Material specific lateralisation of medial temporal lobe function: an fMRI investigation

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Abstract

The theory of material specific lateralisation of memory function posits that left and right MTL regions are asymmetrically involved in mnemonic processing of verbal and nonverbal material respectively. Lesion and functional imaging (fMRI) studies provide robust evidence for a left MTL asymmetry in the verbal memory domain. Evidence for a right MTL/non-verbal asymmetry is not as robust. A handful of fMRI studies have investigated this issue but have generally utilised nonverbal stimuli which are amenable to semantic elaboration. This fMRI study aimed to investigate the neural correlates of recognition memory processing in 20 healthy young adults (mean age = 26 years) for verbal stimuli and nonverbal stimuli that were specifically designed to minimise verbalisation. Analyses revealed that the neural correlates of recognition memory processing for verbal and nonverbal stimuli were differentiable and asymmetrically recruited the left and right MTL respectively. The right perirhinal cortex and hippocampus were preferentially involved in successful recognition memory of items devoid of semantic information. In contrast, the left anterior hippocampus was preferentially involved in successful recognition memory of stimuli which contained semantic meaning. These results suggest that the left MTL is preferentially involved in mnemonic processing of verbal/semantic information. In contrast, the right MTL is preferentially involved in visual/non-semantic mnemonic processing. We propose that during development, the left MTL becomes specialised for verbal mnemonic processing due to its proximity with left lateralised cortical language processing areas while visual/non-semantic mnemonic processing gets 'crowded out' to become predominantly, but not completely, the domain of the right MTL.

Introduction

Lesion studies provide strong evidence that the recruitment of structures within the medial temporal lobe (MTL) during memory tasks is at least partly lateralised depending on the type of material being processed. Seminal publications by Milner and colleagues (1954, 1958) demonstrated that verbal memory was impaired following resection of the left MTL for the treatment of intractable medial temporal lobe epilepsy while nonverbal memory remains intact. In contrast, resection of the right MTL was associated with impairments in picture comprehension but intact verbal memory (Milner et al., 1954, 1958). Similar patterns have been consistently observed in more recent studies (Jones-Gotman, 1986; Helmstaedter and Elger, 1996; Seidenberg et al., 1996; Jones-Gotman et al., 1997; Gleissner et al., 1998; Pillon et al., 1999; Savage et al., 2002). While important insights into MTL functions have been gained from these clinical studies, these have been gleaned in patients with (often) lifelong disorder where the MTL has undergone a substantial functional reorganisation or compensatory processes over time (Adcock et al., 2003; Thivard et al., 2005).

The extent to which results from these studies are reflecting MTL functions in healthy individuals remains to be demonstrated. Only a handful of neuroimaging studies have investigated the neural correlates of memory processing for verbal and nonverbal stimuli in healthy individuals and have generally focussed on encoding. These investigations have consistently observed differences in MTL recruitment for verbal and nonverbal material, in that the left MTL is recruited during encoding of verbal materials such as words and the right MTL is recruited during encoding of nonverbal stimuli such as patterns, designs or faces (Kelley et al., 1998; Golby et al., 2001; Powell et al., 2005; Rosazza et al., 2009). Importantly, however, while evidence that the left MTL is important for verbal memory is strong, the link between nonverbal memory and the right MTL is more tenuous (Bell and Davies, 1998). Indeed, bilateral MTL recruitment has been observed during encoding of scenes, faces,

pictures and line drawings of objects (Golby et al., 2001; Powell et al., 2005; Rosazza et al., 2009), indicating that verbal and nonverbal memory processing may not be entirely lateralised (Saling, 2009).

Golby and colleagues (2001) suggested that lateralisation effects are determined by how verbalisable the information to be encoded is. Many studies investigating the neural correlates of nonverbal memory have utilised stimuli which are amenable to some degree of verbalisation or semantic elaboration, such as faces (Kelley et al., 1998), patterns (Golby et al., 2001; Bunge et al., 2004) and abstract designs (Jones-Gotman et al., 1997). It is therefore plausible that the many observations of bilateral MTL involvement during nonverbal tasks are related to the verbalisability of the stimuli. Ideally, nonverbal stimuli which are truly not amenable to verbalisation are necessary in order to identify MTL contributions to verbal and nonverbal memory processing. However, one of the primary currencies of human cognition is verbalisation. This makes the task of creating wholly nonverbalisable stimuli challenging. Avoiding overtly verbalisable concept laden elements such as colour or texture may be helpful in making verbalisation more difficult. In addition, the variable task demands across studies further limit direct comparisons across studies and between verbal and nonverbal studies. Indeed, it has been argued that lateralisation effects may result from engaging different mnemonic processes rather than a result of differences in the material to be learned (Kennepohl et al., 2007).

