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Levels of processing and the parietal memory network  
by  
Hung-Yu Chen

A dissertation presented to  
The Graduate School  
of Washington University in  
partial fulfillment of the  
requirements for the degree  
of Doctor of Philosophy

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Hung-Yu Chen

*Washington University in St. Louis*

*August 2018*

Dedicated to my parents.

## ABSTRACT OF THE DISSERTATION

Levels of processing and the parietal memory network by

Hung-Yu Chen

Doctor of Philosophy in Psychological and Brain Sciences

Washington University in St. Louis, 2018

Kathleen B. McDermott, Chair

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The parietal memory network (PMN) is a functional brain network that has been recently described through the convergence of task-based fMRI and resting-state functional MRI studies (Gilmore et al., 2015). The network's characteristic encoding/retrieval flip (deactivation at encoding and activation at later retrieval, discussed by Gilmore and colleagues) and its manifestation of a negative subsequent memory effect (greater deactivation at encoding for items that will later be recognized—i.e., subsequent hits—than for those that will not—subsequent misses) (Cabeza et al., 2004; Daselaar, Prince, & Cabeza, 2004; De Chastelaine & Rugg, 2014; Elman, Rosner, Cohn-Sheehy, Cerreta, & Shimamura, 2013; Kim, 2011; Otten & Rugg, 2001) and other memory-related contrasts suggest possible ties to effective encoding of memory. This study sought to use task-based functional MRI to further investigate this tie between the PMN and encoding through the use of the levels of processing paradigm ( Craik & Lockhart, 1972; Craik & Tulving, 1975). Specifically, I hypothesized that the PMN—which demonstrates the negative subsequent memory effect—would deactivate more for conditions that lead to more effective encoding such as a deeper level of processing.

Partial support for greater deactivation in the PMN for deeper processing was observed in two of the three regions that form the network (specifically within precuneus and mid cingulate): Precuneus (and to a lesser extent) mid cingulate deactivated for deeper, semantic processing than for the more shallow orthographic processing. However, the two regions did not show differential activity between semantic and phonological processing (presumably shallower than semantic processing), despite behavioral differences; The third region of the network, PIPL, did not show a consistent levels of processing effect in the univariate analyses, nor did it show the negative subsequent memory effect despite all other PMN regions showing the effect. Linear-mixed effect modeling of PMN regions showed that trial-by-trial variation in levels of BOLD activity in precuneus and mid cingulate predicted subsequent memory, above and beyond the level of processing manipulation as well as contribution from left inferior frontal gyrus (IFG), a region consistently identified in subsequent memory studies (Kim, 2011). Attempts to use multivariate pattern analysis to classify subsequent memory using only individual PMN regions led to above chance classification (hit or miss) for all PMN regions. The ability to predict subsequent memory using only activity from PMN regions (and beyond the contribution of left IFG) supports the role of the PMN in encoding, showing that a sufficient level of deactivation in PMN regions is associated with successful encoding regardless of the level of processing. Overall, the study supported the conclusion that two members of the PMN—the precuneus and mid cingulate—contribute to effective encoding of memory.



# Chapter 1: Introduction

## 1.1 A wide range of memory contrasts reveal a sparse set of regions in parietal cortex

Since the turn of the century, there has been an increased interest in the role of the parietal cortex in episodic memory (Cabeza, Ciaramelli, & Moscovitch, 2012; Cabeza, Ciaramelli, Olson, & Moscovitch, 2008; Wagner, Shannon, Kahn, & Buckner, 2005). Recently, Gilmore et al. (2015) observed commonalities in a sparse set of parietal regions across a wide range of memory-related contrast to a set of regions that include precuneus, mid cingulate and dorsal angular gyrus (also known as posterior inferior parietal lobule, or PIPL). For instance, the “encoding/retrieval flip” (**Figure 1.1**) can be seen in precuneus, mid cingulate, and PIPL; that is, the regions deactivate during encoding and activate during retrieval.

