

A mini-review of fMRI studies of human medial temporal lobe activity associated
with recognition memory

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Abstract

This review considers event-related functional magnetic resonance imaging (fMRI) studies of human recognition memory that have or have not reported activations within the medial temporal lobes (MTL). For comparisons both between items at study (encoding) and between items at test (recognition), MTL activations are characterised as left/right, anterior/posterior and hippocampus/surrounding cortex, and as a function of the stimulus material and relevance of item/source information. Though no clear pattern emerges, there are trends suggesting differences between item and source information, verbal and spatial information, and a role for encoding processes during recognition tests. Important future directions are considered.

The recognition memory paradigm has been used with functional neuroimaging to study human long-term memory for over a decade. In this paradigm, participants are exposed to a series of items during a “study” phase, which are later repeated in a “test” phase (“old items”) intermixed with further items that were not studied (“new items”). The participant’s basic task is to distinguish old items from new items, though this task is often extended to include, for example, confidence judgments, or judgments about some aspect of the context in which an old item was studied (so-called “source information”).

Both psychological and neuroanatomical theories of recognition memory have been the subject of considerable debate. For example, some psychologists have proposed that recognition memory is supported by two distinct processes, such as recollection and familiarity (Mandler, 1980; Yonelinas, 2002). Recollection generally refers to retrieval (recall) of source information; familiarity refers to a feeling attributed to recent exposure to an item, in the absence of retrieval of contextual information. Others however have argued that behavioural data from the recognition memory paradigm can be explained by assuming only a single continuum of memory strength (usually within the context of signal detection theory, Heathcote, 2003; Dunn, 2004). Regarding neuroanatomical theories, some have argued for two MTL subsystems: for example - one involving hippocampus and anterior thalamus and the other involving perirhinal cortex and medial dorsal thalamus - that subserve functions analogous to recollection and familiarity respectively (Aggleton & Brown, 1999). Others however have argued that the MTL is an integrated system and that current simple dichotomies do not capture functional differences that might exist between its components (Squire, Stark & Clark, 2004).

This mini-review focuses on two basic contrasts that can be examined with functional imaging: 1) between items in the study phase that are later recognised (“subsequent hits”) and those later forgotten (“subsequent misses”), and 2) between old items in the test phase that are recognised (“hits”) and new items that are not recognised (“correct rejections”). The former contrast is called the “subsequent memory effect” and is used to investigate encoding of items into memory. The latter is called the “old-new effect”, and is used to investigate successful recognition (see Figure 1). The main interest is whether various experimental

manipulations at either study or test have consistently revealed dissociable patterns of activity within MTL associated with such encoding and/or recognition.

The remit of this mini-review is further constrained as follows. Firstly, I only review event-related fMRI experiments. The inferior spatial resolution of Positron Emission Tomography (PET) means that it can be difficult to determine the precise location of activations within the MTL. Moreover, the fact that PET normally requires averaging over tens of seconds of a cognitive task (restricting it to so-called “blocked” experimental designs) means that it is difficult to test the two comparisons above. For the same reason, I do not consider blocked fMRI experiments (see Rugg & Henson, 2002 and Herron et al, 2004, for further discussion). I also only consider group-averaged data from healthy individuals.

I distinguish two types of MTL activity: that in hippocampus, and that in surrounding medial temporal cortex (MTC). The latter encompasses both rhinal and parahippocampal cortex. (Although hippocampus is also cortex, I use “MTC” simply to distinguish hippocampal archicortex from surrounding transitional- and neo- cortex.) The reason for such a coarse distinction, even with the superior resolution of fMRI over PET, is that precise localisation within MTL rarely achieved, given the susceptibility-induced distortions associated with echo-planar fMRI (Constable et al., 2000) and the fact that most authors report mean locations within brains that were normalised to a common space and spatially smoothed, which reduce spatial resolution. The reason for choosing this particular distinction is to evaluate theories of functional specialisation that distinguish hippocampus from surrounding MTC, like that of Aggleton and Brown (1999).

In the present review, I rely on the authors’ anatomical classifications (i.e, have not attempted to validate them), though I do attempt to characterise activations further as anterior or posterior (as well as left/right), based on a second proposal for a functional dissociation along the anterior-posterior axis (Lepage et al., 1999; Schacter & Wagner, 1999). For this I used an arbitrary division of $y=-20$ in Talairach space (when such coordinates are reported), so this is again a coarse classification (and it should be noted that these coordinates are the maxima of diffuse activations that can extend across the above divisions). I decided not to tabulate Talairach coordinates because they are determined in different ways across

experiments and because they can be misleading for anatomically-distinct regions within close proximity (Maguire, 1998). Finally, different authors use different statistical criteria for the definition of “reliable” activations, which are difficult to inter-relate, particularly when authors focus on a priori regions of interest. The reader should therefore remember that some differences across experiments may reflect different levels of statistical stringency.

In order to see whether any patterns emerge in the conditions under which MTL is activated (in particular, whether those conditions differ for hippocampus and MTC), I also categorise the experiments along different dimensions. There would appear to be only a few such dimensions along which categories can be distinguished that include appreciable numbers of experiments. Apart from the encoding/recognition distinction above, the most obvious is the type of stimulus material (e.g, words, objects or scenes). The next most obvious is the type of task or instructions used at study and at test. These differ across nearly all experiments, so I grouped the task/instructions into those that engender encoding of, or require retrieval of, source information, and those that do not (for which “item information” is sufficient). By source information, I refer to some form of episodic context (e.g, spatiotemporal characteristics of the study episode), but do not distinguish between extrinsic or intrinsic context (Baddeley, 1982), or external and internal source (Johnson et al., 1993). Though obviously related to the distinction between recollection and familiarity (Mandler, 1980; Yonelinas, 2002), I use the source/item distinction here as an operational distinction based on task requirements, rather than the more theoretically-loaded terms of recollection and familiarity. In Tables 1 and 2, experiments are therefore grouped first by stimulus material, and then by whether or not the comparison separates source and item information.

