be stronger for more recent events, and the neural substrates outside the perirhinal cortex have been provided by neurophysiological studies demonstrating familiarity/recency neurons in the monkey area TE (Xiang and Brown, 1998; Brown and Aggleton, 2001). It is also possible that the non-relational processes involve other implicit processes: perceptual fluency, fluent reprocessing of perceptual aspects of recently experienced stimuli thought to support repetition priming effects on implicit perceptual memory tests (Wagner and Gabrieli, 1998), may serve as a cue to relative recency. Moreover, the non-relational processes might involve semantic memory system, especially in light of the cortical localization of the activation in the anterior lateral temporal cortex that has repeatedly been implicated in semantic memory (Martin and Chao, 2001; Hodges et al., 1992; Kapur et al., 1992; Damasio et al., 1996; Gorno Tempini et al., 1998; McClelland and Rogers, 2003; Tsukiura et al., 2002).

The left hemisphere of the temporal cortex has been implicated in word-related processing in the context of episodic memory (Kelley et al., 1998; McDermott et al., 1999). Although the presentation of Japanese characters might account for the right hemispheric activation of the lateral temporal region, the right hemispheric activation in the present study is consistent with the previous neuropsychological literature: the right lateral temporal cortex is involved in newly learned, but not familiar, semantic knowledge (Tsukiura et al., 2002), as opposed to the left lateral temporal cortex typically implicated in semantic memory system proper, regardless of the stimulus modality (e.g. word and face) (Hodges et al., 1992; Kapur et al., 1992; Damasio et al., 1996; Gorno Tempini et al., 1998; Martin and Chao, 2001; McClelland and Rogers, 2002; Tsukiura et al., 2002). Although more precise accounts of the lateral temporal activation need further exploration, the present study suggests that the lateral temporal region implements item-based recency judgements that are recruited as an alternative to relational recency judgements.

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