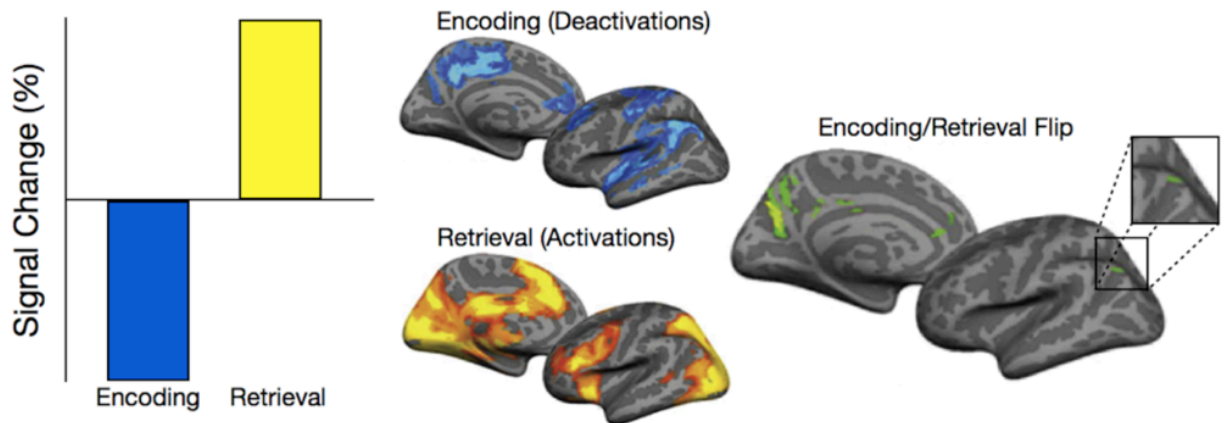
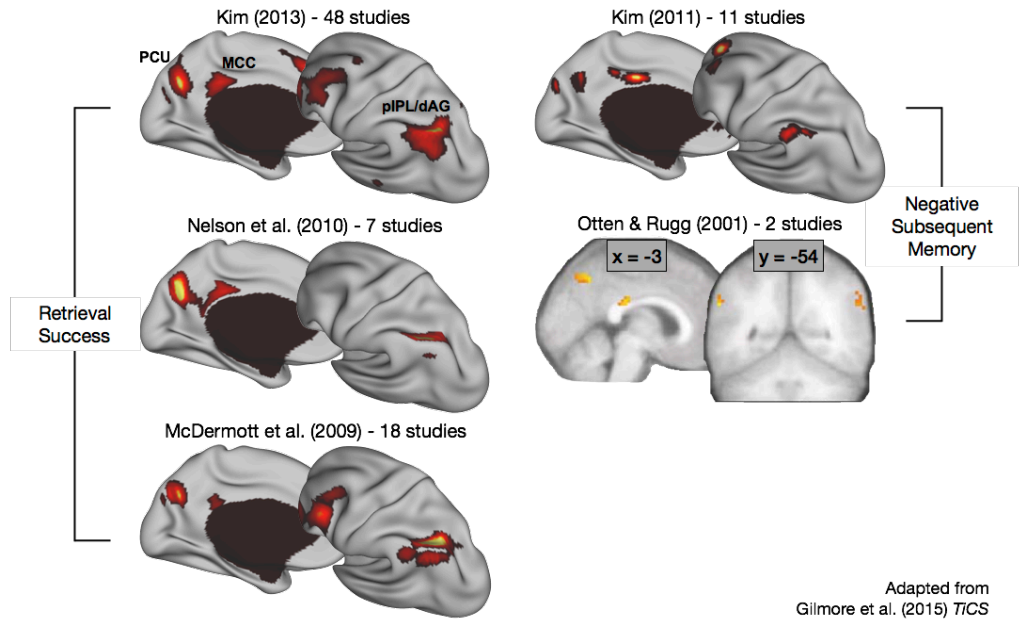


Figure 1.1. The “encoding/retrieval flip” revealed a sparse set of regions within parietal cortex. In other words, in examining which regions show qualitatively different patterns at encoding and retrieval (i.e. deactivate during encoding and activate during retrieval), three regions emerged (precuneus, mid cingulate and inferior parietal lobule, shown in figure). (Adapted from Gilmore et al., 2015; data from Huijbers et al., 2012).