As regards further dimensions relevant to animal experiments of recognition memory (like those reported in other articles in this special issue), it is interesting to note that in the present human experiments: 1) the items are invariably trial-unique (though they may differ in their level of pre-experimental familiarity, particularly for verbal material), 2) only a few experiments explicitly manipulate the similarity between old items and new items, 3) the test format is more often a variant of “yes/no” recognition to single items, rather than “forced choice” between two or more items, and 4) nearly all experiments use visual items, most

often words.

Encoding (subsequent memory effects)

Table 1 shows comparisons that examined subsequent memory effects at study. For the basic comparison of subsequent hits (sHt) versus subsequent misses (sMs) according to a yes/no recognition memory test for single words, three experiments reported activation in left anterior hippocampus (Fletcher et al, 2003; Morcom et al, 2003; Otten et al, 2001), three reported activation in left or right MTC (Morcom et al, 2003; Otten et al, 2002; Wagner et al, 1998) and five failed to find reliable MTL activations (Baker et al, 2001; Buckner et al, 2001; Henson et al, in press; Kirchoff et al, 2000; Otten & Rugg, 2001). One potentially important factor is whether hits are confined to confident recognition decisions, as is the case in many but not all of the above experiments. This is important because some hits (those typically made with low confidence) can be guesses (Otten et al, 2001) and will therefore weaken the ability to detect true subsequent memory effects. Another potential factor is the type of study task. In all the above experiments, participants were not informed that their memory would be tested later (so-called “incidental” encoding). Nonetheless, the type of incidental task varied, from semantic to orthographic decisions, or even recognition decisions from a previous study phase (Buckner et al, 2001). Of the four experiments that directly compared MTL activity in different study tasks, none found a reliable interaction between study task and subsequent memory effects within the MTL (though such interactions were found elsewhere, e.g, in prefrontal and parietal cortices, Otten et al, 2002): for either semantic and orthographic tasks (Fletcher et al, 2003; Otten et al, 2001) or semantic and phonological tasks (Otten & Rugg, 2001; Otten et al, 2002). This suggests the type of processing performed on study items, though it might affect the overall level of memory, does not affect differences between remembered and forgotten items in the MTL.

< insert Table 1 about here >

This apparent independence of MTL subsequent memory effects from participants’ intention to memorize or type of task is supported by Reber et al (2002), who found left

posterior hippocampus and MTC activation related to subsequent memory for words, regardless of whether each word was followed by a cue to either remember it or forget it (the “directed forgetting” paradigm, Bjork, 1989). This suggests that the MTL automatically encodes experiences. However task-independence is not supported by Davachi et al (2002), who asked participants to either repeat triplets of words verbatim (Rote condition) or reorder them according to semantic attributes (Elaborate condition). Only in the Elaborate condition did responses in left anterior and right posterior hippocampus increase with the number of words per triplet later recognised (when presented individually at test). This suggests that hippocampal activation only predicts subsequent memory when a certain level of semantic elaboration is performed. Interestingly, Davachi et al (2002) also found right posterior MTC responses that decreased as the number of recognised words increased (a similar decrease in right MTC was found for subsequent Remember versus subsequent Know judgments to single words, Henson et al, 1999, and sHt versus sMs for face-name pairs during a recognition test, Kirwan & Stark, 2004; see below).

An experiment by Kensinger et al (2003) examined subsequent recognition as a function of whether an incidental semantic task was performed concurrently with either an “Easy” or “Hard” secondary task. Left MTC showed activation related to subsequent memory in both Easy and Hard conditions, whereas left hippocampus only showed subsequent memory effects in the Easy condition. Taken together with those above, these findings suggest that, while encoding in MTL may be “automatic” in one sense (i.e, occur under incidental tasks, regardless of instructions to forget or the type of *information* emphasised by the task), it does depend on a certain level of attentional resources and possibly a certain type of *processing* (e.g, elaboration) of that information.

The above experiments did not directly test whether correct subsequent recognition was based on item or source information (though there is evidence that source information is less well encoded under demanding dual-task conditions, Kensinger et al, 2003). Two experiments using words attempted to isolate encoding that leads to later retrieval of source information. In the experiment of Davachi et al (2003), participants saw words and were randomly cued to either imagine scenes associated with those words, or imagine how they

would sound if read backwards. In a later recognition test, they were asked whether each item was old, and if so, whether it was imaged or read backwards. Left anterior MTC activation predicted subsequent item memory, but did not differ according to whether the study task was retrieved correctly. Bilateral hippocampus and left posterior MTC however were more responsive to items for which the study task was retrieved correctly than to items that were recognised but their study task not retrieved. These results suggest that anterior MTC (which was identified as perirhinal cortex) encodes item but not source information, whereas hippocampus and posterior MTC (which was identified as parahippocampal cortex) encode only source information.

An experiment by Ranganath et al (2004) came to similar conclusions. At study, words were presented in two colours, which cued one of two incidental tasks; at test, participants made a six-way confidence judgment for item recognition, followed by a colour/task source judgment. Left anterior MTC activity increased linearly with subsequent confidence levels 1-5 (excluding the most confident level 6). For items recognised with high confidence (rated 4 or more), right posterior hippocampus and right posterior MTC were more active for those associated with correct versus incorrect source judgments. This pattern is generally consistent with the interpretation of Davachi et al (2003).

An experiment by Cansino et al (2002) used objects rather than words, which were presented at study in one of four spatial locations (corners of the screen). They failed however to find any subsequent memory effects within MTL, even when comparing subsequent correct versus incorrect retrieval of the spatial source. The reason for this is unknown, though they did find MTL differences at test (see later).