This study aimed to investigate the neural correlates of recognition memory processing for verbal and nonverbal stimuli in the same group of individuals. Importantly, in light of the argument presented above, we utilised nonverbal stimuli which were difficult to verbalise and also ensured that the task demands for the verbal and nonverbal tasks were matched. We predicted that recognition memory of verbal stimuli would preferentially recruit

regions within the left MTL whereas recognition memory of nonverbal stimuli would be associated with the recruitment of right MTL regions predominantly.

Materials and Methods

Participants.

Twenty right-handed healthy volunteers (15 females) (mean age = 26 years, range = 21 – 37 years) were recruited for this study. All were native English speakers with normal or corrected to normal vision and free of significant neurological or psychiatric disorders. Other exclusion criteria included a history of significant traumatic brain injury, drug or alcohol abuse or use of medications with central nervous system side effects. This study was approved by the University of New South Wales Human Ethics Research Committee and all participants provided written informed consent.

Stimulus materials

This study comprised one verbal and one nonverbal recognition memory task. For the verbal task, stimuli comprised 60 two- or three-syllable compound words (e.g., *gateway*, *highchair*). For the nonverbal task, stimuli included 60 pairs of symbols with no evident semantic meaning recreated from rare and extinct languages and from modified Japanese kanji and hiragana characters (Figure 1). Importantly, none of the participants were familiar with Japanese or Chinese languages. All stimuli were printed in black on a white background. Three different versions of each task were created and lists were randomly allocated across participants.

***** INSERT FIGURE 1 AROUND HERE *****

Procedure

The entire experiment was conducted in the scanner and functional magnetic resonance imaging data were acquired during both encoding and test phases. All responses were recorded using an MR compatible button box. The stimulus presentation procedure was identical for both the verbal and nonverbal tasks. At encoding, 60 stimuli were presented on a Philips LCD monitor. During the verbal task, stimuli were presented one compound word at a time and during the nonverbal task, one symbol pair at a time. Each stimuli was presented in the centre of the screen for 2000 ms, followed by a fixation point for 1000 ms. To ensure optimal attention to the stimuli at encoding, participants were instructed to indicate for each stimulus of the verbal task whether the word was pleasant, unpleasant or neutral. For the nonverbal task participants were instructed to visually inspect each pair of symbols as a pair.

At test, 60 stimuli were presented one at time following the same procedure used during encoding. Twenty stimuli were identical to the ones seen at study (old), 20 were novel stimuli not seen at study (new) and 20 stimuli were the combination of two stimuli seen at study. For example, for the verbal task, *highchair* and *gateway* at encoding were recombined to become *highway* at test. These recombined items were introduced to increase task difficulty. Memory for the stimuli seen at study was tested using a yes/no recognition procedure. For each item, participants were instructed to indicate 'yes' if they thought the stimulus had been presented at encoding, or 'no' if they thought the stimulus had not been seen at encoding. Participants were also instructed to respond within the 2000 ms stimulus

presentation window. At test, the order of presentation of old, recombined and new stimuli was pseudo-randomized, in that no more than 2 items from the same category were seen in succession. In order to get familiarised with the general procedure, participants took part in a practice trial of the encoding and test phases outside the scanner but were not informed about the recombined items. As such, participants knew that they were participating in a memory task while in the scanner.

Behavioural data analyses

A response accuracy index was derived by computing the following formula: [Hits (i.e., "Yes" responses to old items) minus False Alarms (i.e., "Yes" responses to new items)]. Repeated-measures analyses of variance (ANOVA) were conducted on response accuracy and response latency scores. Significant main effects or interactions were followed by Tukey post-hoc tests.