In addition to the encoding/retrieval flip, these regions were also revealed in other memory-related comparisons, such as the retrieval success effect (greater activity for successfully retrieved old items than correctly rejected new items) (Kim, 2013; McDermott, Szpunar, & Christ, 2009; Nelson et al., 2010) (**Figure 1.2 left**); greater deactivation during encoding for items that would later be recognized (i.e., subsequent hits) than those not later recognized (i.e., subsequent misses) (Cabeza et al., 2004; Daselaar et al., 2004; De Chastelaine & Rugg, 2014; Elman et al., 2013; Kim, 2011; Otten & Rugg, 2001) (**Figure 1.2 right**; negative subsequent memory effect); greater activity for subsequent versus initial item presentations (Jessen et al., 2001; Nelson, Arnold, Gilmore, & McDermott, 2013); greater activity for intentional retrieval versus intentional encoding (McDermott et al., 1999); greater activity for false alarms versus misses (Wheeler & Buckner, 2003); greater activity for higher versus less confidently retrieved items (Yonelinas, Otten, Shaw, & Rugg, 2005); and greater activity for items retrieved with contextual information versus items without contextual information (Frithsen & Miller, 2014; Raposo, Han, & Dobbins, 2009). These contrasts support the contribution of these regions to memory, as well as demonstrate the cohesiveness of these regions across memory-related contrasts.



Adapted from  
Gilmore et al. (2015) *TICS*

Figure 1.2. Task-based fMRI meta-analyses of retrieval success and negative subsequent memory effects revealed a common set of regions. Adapted from (Huijbers et al., 2012).

## 1.2 Resting-state functional connectivity studies have revealed a sparse network that aligns with the parietal regions emerging from memory studies

In parcellation studies using resting-state functional connectivity, researchers typically collect resting-state data while participants stare at a fixation cross; researchers then apply various algorithms to organize brain regions into correlated networks. In its most basic definition, a network is a “collection of points, or nodes, joined by lines, or edges”(Newman, 2008). When applied to the organization of the human cerebral cortex using functional connectivity, a network then refers to a collection of interconnected brain regions (as measured by functional connectivity)(Yeo et al., 2011). Despite the differences in the algorithms used, researchers using independent component analyses (Doucet et al., 2011; Shirer, Ryali, Rykhlevskaia, Menon, & Greicius, 2012; Smith et al., 2013) and other clustering algorithms

(Power et al., 2011) have identified a distinct functional network that shows strong correspondence with the regions described in the task-based memory studies (**Figure 1.3**). It is thought that resting state data capture a lifetime history of co-activation between brain regions (Dosenbach et al., 2010; Gilmore, Nelson, & McDermott, 2015; Lewis, Baldassarre, Committeri, Romani, & Corbetta, 2009; Wig, Schlaggar, & Petersen, 2011) and thus these data suggest that these regions work in concert over the lifetime. Wig, Schlaggar and Petersen argued that regions that share high correlations with each other during resting state might be mediated by a “Hebbian-like” mechanism such that continual recruitment of a common set of regions might lead to changes in synaptic efficiencies between these regions. Recently, Warren and colleagues (2014) demonstrated the functional significance of using resting-state functional connectivity to study brain organization by showing that network measures of resting state data can be used to predict disruption caused by lesions. More specifically, damage to connector hubs (regions with high system density and high participation coefficient) led to severe and widespread cognitive deficits.