Three experiments looked at associative recognition, in which pairs of items at study were either presented again during test (“intact”) or rearranged such that the two items in a test pair came from different study pairs (“rearranged”). Since intact and rearranged pairs cannot be distinguished using item information alone, their comparison is believed to isolate associative or relational information (which I characterise in Tables 1-2 as another example of source information, for simplicity). Jackson et al (2004) used pairs of words and found left anterior hippocampus and bilateral anterior MTC activation for intact pairs recognised as

“intact” than for intact pairs judged to be “rearranged” (pairs in which one or more items were not recognised at all were classified separately). Sperling et al (2003) presented pairs consisting of a face and a name, followed by two-alternative forced choice (2AFC) for two names presented with a face (one name paired with that face at study, the other paired with a different face at study). Study pairs later attracting high confidence, correct decisions produced greater responses in bilateral anterior hippocampus than those with later incorrect decisions. Kirwan and Stark (2004) also used face-name pairs but an intact/rearranged/new decision at test (similar to Jackson et al, 2004) rather than 2AFC. They found right hippocampal and right posterior MTC (identified as parahippocampal cortex) activation for intact pairs called “intact” versus intact pairs called “rearranged”. Assuming that two items in a study pair were not unitised into a single “item”, all three experiments suggest that hippocampus is important for encoding associations between items. If the requirements for encoding associations between items are equivalent to those for encoding associations between an item and contextual information, then these results are consistent with those from source memory tasks considered above.

Kirwan and Stark (2004) also found that more anterior regions in right MTC (including what was identified as perirhinal cortex) showed comparable levels of activation for both intact pairs called “intact” and intact pairs called “rearranged” relative to intact pairs called “new” (by virtue of the face and/or name being forgotten). This is consistent with the suggestion of Davachi et al (2003) that perirhinal cortex supports subsequent item memory, whereas hippocampus and parahippocampus support subsequent source memory (though see Kirwan & Stark, 2004, for further discussion).

Four experiments used visual scenes rather than words. All four reported bilateral MTC subsequent memory effects (Brewer et al, 1989; Kirchhoff et al, 2000; Stark & Okado, 2003; Weis et al, 2004), in addition to bilateral posterior hippocampus in the Kirchhoff et al (2000) and Stark and Okado (2003) experiments. Only Brewer et al (1989) made an attempt to distinguish item from source information, by using Remember/Know (R/K) judgments at test (Tulving, 1985). They found that bilateral posterior MTC responses increased successively from sMs to subsequent K (sK) to subsequent R (sR) judgments. Given that R

judgments are likely to involve source retrieval, this is consistent with the above suggestion that posterior MTC (which was identified as parahippocampal cortex) is involved in encoding source information. Though direct, within-experiment comparisons between stimuli are clearly needed, it is noteworthy that MTL subsequent memory effects are more often seen with scenes than with words (and more often seen bilaterally, though see Kirchoff et al, 2000).

Recognition (old-new effects)

Table 2 shows experiments that examined variants of old-new effects at test. With regard to the basic activation for hits (Ht) relative to correct rejections (CR) in Y/N tests using words, one found left posterior MTC (Daselaar et al., 2001) and one found left posterior hippocampus (Donaldson et al, 2001), but eight did not find activations within MTL (Donaldson et al, 2000; Henson et al, 2000; Herron et al, 2004; Jessen et al, 2001; Konishi et al, 2000; McDermott et al, 2000; Ranganath et al, 2000; Rugg et al, 2003). Four of the latter experiments did, however, find “deactivations” for Ht versus CR. These were generally in anterior MTC rather than hippocampus (Henson et al, in press; Herron et al, 2004), though extending more posteriorly in Rugg et al (2003) and Jessen et al (2001) and the laterality varied. Similar deactivations were found in re-analysis of further experiments, with a common locus believed to be perirhinal cortex (Henson et al, 2003). Moreover, these MTC deactivations associated with old items (or conversely, activations associated with new items; see later) did not appear sensitive to source retrieval (see Henson et al, 2003, for further discussion).

< insert Table 2 about here >

Konishi et al (2002) used a 2AFC Recency task, rather than Y/N task, in which participants saw two old words and judged which was studied more recently. The two words were either close together (High demand condition) or far apart (Low demand condition) in the study list. Bilateral posterior MTC activation was found for High versus Low demand trials (with accuracy close to ceiling in both).

Three experiments used R/K judgments (Tulving, 1985). Two reported MTL activation for R-hits vs K-hits: in left anterior hippocampus and right posterior MTC (Eldridge et al, 2000) and in, or near, bilateral anterior hippocampus (Wheeler & Buckner, 2004). The third only found activation in, or near, left posterior hippocampus for R-hits vs CRs (Henson et al, 1999). Two factors are potentially important in these experiments: The first is whether the R/K decision follows an old-new (O/N) decision (as in Eldridge et al, 2000), or whether a single R/K/N decision is made (as in Henson et al, 1999, and Wheeler & Buckner, 2004). The former is better for isolating recollection (Eldridge & Knowlton, 2002) while the latter is better for comparing R/K with N judgments (e.g, CRs). The second is whether K responses are more accurate than guesses (as in Henson et al, 1999, and Wheeler & Buckner, 2004, but not necessarily in Eldridge et al, 2000, depending on how R and K judgments are related). The experiment by Kensinger et al (2003) mentioned earlier did not use R/K judgments during fMRI, but did find more R than K judgments under Easy than Hard dual-task study conditions in a separate behavioural experiment, together with left anterior hippocampal activation for hits in a Y/N task following Easy than following Hard dual-task conditions at study.

While R/K judgments might be viewed as a subjective means of distinguishing source information (R) from item information (K), several experiments used objective tests of memory for study context. Wheeler et al (2003) asked participants to study words presented together with either a sound or a picture related to that word. At test, they were asked to indicate whether words were new, or whether they had previously been paired with a sound or picture. Those test words that were repeated 20 times at study (for which accuracy of remembering the associated sound/picture was close to perfect) produced left anterior hippocampal and bilateral posterior MTC activation relative to CRs. A similar experiment was performed by Okado and Stark (2003). At study, participants heard names of objects, and then either saw or imagined a picture of that object. At test, they heard old and new object names and were asked whether or not they saw pictures of those objects at study. No MTL differences however were found between hits (true memories), false alarms for objects that were only imagined at study (false memories), or correct rejections of objects imagined at

study.