MR imaging protocol

Functional and structural brain MR images were acquired on a 3-Tesla Philips Achieva MRI scanner with standard quadrature head coil (16 channels). The following scanning parameters were used for the collection of functional data: 33 slices were collected per image volume covering the whole brain. Scanning parameters for the echo planar imaging (EPI) sequence were as follows: orientation plane axial; matrix 120 x 120; field of view 240 x 240; repetition time/echo time (TR/TE) 2000ms/1000ms; flip angle 80°; slice thickness 3.5mm with a 0 mm interslice gap; voxel size 2 x 2 x 3.5 mm. For each task, two encoding and two test runs were collected (75 acquisitions per run). Each encoding run was immediately followed by a test run. In addition, all participants underwent a whole-brain T1

coronal orientation, matrix 256 x 256, 200 slices, 1 mm isotropic, TR/TE = 5.4/2.5 ms, flip angle 80°. These images were used for co-registration with the functional imaging data.

fMRI data analysis

Images were analysed using FEAT (FMRI Expert Analysis Tool) version 5.98, a part of FSL (FMRIB's Software Library, www.fmrib.ox.ac.uk/fsl). Pre-processing of each individual's fMRI dataset included: removal of non-brain structures from the T1 structural scans using BET (Brain Extraction Tool), motion correction using MCFLIRT, non-brain structures were removed from the echoplanar imaging volumes using BET, spatial smoothing using a Gaussian Kernel of FWHM 5 mm; mean based intensity normalisation of the entire 4D dataset by the same multiplicative factor; high pass temporal filtering (Gaussian weighted least-squares straight line fitting, with σ = 100s). Time series statistical analysis was performed using FILM with local autocorrelation correction. Functional scans were registered to the high resolution T1 structural scan per participant and to the standard Montreal Neurological Institute (MNI 152) standard space template image using affine registration with FLIRT. Coordinates (x, y, z) of activation are reported in MNI space.

For each participant, a fixed effects model was used to estimate effects for each condition. The following contrast was modelled for the verbal and nonverbal tasks separately: old item hits vs correct new item rejection (Ranganath et al., 2000; Hornberger et al., 2006). The resulting data were then entered into a mixed effects higher-level analysis to investigate activation across participants for each comparison. Z statistic images were thresholded using clusters determined by Z > 2.3 and a corrected cluster significance threshold of p < .01.This analysis yielded no significant corrected results. We therefore ran an additional uncorrected analysis with a p value of .001. This value was selected in order to minimise the risk of false

positive results. In addition, the % signal change within each significant cluster was extracted for each stimulus condition.

Results

Behavioural results

Response accuracy

A repeated-measures ANOVA revealed significant main effects of condition (new, old) [$F(1,30) = 189.604$, $p < .001$], denoting higher overall response accuracy to new (correct rejection of novel items) than to old items (correct identification of old items - false alarms to recombined items), and material type (verbal, nonverbal), [$F(1,29) = 53.507$, $p < .001$], reflecting higher overall response accuracy to verbal than to nonverbal items. In addition, a significant condition by material type interaction was also observed [$F(1,14) = 14.725$, $p = .002$]. Investigating the interaction further with post hoc tests revealed significantly higher response accuracy for verbal (85%) than nonverbal (51%) old items ($p = .001$) and for verbal (94%) than nonverbal (70%) new items ($p = .004$). In addition, significant differences in response accuracy between old (85%) and new (94%) items on the verbal task ($p < .001$) and between old (51%) and new (70%) items on the nonverbal task ($p < .001$) were also observed (Figure 2).

***** INSERT FIGURE 2 AROUND HERE *****

Response latency

A repeated-measures ANOVA on response latency uncovered a significant main effect of material type (verbal, nonverbal) [$F(1,119) = 56.060$, $p < .001$], reflecting significantly slower responses to nonverbal (1304 ms) than to verbal items (1091 ms). No significant main effect of condition (new, old) was observed [$F(1,79) = .005$, $p = .944$].

In addition, a significant condition by material type interaction was also observed [$F(1,119) = 17.329$, $p < .001$]. Investigation of the interaction with post hoc tests further revealed that participants responded significantly faster to verbal (1042 ms) than to nonverbal (1275 ms) old items ($p < .001$) and to verbal (1026 ms) than to nonverbal (1284 ms) new items ($p = .004$). In contrast, no significant differences in response latency were observed between old and new items on the verbal ($p = .999$) or nonverbal ($p = 1.0$) task.

Functional imaging results

All coordinates (x, y, z) of activation are reported in MNI space. The neural correlates of recognition memory were established by contrasting neural activation associated with correct recognition of old items and that associated with correct rejection of new items (i.e., old vs new). The mean number of responses included in the contrast for each condition are provided in supplementary table 1. Given the hypotheses and aims of the study, regions of interest analyses were conducted on the MTL and its subregions. Activation outside the MTL are therefore mentioned but not discussed in detail.