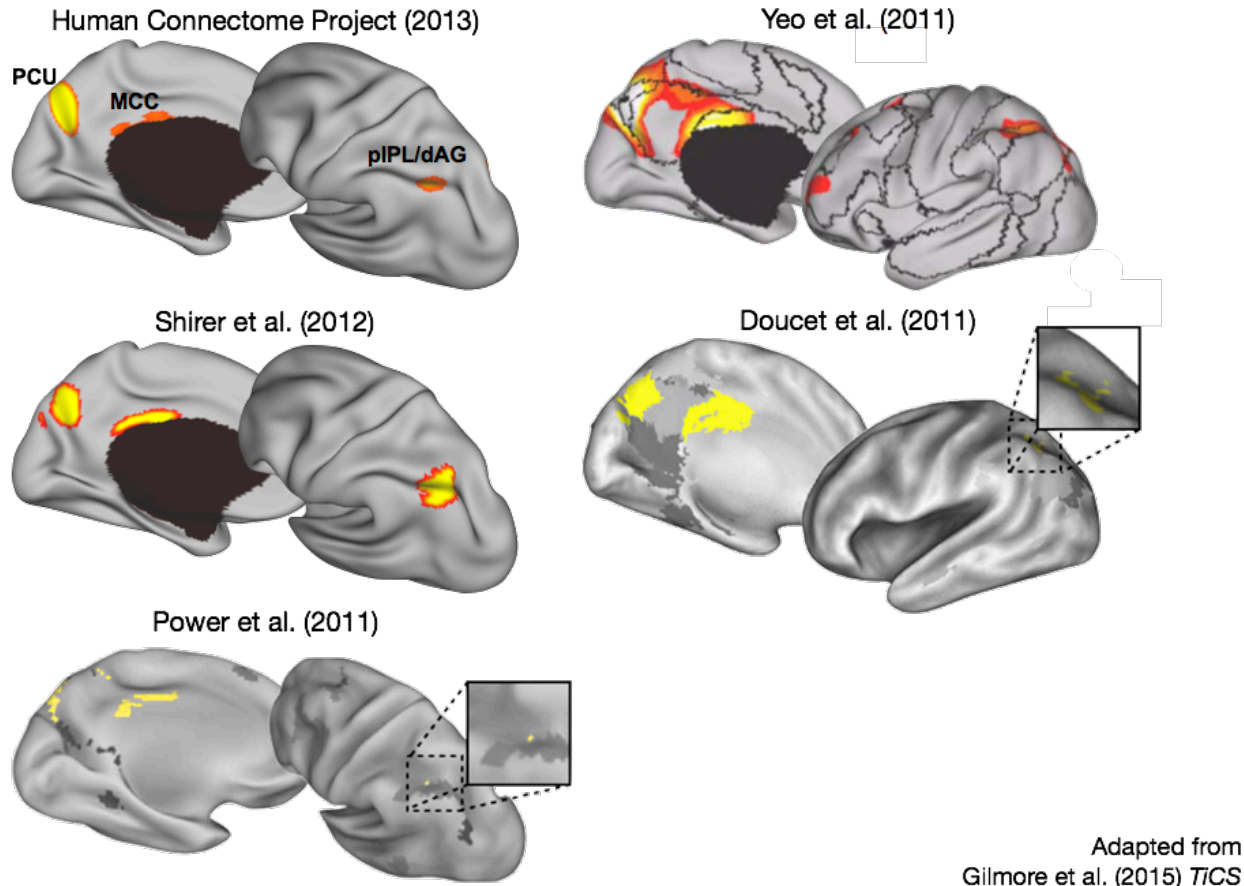


Figure 1.3. Independent resting-state functional connectivity studies have revealed that the regions within mid-cingulate cortex, precuneus, and posterior IPL form a distinct functional network.

### **1.3. The convergence of task-based memory studies and resting state functional connectivity studies led to the hypothesis that this collection of regions forms a functional network that contributes to human memory encoding and retrieval.**

Gilmore and colleagues observed that both task-based memory studies as well as resting state functional connectivity led to the same collection of regions: precuneus, mid cingulate and PIPL. The convergence of the analysis stream led them to the hypothesis that this collection of

regions forms a functional network that contributes to encoding and retrieval of human memory. Gilmore et al. named this collection of regions the parietal memory network. The convergence of task-based fMRI and resting-state fMRI has previously led to the discovery of other functional networks such as the default mode network, frontal parietal control network and cingulo-opercular network (J D Power et al., 2011b). Perhaps the best-known example is the default mode network, which typically deactivates during goal-directed behaviors (Greicius, Supekar, Menon, & Dougherty, 2009; Raichle et al., 2001). The convergence is important because if functional networks reflect a history of co-activation over the lifetime, researchers should be able to identify the same network across a variety of contrasts and task states.

## **1.4 Manipulating the level of processing employed during encoding allows us to examine the tie of PMN deactivation to the quality of encoding**

Manipulating the level of processing employed during encoding offers a way to further explore the role of PMN regions in encoding. As mentioned above, one of the contrasts that consistently identified PMN regions is the subsequent memory contrast. PMN regions typically deactivate more during encoding for subsequent hits. Nevertheless, it is not clear what deactivation in PMN represents. One possibility is that deactivation in PMN indexes the quality of probe processing such that the nature of processing of encoding probes would lead to different levels of PMN activity. Alternatively, PMN activity could index something not directly tied to the nature of probe processing, such as attentional processes or uncontrolled item effects (Cortese, Khanna, & Hacker, 2010; Cortese, McCarty, & Schock, 2015).