Dobbins et al (2003) cued participants for either a pleasant/unpleasant or concrete/abstract decision to words. At test, two old words were presented for one of two types of 2AFC: to select the word seen more recently in the study phase (Recency task) or to select the word judged for pleasantness in the study phase (Source task). Activation for correct versus incorrect decisions was found in left anterior hippocampus and left MTC in the Source task, but not in the Recency task. Using a similar source task but with Y/N recognition, Kahn et al (2004) found bilateral posterior MTC activation for words whose study task was correctly identified relative to words that were recognised as studied but their study task not identified. Interestingly, this activation was found for words from the visual imagery task, but not those from the read-backwards task (see the earlier description of Davachi et al, 2003, which reported encoding data using the same paradigm). Moreover, the same regions were activated (though to a lesser extent) for false alarms to new items that were (erroneously) judged to have been imaged at study, but not false alarms judged to have been read backwards. This pattern suggests that bilateral posterior MTC activity (particularly in parahippocampal cortex) is associated with episodic retrieval of visual imagery, even if that is cued by a nonstudied item (perhaps reflecting confusion of that item with a different, but related, study item).

Considering the above experiments using source judgments together with those using R/K judgments, it appears that source retrieval is normally correlated with MTL activation (indeed, the likelihood that not all hits are associated with source retrieval in standard y/n recognition tasks may explain why MTL activation is less common in the basic "old-new" contrast of hits versus correct rejections considered earlier). Whether that activation is in hippocampus or MTC, anterior or posterior, or left or right, varies however (though the MTC activations are more often in parahippocampus than rhinal cortex). The differences may depend on the type of source information. Note also that, though explicit source judgments can objectify whether a specific type of contextual information was retrieved, it is possible that items for which that particular information was not retrieved were nonetheless associated with retrieval of other aspects of study context (so-called "non-criterial" source retrieval).

Thus both procedures -- objective source decisions and subjective R/K judgments -- are valuable.

Four experiments examined recognition memory using new items that were related in some way to studied items. For such “lures”, one can look at both false alarms and correct rejections. According to some models (e.g, Jones & Jacoby, 2001), false alarms to lures are attributed to an increased feeling of familiarity in the absence of recollection, whereas correct rejections of lures are attributed to recollection of the related studied item(s) and hence rejection of their increased familiarity (a “recall-to-reject” strategy). Using compound nouns as lures (rearranged from two studied nouns), McDermott et al (2000) did not find MTL differences between hits, correct rejections of lures and correct rejections of unrelated new items. Using semantically-related lures, von Zerssen et al (2001) found left posterior MTC activation for hits and correct rejection of lures, relative to correct rejection of unrelated items. They failed to find MTL differences between false alarms to lures and correct rejections of unrelated items. Cabeza et al (2001) on the other hand found bilateral posterior hippocampus activation for both hits and false alarms to lures, relative to correct rejections of unrelated items, and left posterior MTC activation for hits relative to both false alarms to lures and correct rejections of unrelated items. This pattern was interpreted as hippocampus being sensitive to retrieval of semantic information, which would not distinguish targets from lures, and parahippocampus being sensitive to retrieval of perceptual information, which would distinguish targets from lures.

However, this hippocampal pattern (hits and false alarms greater than correct rejections) was also found by Slotnick and Schacter (2004) using abstract shapes, which presumably have little semantic content. This suggests that hippocampus is activated by false memory for “gist”, even if that gist is a nonverbal visuospatial prototype. Furthermore, Slotnick and Schacter found that it was relatively “early” visual regions, rather than “late” (e.g, parahippocampal) visual regions, that showed differences between hits and false alarms to lures. This difference between the two studies may reflect a difference in the types of source information retrieved for true memories (hits): one of two speakers from a video clip (Cabeza et al, 2001) versus presentation left or right of fixation (Slotnick & Schacter, 2004).

These findings using lures raise interesting interpretations (e.g, left posterior MTC activation associated with valid recollection/source retrieval), but more experiments are needed to establish their typicality and robustness. There are also likely to be multiple factors that affect results and their interpretations, such as whether the lures are internally-generated at study, whether false recollection occurs in addition to misattributed familiarity, and the type of item and source information – e.g, perceptual or semantic – contributing to the recognition decision.

Two experiments examined recognition of items previously studied in emotionally positive, neutral or negative contexts (either words within sentences, Maratos et al, 2001, or objects within background scenes, Smith et al, 2004). Maratos et al (2001) found left posterior MTC activation for hits relative to correct rejections of words, collapsing across study context, and left anterior hippocampal activation for negative-hits relative to neutral-hits. Smith et al (2004) did not find MTL activation for hits relative to correct rejections of objects, but found right posterior hippocampal and left posterior MTC activation for negative-hits relative to neutral-hits. Though these experiments had no objective measure of source retrieval, the difference between negative and neutral hits may reflect differences in the amount (and/or emotional content) of the source information retrieved.

Four experiments looked at variants of the associative recognition task. Using pairs of objects, LePage et al (2003) did not find MTL differences between intact, rearranged or new pairs. Using pairs consisting of a central face and an peripheral object presented in one of four corners of the screen (for multiple learning trials), Duzel et al (2003) found right posterior MTC activation for studied relative to new pairs, but right anterior hippocampus activation for new pairs relative to studied pairs, regardless of whether recognition decisions were based on the spatial position of the studied object (relative to the face) or the identity of the object (relative to the one studied with that face). In an experiment also described earlier, Kirwan and Stark (2004) found bilateral anterior MTC, right posterior MTC and right anterior hippocampus for intact face-name pairs called “intact” relative to intact pairs called “rearranged”. Giovanello et al (2004) found bilateral anterior hippocampal activation (stronger on left) for intact word-pairs called “intact” in an associative recognition task

relative to correct recognition for both items of a rearranged pair in an item recognition task. The latter three experiments are all consistent with a hippocampal role in retrieval (as well as encoding; see earlier) of associations between pairs of items, though note that different comparisons were used in each case.

Of the experiments using visual objects, Henson et al (2002a) failed to find MTL old-new effects with either familiar or unfamiliar faces during a continuous recognition memory task. Tsivilis et al (2003) also failed to find MTL differences between old or new objects, or between old objects presented in the same or a different background scene as during study. Slotnick et al (2003) used unfamiliar, nonverbalisable abstract shapes, and found left anterior MTC activation for hits versus correct rejections in an item recognition task (but no reliable differences in a source recognition task in which participants recollected whether the shapes were studied left or right of fixation).