Correct recognition memory for verbal stimuli was associated with increased activation of the left anterior hippocampus (Figure 3 and Table 1). This region, however, was

not recruited during the same condition on the non-verbal task (Figure 3; Bar Chart). Additional clusters of significant activation were found outside the MTL, including the lateral occipital cortex, middle frontal gyrus, frontal pole and thalamus (Supplementary Table 2). In contrast, correct recognition memory for nonverbal stimuli was associated with significant activation of six regions within the MTL, four in the right hemisphere and two in the left (Figure 3 and Table 1). The specificity of each of these clusters to the nonverbal rather than verbal tasks is represented in the bar graphs in Figure 3. On this task, additional clusters of activation outside the MTL were also observed in a number of regions of the left hemisphere, including the angular gyrus, frontal pole and middle frontal gyrus (Supplementary Table 2).

*****   INSERT FIGURE 3 AROUND HERE   *****

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Discussion

This study investigated the neural correlates within the MTL of recognition memory for verbal and nonverbal stimuli in a single group of healthy individuals. For the verbal task, increased activation of the left hippocampus was observed during correct identification of stimuli that were identical between study and test compared to those that were novel (i.e., reflecting recognition memory). In contrast, activation in a distinct set of brain regions (right

perirhinal cortex, right posterior hippocampus, bilateral mid hippocampus and left posterior parahippocampus) was found during the nonverbal task.

The prediction that recognition memory of nonverbal stimuli asymmetrically recruits regions of the right MTL received partial confirmation, with increased brain activation observed in a number of clusters within the right MTL structures during successful recognition memory of nonverbal stimuli. Of particular interest is the participation of the perirhinal cortex in this process, a brain region central for the representation, recognition and discrimination of complex visual stimuli. The perirhinal cortex has previously been implicated in the ability to discriminate among perceptually complex items in the animal and human literature (Bussey and Saksida, 2002; Bussey et al., 2002; Ryan et al., 2012). Functional imaging studies and human lesion model studies have also highlighted the importance of the perirhinal cortex during representation of complex objects (Lee et al., 2005b; Lee et al., 2005a; Lee et al., 2006; Barense et al., 2007). Here, the complex symbol pairs are not easily imbued with a semantic label. In the absence of a semantic 'anchor', correct discrimination required successful retrieval of mental representations for the visually complex symbols. Our results demonstrate the contribution of the right perirhinal cortex to recognition memory of visually complex stimuli and provide support to theories implicating the perirhinal cortex in mnemonic processes.

Activation was also observed in the right hippocampus, a finding previously reported during the encoding and recognition of nonverbal stimuli (Papanicolaou et al., 2002; Kennepohl et al., 2007). Of note, however, is that MTL recruitment was not entirely lateralised during the nonverbal task with clusters of activation observed in the left hippocampus and the left posterior parahippocampal gyrus. This left hemisphere recruitment may reflect an attempt to verbalise or engage in elaborative processing as a mnemonic technique (Kondo et al., 2005), even in the context of stimuli that were designed specifically

to be difficult to verbalise. Taken together, our results extend previous findings and confirm the asymmetric and preferential recruitment of right MTL structures during memory processing of nonverbal stimuli (Golby et al., 2001). Further, our results underline the contribution of the perirhinal cortex during mnemonic processing of complex, poorly verbalisable, nonverbal stimuli.

The prediction that recognition memory of verbal stimuli preferentially recruits left MTL regions also received confirmation. Findings from the verbal task are consistent with previous research which implicates structures of the left MTL in verbal-semantic memory processing (Binder et al., 2003; Daselaar et al., 2003; Parsons et al., 2006). The left anterior hippocampus was specifically involved during recognition memory for compound words, in line with previous studies (Koutstaal et al., 2003; Giovanello et al., 2004; Jackson and Schacter, 2004; Park and Rugg, 2011). Importantly, however, data from our experiments revealed that left anterior hippocampal clusters recruited during the verbal recognition memory task were deactivated during the nonverbal task. This finding indicates that the left hippocampus appears to be central to recognition memory processes which comprise a semantic, and intrinsically verbalisable element, and may not participate in recognition memory for nonverbal stimuli.