If PMN indexes the quality of probe processing, manipulations that lead to more effective encoding should also lead to more PMN deactivation. Manipulating the level of processing at encoding offers one such opportunity because the level of processing has been shown to

influence later memory performance ( Craik & Lockhart, 1972; Craik & Tulving, 1975; Nyberg, 2002; Wagner et al., 1998). The levels of processing framework focuses on the idea that memory traces can be altered by how information is processed at encoding, whether those processes are for the purpose of perception or comprehension. Deeper, or more semantic levels of processing lead to more durable traces. In a study by Craik and Tulving (1975), they had participants make three kinds of judgments at encoding: semantic, phonological, and orthographic. The consistent finding across multiple experiments was that semantic processing led to the best memory performance later, and their finding could not be explained by differences in encoding time. Craik and Tulving surmised that the durability of the memory trace is influenced by the depth of processing: the deeper, the more semantic the processing, the more durable the memory trace. Thus, manipulating the level of processing allows us to explore the link between the nature of the active processing of the encoding probes and PMN activity, by prospectively predicting that deeper levels of processing would lead to more effective encoding and greater deactivation in PMN.

## **1.5 Does trial-by-trial variability in PMN regions predict subsequent memory?**

It will be another step forward for our understanding of PMN regions if we can demonstrate that trial-by-trial variability in PMN regions can predict the likelihood of subsequent recognition memory, using linear mixed effects (LME) models and multivariate pattern analysis (MVPA) (described more in the methods section). On one hand, studies that revealed PMN regions in negative subsequent memory contrasts averaged across trials and participants (Daselaar et al., 2004; De Chastelaine & Rugg, 2014; Elman et al., 2013; Otten & Rugg, 2001) and thus cannot inform as about the usefulness of using trial-wise PMN activity to predict

subsequent memory. On the other hand, even though using trial-wise neural activity to decode subsequent memory (Kuhl, Rissman, & Wagner, 2012; Watanabe et al., 2011; Xue et al., 2010) or memory retrieval (Chadwick, Hassabis, Weiskopf, & Maguire, 2010; Rissman, Greely, & Wagner, 2010) is not a new practice, no study has focused solely on PMN regions. Among these studies, Xue and colleagues' study is the most relevant to our study, as the other studies either used whole-brain masks or ROIs not containing PMN regions for decoding. Xue and colleagues found that anatomically-defined left inferior parietal lobule showed greater pattern similarity across repeated study episodes for subsequently recalled than recognized or forgotten words. However, Xue and colleagues' left inferior parietal lobule mask also included non-PMN regions such as supramarginal gyrus and angular gyrus. As a result, it was not clear which region in left inferior parietal lobule contributed to the higher pattern similarity across study episodes for subsequent recalled items.

Another research question that can be answered via LME analysis is whether PMN can predict subsequent memory above and beyond contribution from another region known for showing the subsequent memory effect. For instance, left inferior frontal gyrus (IFG) was identified by Kim's (2011) meta-analysis on subsequent memory as one of the regions that showed greater activity for subsequent hits than misses. Including PMN regions as well as left IFG in the same LME model for subsequent memory could assess the relative contribution of positive and negative subsequent memory regions to subsequent memory.

To summarize, if PMN activity is tied to the quality of processing probes at encoding, it should deactivate more for deeper levels of processing. If it, however, also indexes uncontrolled item effects or attention, it would show a subsequent memory effect above and beyond the levels of processing manipulation. Failure to observe the subsequent memory effect in PMN regions



above and beyond the contribution from left IFG would challenge the role of the PMN at encoding as well as the usefulness of predicting subsequent memory with PMN regions.

## **Chapter 2: Methods and Approach**

### **2.1 Participants**

Participants were 30 18-35 year olds recruited from Washington University and the St. Louis area. All participants reported being right-handed, native speakers of English, who possessed normal or corrected-to-normal vision, and were neurologically healthy. All participants provided consent and received compensation (\$25 an hour) in accordance with the guidelines set forth by the Human Research Protection Office at Washington University. One participant was excluded due to excessive motion, leaving 29 for the analysis. Among the 29 participants (16 female, ages 18-31), only 23 had functional connectivity data as six participants' data were collected along with a separate study.