Stark and Squire (2001) presented either objects at study and test, object names at study and test, or objects at study and their names at test. Comparing hits with correct rejections, they found left hippocampal activation in the name-name condition and right hippocampal activation in the object-name condition (probably including both anterior and posterior loci in both cases). Right hippocampal activation was found in the object-object condition only when the recognition test was repeated (which the authors attributed to a high level of encoding-related activation for the new objects; see later). Interestingly, no hippocampal differences were found for hits across the three conditions, suggesting that retrieval of the object associated with a name cue does not engage hippocampus any more than retrieval associated with an object or word copy cue (Tulving, 1982).

Participants in the Cansino et al (2002) performed an incidental semantic task on objects presented in one of four corners of the screen (as described in the encoding section), then at test saw a central object and indicated in which of the four positions it appeared at study, or that it was new. Right anterior hippocampus and left posterior MTC were activated for source hits versus source misses. This experiment thus resembles both the source judgment tasks described above using words, and the associative recognition task using objects and locations by Duzel et al (2003), though the only common activation would appear

to be posterior MTC.

Three experiments examined recognition memory for scenes (e.g, landscapes, buildings). Rombouts et al (2001) found deactivations in bilateral anterior MTC and right anterior hippocampus for hits relative to correct rejections, while Weis et al (2004) found deactivations in left anterior MTC for confident hits relative to confident misses. These “deactivations” associated with recognition, at least with regard to anterior MTC, are analogous to those for words described earlier (and Henson et al, 2003). Furthermore, that the deactivation was found relative to misses by Weis et al (2004) suggests that it is likely to reflect participants’ explicit memory, rather than (implicit memory for) the objective old/new status of the item (see also Henson et al, in press).

Stark and Okado (2003) on the other hand found no MTL differences for the usual comparison of hits versus correct rejections. However, when they restricted correct rejections to those new items that were not recognised in a second subsequent recognition test, they found bilateral activation in hippocampus and MTC. The lack of MTL differences for the usual hits versus correct rejection comparison was therefore attributed to encoding-related activation for those new items that were recognised in the second test (see later).

Finally, one experiment by Burgess et al (2001) used virtual reality to distinguish retrieval of different types of source information. Participants were told to remember objects given to them by virtual people at specific locations within a virtual environment. During test trials, they were shown two objects, again in the context of a specific person and location, and cued to choose either 1) which of an old and a new object was studied (“Object” trials), 2) which of two old objects was studied together with that person (“Person” trials), 3) which of two old objects was studied in that location (“Place” trials), or 4) which of two old objects was “wider” (Control trials). Bilateral posterior MTC was activated for hits in the Place trials versus hits in the Object, Person and Control trials. Since the person trials required retrieval of source information, this result suggests that these regions are specifically involved in retrieval of (allocentric) spatial information. Left (and right at a lower threshold) posterior hippocampus was also activated in the Place versus Control trials, but showed intermediate levels of activity (on the left) in the Person and Object trials, suggesting a more general role

in item and/or source retrieval.

Summary

Returning to look at Tables 1 and 2 as a whole, I think there is little doubt that structures within MTL show memory-related differences in haemodynamic activity during both the study and test phases of recognition memory tasks. Unfortunately however, no *clear* pattern emerges (at least to my eye!) for functional divisions between hippocampus and MTC, between anterior or posterior MTL, or even left versus right MTL. One possibility is that, contrary to proposals such as that by Aggleton and Brown (1999), there is no functional division of labour within the MTL, or at least, any functional division that exists does not conform to the dichotomies considered here (Squire et al, 2004).

Having said this, some trends do appear to be emerging. One trend is that hippocampus and posterior MTC (specifically, parahippocampal cortex) appear particularly important for encoding and retrieving source information and associations between distinct items. Anterior MTC (most likely perirhinal cortex) on the other hand seems more concerned with item information (see below). Indeed, a clearer functional dissociation might be between (peri)rhinal and parahippocampal cortex rather than hippocampus and MTC (unfortunately not all the experiments reviewed here allowed a clear distinction between perirhinal and parahippocampal activation).

Another trend, regarding the stimulus material, is that scenes seem particularly effective at eliciting memory-related MTL activations (at least relative to words). This may reflect the novelty, complexity or spatial components of scenes. It may even relate to the impression scenes give of being present in an allocentric environment. It is noteworthy therefore that all three experiments that explicitly examined retrieval of spatial relations found right hippocampal activation, whether those relations were likely to be egocentric (Cansino et al, 2002; Duzel et al, 2003) or allocentric (Burgess et al, 2001). Furthermore, there is a slight trend for left-lateralisation of activations associated with verbal information (particularly at test), in contrast with bilateral activation for scenes.

Another trend is for decreased responses in anterior MTC for old relative to new items during recognition tests. This resembles decreased firing rates associated with

familiarity in perirhinal neurons in animals (Brown & Xiang, 1998). Alternatively (or perhaps equivalently), this pattern could reflect increased responses to new items (e.g. a novelty response). Indeed, such increases may even reflect encoding-related processes, given that another interesting possibility concerns encoding-related activation during recognition tests: Three experiments examined differences between new items in one test as a function of whether they are recognised in a second test, and two found MTL activation (Kirwan & Stark, 2004; Stark & Okado, 2003). If MTL is involved in encoding new items, as well as recognising old items, this could explain why MTL activations are less often seen in the basic comparison of hits versus correct rejections during recognition tests. It may only be when old items are associated with high levels of source or associative retrieval (see above) that they produce activity over and above that produced by the encoding of new items.

Future Directions

Many future experiments are suggested by the above findings. Firstly there is a need to examine a larger range of stimulus material, given the current dominance of verbal material (probably reflecting the long tradition of verbal learning in human behavioural experiments). One reason is that nonverbal stimuli are easier to compare with those used in animal experiments. Another reason is that words are also confounded with pre-experimentally familiarity, making it difficult to separate intra- and extra-experimental sources of information (given that even a simple y/n recognition memory test can be viewed, at least for familiar items, as a source memory test for whether items were seen in a specific context, viz the study phase). A related need is to examine recognition memory for nonvisual material, since some MTL activations may be specific to memory for visual information. Future experiments would benefit from using both visual and nonvisual (and/or verbal and nonverbal) material, in order to make direct, within-experiment statistical comparisons (e.g., Duzel et al, 2003; Kirchhoff et al, 2000), rather than relying on comparisons across experiments.