Words are associated with a range of contextual information and concepts and recruitment of the left anterior hippocampus during the verbal task may be a result of the nature of the stimuli. In this study, the way in which each item was remembered was not controlled. In post task debriefings, however, participants commonly mentioned the use of mental imagery and associations as mnemonic tools to help remember each item. For example, the word 'bluebird' may be remembered by evoking the concept of a bluebird, a 'Nissan bluebird' automobile or the movie 'the bluebird' with Shirley Temple. Associating a conceptual mental image with the stimuli may have the effect of making the task more akin to

an associative memory task. Such tasks, which require the integration of information from different perceptual or conceptual domains, tend to recruit the hippocampus (Diana et al., 2007; Mayes et al., 2007), similar to the pattern of activation observed. Given the nature of the nonverbal stimuli, such a strategy was not available in the nonverbal version of the task. This explanation appears to support the claim that the anterior hippocampus is preferentially involved in processing integrated domain-general memory representations (in this instance words and their conceptual associations) whereas content specific processing may be carried out by extra-hippocampal MTL cortices (Liang et al., 2013).

Alternatively, the left hippocampal recruitment observed during the verbal condition in the current study, may reflect mental imagery related to the concepts evoked by the words themselves. Bilateral anterior hippocampal recruitment has previously been observed during mental imagery of scenes (Zeidman et al., 2015). Speculatively, the words used in the current study, may indeed have induced the mental image of a scene in our participants. While bilateral hippocampal recruitment may be involved during visuospatial mental imagery, MTL substructure recruitment during visualisation of concepts associated with words and symbols such as those used in the current experiment has not, to our knowledge, been investigated. It remains to be seen whether mental imagery of verbal and nonverbal stimuli is lateralised.

The left hemisphere is dominant for language in the majority of humans, regardless of handedness (Knecht et al., 2000). Whether this indicates a genetic component to the lateralisation of function remains unclear. Specific genes are associated with biological pathways for left-right asymmetry (Scerri et al., 2011). Environmental effects in early neurodevelopment, however, also influence the lateralisation of function (Raj and van Oudenaarden, 2008; Bishop, 2013). In parallel with left hemisphere dominance for language, it appears that the left MTL is dominant for mnemonic processing of verbal stimuli. In contrast, our results indicate that the right MTL is preferentially recruited during mnemonic

processing of nonverbalisable stimuli. What could account for this asymmetry of MTL function?

We speculatively argue that material specific asymmetry of function within the MTL may result from functional reorganisation during the development of language. Prior to language and semantic knowledge development, experience is primarily perceptually based. It is therefore plausible that left and right MTL are equally involved in mnemonic processing of visual stimuli during the period preceding the acquisition of language. As language and semantic knowledge develop, however, the left MTL becomes functionally invaded by and recruited for verbal mnemonic processing due to its proximity with left lateralised language processing regions. As left MTL real estate is progressively appropriated for verbal mnemonics, visual aspects of mnemonic processing become asymmetrically dependent upon the right MTL. Complete translocation of function may not occur however, resulting in the continued involvement of the left MTL on nonverbal mnemonic processing, albeit to a lesser degree than the right. This explanation accommodates recent observations relating to the asymmetric, but not complete, material specific lateralisation of function in the MTL. Future studies may wish to test this position further by examining individuals with right hemisphere language dominance, in whom a reversed pattern of activation would be predicted. In addition, advances in high-resolution functional imaging will allow further investigations on how (and which) subregions of the MTL differentially contribute to verbal and non-verbal mnemonic processing.

The dual process theory of recognition memory states that the hippocampus is important for recollection and the perirhinal cortex underlies familiarity (Mayes et al., 2007). Concurrently, human lesion studies suggest that damage to left and right MTL structures impairs performance on verbal and nonverbal learning tasks respectively (Jones-Gotman, 1986; Helmstaedter and Elger, 1996; Seidenberg et al., 1996; Jones-Gotman et al., 1997;