### **2.2 Materials**

Stimuli consisted of 288 words, all collected via the English Lexicon Project (Balota et al., 2007). The stimuli followed a 2 (2 vs. 3 syllable words) x 2 (Living vs. Non-living) x 2 (Upper vs. Lowercase) design. Half (144) of the words represented living things and the other half represented non-living things. Half of the words contained two syllables, and the other half contained three syllables. Finally, half of the words appeared in upper-case letters and the other half appeared in lower-case letters.

An Apple MacBook Air portable computer running PsychoPy version 1.82.01 (Peirce, 2007) was used to display stimuli while participants were in the scanner. An LCD projector (Sharp PG-C20XU) was used to project encoding stimuli onto an MRI-compatible rear-

projection screen (CinePlex) at the head of the scanner bore (screen resolution: 1024x768). Subjects viewed the screen through a mirror attached to the top of the head coil (field of view = 21° of visual angle). The same MacBook Air was used to present retrieval stimuli (screen resolution: 1366x768) outside the scanner. All stimuli were centrally presented to participants in white Arial font on a black (RGB: 0, 0, 0) background. Encoding stimuli subtended 1.05° of visual angle. Retrieval stimuli subtended approximately 0.90° of visual angle.

## **2.3 Design and procedure**

The experiment consisted of four phases: (i) one 7-min resting-state functional connectivity scan; (ii) another 7-min resting-state functional connectivity scan; (iii) three 6-min encoding runs; (iv) a 15-min retrieval task performed outside of the MRI scanner. For the 23 participants who had resting-state functional connectivity data, the data were collected as part of another experiment one day prior to phases three through four. During the third phase (encoding), participants encoded 144 words across three different runs (48 words per run). Words were presented in one of three encoding conditions: (i) orthographic (Upper vs. Lowercase), (ii) phonological (2 vs. 3 syllables), or (iii) semantic (Living vs. Non-Living). Due to some concern about the PMN's sensitivity to task switching (through a literature search and earlier data collected from our lab), the conditions in which the words were presented were blocked, such that participants were not switching between conditions on a trial-by-trial basis. Blocking the task, however, is not without potential drawbacks. For instance, trials within a block might have sequential dependencies in RTs or judgments. In each scanning run, there were three blocks of 16 words. The order of the blocks within runs (e.g., orthographic → phonological → semantic) was counterbalanced within and across participants.

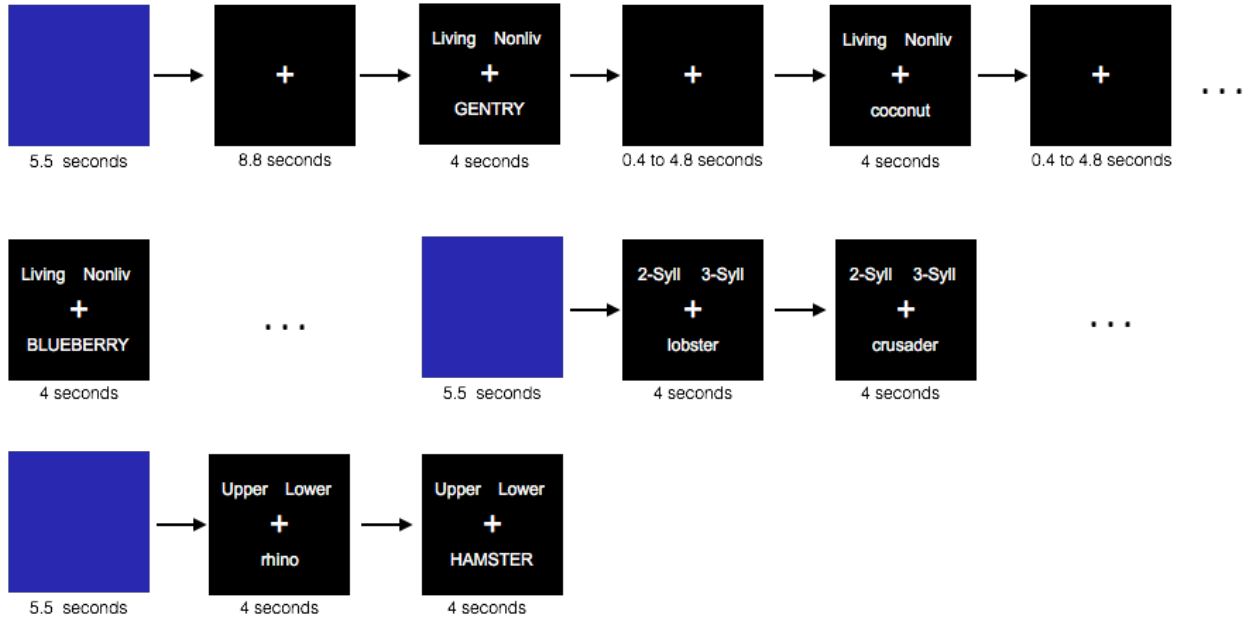


Figure 2.1. Sample schematic for one run of encoding trials. Prior to each block of 16 words, a blue screen oriented the subject to a change in task set. Words were presented for 4 seconds, with an ISI of .4-4.8 seconds.