Another need is to further characterise and contrast different types of source information, such as time and space (see above), or conceptual versus perceptual information (see also recent interest in “content effects” at retrieval, e.g, Wheeler et al, 2000). Of

particular importance is the theoretical characterisation of the commonalities or differences between context information (as tested in source judgments) and associative information (as tested in associative recognition judgments). This may include the role of intrinsic versus extrinsic source (Baddeley, 1982), internal versus external source (Johnson et al, 1993), the difference between unassociated versus associated items, and associations between different types of information (Mayes et al, 2004). It is also important to characterise more precisely the theoretical relationship between encoding and novelty (Kirchhoff et al, 2000).

Other factors that may be relevant to MTL activation include the question of explicit (conscious) versus implicit (unconscious) retrieval of information (Henke et al, 2003) and the related question of the relationship between the present findings from recognition tests (“direct” memory tests) and analogous comparisons between novel and repeated items in indirect memory tests (e.g, Donaldson et al, 2001; Henson et al, 2002a; Saykin et al, 1999), where target-related effects are less likely (Herron et al, 2004).

Future recognition experiments would benefit from more comparisons involving misses and false alarms, provided they can be collected in sufficient numbers (e.g, Wheeler et al, 2003, Kahn et al, 2004; Slotnick & Schacter, 2004). This might include the use of lures (see earlier). Future experiments would also benefit from direct statistical comparisons between different MTL regions, such as hippocampus versus perirhinal cortex, or left versus right hippocampus: current experiments tend to report only reliable findings within each region, with the danger that other regions show similar effects that simply did not reach significance (Henson, in press). Furthermore, the experiments should test for both increases and decreases in the subtraction of different conditions, and might want to consider differences in sustained memory-related “state” effects (Otten et al, 2002; Velanova et al, 2003), as well as between transient “item” effects (as considered here). These tests would benefit from conforming to standardised criteria for allowing for multiple statistical comparisons across voxels within a specified, a priori search space (e.g, MTL), allowing fairer comparison across studies. Most importantly, they should use methods developed for better localisation and coregistration of structures within MTL (e.g, Zienh et al, 2003), including acquisition at higher spatial resolution and efforts to minimise fMRI susceptibility-

effects. The latter is important not only to prevent geometric distortion and hence mislocation of activations, but also to prevent signal loss or “drop-out”, which is particularly common in anterior MTL (another potential reason why some studies in Tables 1-2 failed to find MTL activity). Indeed, it would be valuable if future studies provided information on the degree of signal loss in their fMRI data, in order to evaluate the likelihood of finding MTL activity. Finally, it will be important to compare encoding- and retrieval-related findings from the recognition memory paradigm with those from other paradigms, such as (the technically more challenging) recall paradigms (Henson et al, 2002b; Strange et al, 2002).

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Table 1. Subsequent memory effects at study (encoding): activations for items later “remembered” versus items later “forgotten” (deactivations in ***bold italics***). One row per comparison, ordered by study material and then by information encoded (item, source or possibly both). H = Hippocampus, MTC = Medial Temporal Cortex, l = left, r = right, ant = anterior ($y \leq -20$), pos = posterior ($y > -20$), sHt = subsequent hit, sMs = subsequent miss, Inc = Incidental, Int = Intentional, Obj = Object, Loc = Location, Sem = Semantic, Pho = Phonological, Lex = Lexical, Ort = Orthographic, Rem = Remember cue, For = Forget cue, Elab = Elaborate, Assoc = Associate, Y/N/G = Yes/No/Guess, Recog = Recognition, Conf = Confidence ratings, 2nd = Secondary task, SourceN = N-way source decision, Int = Intact, Rer = Rearranged, Sin = Single item recognised, R = Remember, K = Know, ? = unclear, + = main effect, / = either simple effect, & = both simple effects (see text for further information).