Gleissner et al., 1998; Pillon et al., 1999; Savage et al., 2002; Aly et al., 2010; Cohn et al.,2009; Weintrob et al., 2007). More recently, patients with lesions to specific subregions of the MTL have been recruited to investigate the dual process theory in relation to verbal and non-verbal stimuli. Martin and colleagues (2011) probed familiarity and recollection of verbal and nonverbal stimuli in a patient with a left lateralised MTL lesion. Importantly, the lesion encompassed the perirhinal cortex but spared the hippocampus. As predicted by the dual process theory, this patient was specifically impaired on familiarity for verbal stimuli while recollection remained intact. For nonverbal (faces and abstract pictures) stimuli, however, both familiarity and recollection were intact. In short, the left perirhinal cortex lesion in this patient resulted in impaired familiarity for verbal but not nonverbal stimuli indicating that the processes of familiarity and recollection may also be lateralised. Taking these observations into account, it is plausible that the right perirhinal cortex specifically underlies familiarity for non-verbal stimuli. While this study did not specifically probe familiarity and recollection, both the right perirhinal cortex and hippocampus were recruited during the nonverbal task. As behavioural accuracy was considerably low on the nonverbal task, it is possible that some nonverbal stimuli were recognised based on familiarity, resulting in recruitment of the right perirhinal cortex while others were recollected, resulting in recruitment of the right hippocampus. In contrast, performance on the verbal task remained high and recruitment of the left hippocampus may reflect more confident recollection of the verbal stimuli. These speculative points raise interesting questions relating to material specific lateralisation of familiarity and recollection to be probed in future studies.

On a related note, the stimuli used in the verbal and nonverbal conditions likely differ with regard to their level of processing. At encoding, the compound words can be encapsulated as a single conceptual unit while the symbol pairs require an association between two distinct symbols. While the hippocampus is implicated in contextual associative

processing, the perirhinal cortex has been implicated in associative processing when both elements are items (Mayes et al., 2007). Therefore, our finding of right perirhinal cortex recruitment during the non-verbal task may reflect item-item associative memory processing for the nonverbal stimuli while the left anterior hippocampal recruitment may reflect conceptual/contextual associative processing for the verbal stimuli.

While our results support the hypothesis that different subregions of the MTL are differentially involved in mnemonic processing of verbal and non-verbal material in a lateralised manner, our findings need to be taken with caution. Indeed, differences in neural activity may also reflect other aspects of the task. For example, the items used in the verbal memory task contained, by their very nature, semantic meaning, and were therefore familiar to participants, whereas the nonverbal items did not. As such, participants found the nonverbal task much more difficult than the verbal task, possibly reflecting the absence of prior associations which would support encoding. Therefore, observed differences in neural activity may also reflect difference in difficulty between the verbal and nonverbal tasks, in addition to the effect of type of material. Future studies that include nonsense words which are unfamiliar and carry no semantic weight may help clarify this issue. A related point to consider is that, on the nonverbal task, the number of data points available for the imaging analyses were somewhat reduced because of task difficulty. Nevertheless, while the activation clusters in the MTL may appear small, they are in line with a growing body of literature reporting material specific lateralisation of function within the MTL (Golby et al., 2001; Powell et al., 2005; Rosazza et al., 2009).

These potential limitations notwithstanding, the results of the current study indicate that the neural correlates of recognition memory processing for verbal and nonverbal stimuli are differentiable in the human brain. These results provide evidence that the right perirhinal

cortex and hippocampus are preferentially involved in recognition memory for symbol pairs that are devoid of semantic information. In contrast, the left anterior hippocampus is preferentially involved in associative recognition memory for compound words which contain semantic meaning.

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Figure and Table Legends.

Figure 1. Three examples of the symbol pairs used in the nonverbal task.

Figure 2. Recognition memory performance for each stimulus condition on the verbal and nonverbal tasks. The bar chart shows the percent correct response for each condition (old and new). Error bars represent the standard error of the mean.

Figure 3. Regions of significant difference in BOLD response associated with recognition memory (old vs. new) for verbal (red) and nonverbal (blue) stimuli. Bar charts indicate mean percent signal change associated with each memory condition (verbal old and nonverbal old) within each significant cluster. See Table 1 for the coordinates and cluster sizes of relevant regions

Table 1. Regions of significant BOLD signal increase within the MTL associated with correct recognition memory of verbal and nonverbal stimuli (i.e., contrast of hits for old items vs. correct rejections of new items). Results are reported at p = .001 uncorrected.

Supplementary Table 1. Mean number of hits and correct rejections included in the contrast for each group in each condition (SEM in brackets).

Supplementary Table 2. Regions of significant BOLD signal increase outside of the MTL

for the contrast of old item hits vs. new item hits on the verbal and nonverbal task. Results are

reported at p = .001 uncorrected with a voxel threshold of at least 100 contiguous voxels.