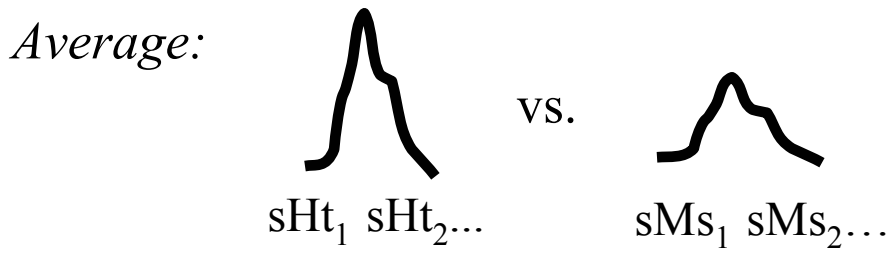
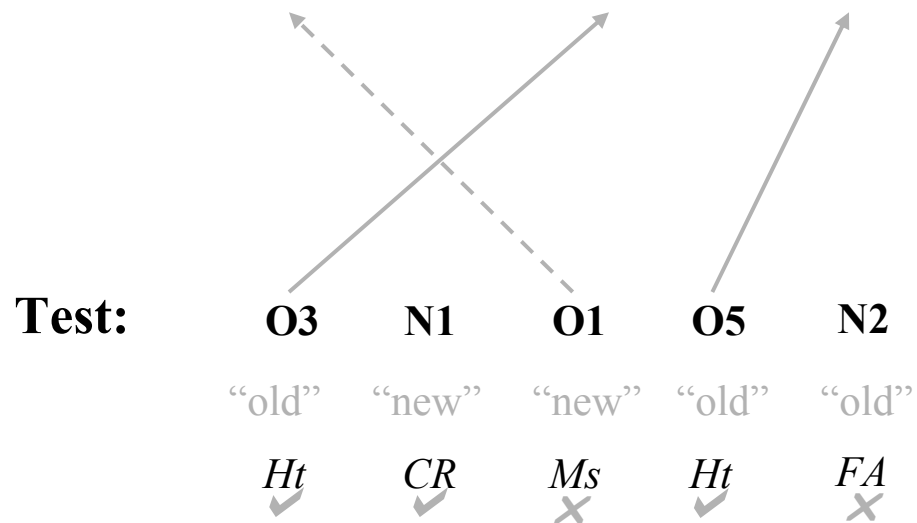
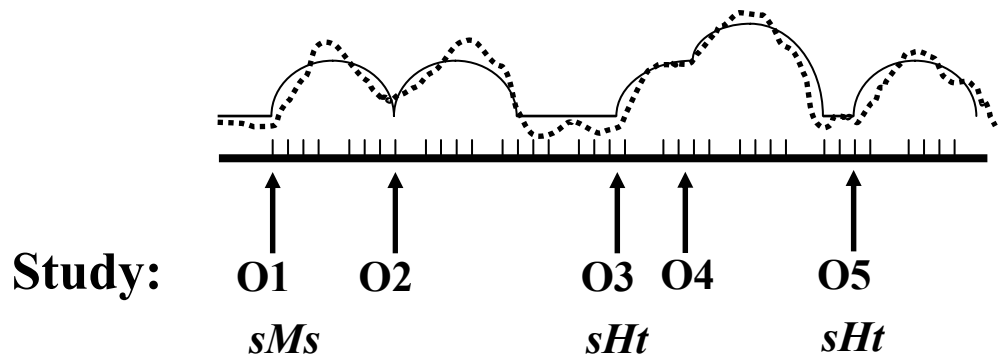
Reference	Study Material	Item/Source	Study Task	Test Task	Comparison	H		MTC	
						l	r	l	r
Baker et al 01	Words	both?	Inc Sem/Ort	Y/N	sHt > sMs, Sem/Ort				
Fletcher et al 03	Words	both?	Inc Sem/Ort	Y/N	sHt > sMs, Sem+Ort	ant			
Henson et al 04	Words	both?	Inc Ort	Y/N	sHt > sMs, Ort				
Wagner et al 98	Words	both?	Inc Sem	Y/N, Conf	sHt > sMs (conf)			pos	
Buckner et al 01	Words	both?	Inc Recog	Y/N/G	sHt > sMs (no guesses)				
Otten & Rugg 01	Words	both?	Inc Sem/Pho	Y/N, Conf	sHt > sMs (conf), Sem/Pho				
Otten et al 01	Words	both?	Inc Sem/Ort	Y/N, Conf	sHt > sMs (conf), Sem&Ort	ant			
Otten et al 02	Words	both?	Inc Sem/Pho	Y/N, Conf	sHt > sMs (conf), Sem only				ant
Morcom et al 03	Words	both?	Inc Sem	Y/N, Conf	sHt > sMs (conf), Sem	ant		ant	ant
Kirchhoff et al 00	Words	both?	Inc Sem	Y/N, Conf	sHt > sMs (conf)				
Reber et al 02	Words	both?	Rem/For	Y/N	sHt > sMs, Rem&For	pos		pos	
Davachi et al 02	3 Words	both?	Inc Elab/Rote	Y/N, Conf	sHt1 to sHt3, Elab only	ant	pos		
<i>Davachi et al 02</i>	<i>3 Words</i>	<i>both?</i>	<i>Inc Elab/Rote</i>	<i>Y/N, Conf</i>	<i>sHt3 to sHt1, Elab only</i>				<i>pos</i>
Kensinger et al 03	Words	both?	Inc Sem+ 2nd	Y/N	sHt > sMs, Hard&Easy			pos	
<i>Henson et al 99</i>	<i>Words</i>	<i>item?</i>	<i>Inc Lex</i>	<i>R/K/N</i>	<i>sK > sR</i>				<i>pos</i>
Davachi et al 03	Words	item	Image/Read	Y/N, Source2	sHt(Inc source) > sMs			ant	
Ranganath et al 04	Words	item?	Inc, 2 Sems	Conf6, Source2	Conf 1 to 5			ant	
Kensinger et al 03	Words	source?	Inc Sem+ 2nd	Y/N	sHt > sMs, Easy only	ant			
Davachi et al 03	Words	source	Image/Read	Y/N, Source2	Cor > Inc Source (sHt)	pos	ant	pos	
Ranganath et al 04	Words	source	Inc, 2 Sems	Conf6, Source2	Cor > Inc Source (4-6)		pos		pos
Cansino et al 02	Obj-Loc	source	Inc Sem	Y/N, Source4	Ht vs Ms, Cor vs Inc Source				
Jackson et al 04	2 Words	source	Inc Assoc	Int/Rer/Sin/New	IntInt > IntRer	ant		ant	ant
Sperling et al 03	Face-name	source	Int Match	2AFC name	sHt > sMs, high conf	ant	ant		
Kirwan & Stark 04	Face-name	source	Int Assoc	Int/Rer/New	IntInt > IntRer		pos		pos
Kirwan & Stark 04	Face-name	item	Int Assoc	Int/Rer/New	IntInt/IntRer > IntNew				both
<i>Kirwan & Stark 04</i>	<i>Face-name</i>	<i>both?</i>	<i>Inc Recog</i>	<i>Y/N</i>	<i>sMs > sHt</i>				<i>ant</i>
Brewer et al 98	Scenes	both?	Inc in/outdoor	R/K/N	sR > sK > sMs			pos	pos
Kirchhoff et al 00	Scenes	both?	Inc in/outdoor	Y/N, Conf	sHt > sMs, high conf	pos	pos	pos	pos
Weis et al 04	Scenes	both?	Int building	Y/N, Conf	sHt > sMs, high conf			pos	ant
Stark & Okado 03	Scenes	both?	Int	Y/N	sHt > sMs	pos	both	both	both

Table 2. Old-new and related effects at test (recognition): activations for old items versus new items (deactivations in **bold italics**). Ht = Hit, CR = correct rejection, Aud = Auditory, Environ = Virtual environment, Snd = Sound, Pic = Picture, Cont = Continuous, Sim = similar to old item (lures); Dis = dissimilar (unrelated) new items, Neg = Negative, Pos = Positive, Neu = Neutral valence, Pers = Person. See text and Table 2 for more information.

Reference	Test Material	Item/ Source	Study Task	Test Task	Comparison	H		MTC	
						l	r	l	r
Daselaar et al 01	Words	both?	Int	Y/N	Ht > CR			pos	
Donaldson et al 01	Words	both?	Inc Sem	Y/N	Ht > CR	pos			
Donaldson et al 00	Words	both?	Inc Sem	Y/N	Ht vs CR				
Henson et al 00	Words	both?	Inc Sem	Y/N Conf	Ht vs CR, high/low conf				
Konishi et al 00	Words	both?	Int	Y/N	Ht vs CR				
Ranganath et al 00	Words	both?	Inc Sem	Y/N, gen/spec	Ht vs CR				
Henson et al 04	Words	both?	Inc Sem/Ort	Y/N	CR > Ht			ant	
Herron et al 04	Words	both?	Inc Sem/Ort	Y/N	CR > Ht				ant
Rugg et al 03	Words	both?	Inc Sem	In/Exclusion	CR > Ht (Inc+Exc)			both	both
Jessen et al 01	Words	both?	Cont recog	Y/N Cont	CR > Ht			pos	
Konishi et al 02	Word pairs	both?	Int	Recency 2AFC	Close > Far (Cor)			pos	pos
Eldridge et al 00	Words	source	Int	Y/N, R/K	R(Ht) > K(Ht)/CR	ant			pos
Henson et al 99	Words	source?	Inc Lex	R/K/N	R(Ht) > CR	pos			
Wheeler et al 04	Words	source	Int	R/K/N/G	R(Ht) > K(Ht)	ant	ant		
Kensinger et al 03	Words	source?	Inc Sem + 2nd	Y/N	Ht: Easy > Hard	ant			
Wheeler & Buck.03	Words	source	Int, Snd/Pic	Snd/Pic/N	Ht(20) > CR	ant		pos	pos
Okado & Stark 03	Aud. word	source	See/Image	Y/N seen	Ht vs FA vs CR				
Dobbins et al 03	Word pairs	source	Inc 2 Sem	2AFC: Rec/Sou	Cor > Inc, Source only	ant		both	
Kahn et al 04	Words	source	Image/Read	Y/N, source	Cor > Inc Source, Image			pos	pos
McDermott et al 00	Words	source	Int	Y/N	CR(sim) vs CR(dis) vs Ht				
von Zerssen et al 01	Words	source	Int	Y/N, Conf	Ht/CR(sim) > CR(dis)			pos	
Cabeza et al 01	Words	item?	Int	Y/N	Ht/FA(sim) > CR(dis)	pos	pos		
Cabeza et al 01	Words	source?	Int	Y/N	Ht > FA(sim)/CR(dis)			pos	
Slotnick et al. 2004	Shapes	source ?	Int	L/R/N, Conf	Ht/FA(sim) > CR	pos			
Maratos et al 01	Words	both?	Valence	Y/N	Ht > CR (Pos+Neu+Neg)			pos	
Maratos et al 01	Words	source?	Valence	Y/N	Neg > Neu (Ht)	ant			
Smith et al 04	Objects	source?	Inc assoc scene	Y/N	Neg > Neu (Ht)		pos	pos	
Lepage et al 03	Object pair	both?	Int Assoc	Int/Rer/New	Int vs Rer vs New				
Duzel et al 03	Obj/Loc	source	Learn	Y/N Obj/Loc	Old > New pairs, Obj/Loc				pos
Duzel et al 03	Obj/Loc	source	Learn	Y/N Obj/Loc	New > Old pairs, Obj/Loc			ant	
Kirwan & Stark 04	Face-name	source	Int Assoc	Int/Rer/New	IntInt > IntRer		ant	ant	both
Giovanello et al 04	Word pairs	source	Inc Sem	Assoc/Item	Assoc > Item (Ht)	ant	ant		
Henson et al 02	Faces	both?	Cont recog	Y/N Cont	Ht vs CR				
Tsivilis et al 03	Objects	both	Inc assoc scene	Y/N	Int vs Rer vs New				
Slotnick et al 03	Shapes	both?	Int	Y/N	Ht > CR			ant	
Stark & Squire 01	Names	both?	Int Names	Y/N	Ht > CR (1st test)	both		?	?
Stark & Squire 01	Names	both?	Int Objects	Y/N	Ht > CR (1st test)		both		
Stark & Squire 01	Objects	both ?	Int Objects	Y/N	Ht > CR (2nd tes)		both		?
Cansino et al 02	Objects	source	Inc Sem	Loc 1-4/N	Cor > Inc source (Ht)		ant	pos	
Rombourts et al 01	Scenes	both?	Int	Y/N	CR > Ht			ant	ant
Weis et al 04	Scenes	both?	Int	Y/N, Conf	Ms > Ht, high conf				ant
Stark & Okado 03	Scenes	both ?	Int	Y/N	Ht > CR(forgotten)	both	both	both	both
Burgess et al 01	Environ	source	Int Assoc	2AFC	Place > Pers/Obj/Width			pos	pos
Burgess et al 01	Environ	source	Int Assoc	2AFC	Place > Width	pos	pos ?		

Figure 1: Schematic illustration of subsequent memory effects at study (encoding) and old-new effects at test (recognition). When scanning at study (left) or test (right), dotted and solid lines illustrate actual and fitted timecourses of event-related fMRI responses, with upward arrows indicating onset of an event. "O1", "O2", etc indicate different "old" (studied) stimuli; "N1", "N2", etc indicate different "new" (unstudied) stimuli. Events are defined on the basis of the participants "old" or "new" response at test, which are either a correct endorsement of an old item, a "hit" (Ht), correct rejection of a new item ("CR"), incorrect rejection of an old item, a "miss" (Ms), or incorrect endorsement of a new item, a "false alarm" (FA). For the subsequent memory effect, hits and misses at test are used to define events at study as either a "subsequent hit" (sHt) or "subsequent miss" (sMs). After effective event-locked "averaging", voxels are identified in which the mean response differs for the critical event-types.

Encoding “Subsequent Memory” effect



Recognition “Old-New” effect