At the start of each encoding scan, a fixation crosshair was presented for 8.8s (**Figure 2.1**). Within each encoding trial, the target word was displayed for 4s below a fixation crosshair, during which the participants made an orthographic, phonological, or semantic judgment about the word. For the orthographic judgment, participants decided if the presented word was upper or lower case; for the phonological judgment, participants determined the number of syllables in the presented word; for the semantic judgment, participants made a living or non-living judgment on the presented word. Condition cues were provided above the fixation crosshair for the duration of the trial. The encoding trials were separated by jittered ISIs of 0.4-4.8s, during which a fixation crosshair was presented. A dark blue (RGB: 0, 0, 89) screen indicating new condition was displayed for 5.5s with no fixation crosshair prior to the first condition block, in between the

first and second condition block, and in between the second and third condition block. Jittered ISIs of 0.4-4.8s bookended the dark blue condition switch screen.

After the third phase of the experiment, participants exited the MRI scanner and completed the fourth phase of the experiment. During this phase (retrieval), participants were presented with 288 words, half (144) of which had been seen during the encoding scans (old). The order in which the words were presented were randomized, with the constraint that a participant could not receive more than three old words or three new words consecutively.

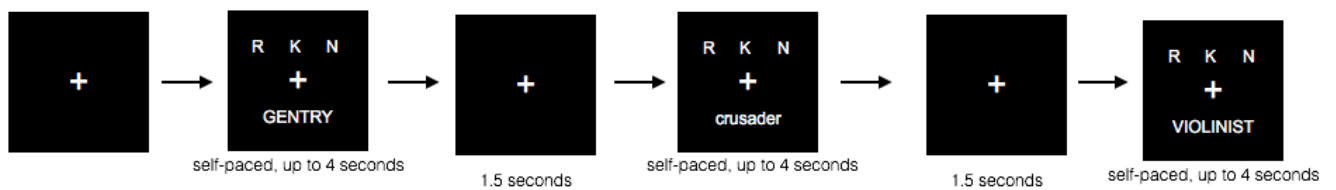


Figure 2.2. Schematic of procedure for the retrieval phase (unscanned).

The retrieval phase used a variant of the “Remember/Know” task originally described by Tulving (1985; see also Gardiner, 1988). At the start of the retrieval phase, a fixation crosshair was presented for 4s (**Figure 2.2**). Within each retrieval trial, the target word was displayed below a fixation crosshair. In response to each target word, participants made a Remember/Know/New judgment (Lindsay & Kelley, 1996; Perfect, Mayes, Downes, & Van Eijk, 1996). They were asked to make a *remember* response when they could retrieve specific episodic details of their initial encoding experience. If they remembered seeing the word during the encoding phase but could not recall specific details about its occurrence, they were instructed to make a *know* response. If they did not recognize seeing the word during the encoding phase, they were instructed to make a *new* response. Response option cues were provided above the fixation crosshair for the duration of the trial. The retrieval trials lasted until the participant recorded a response, up to a maximum of 4s. Responses made in fewer than 0.3s were not

accepted to minimize the recording of inadvertent button presses. An ISI of 1.5s separated each retrieval trial, during which a fixation crosshair was displayed. Additionally, one-third (96 words) and two-thirds (192 words) of the way through the retrieval phase, participants were allowed to pause for a self-determined length of time before continuing to the next trial.

## **2.4 MRI data acquisition**

MRI scanning was performed on a Siemens MAGNETOM Prisma 3.0T scanner (Erlangen, Germany) using a Siemens 32 channel Head Matrix Coil, designed for functional MRI. A shielded LCD projector (Sharp model PG-C20XU) displayed stimuli onto an MRI-compatible screen situated at the head of the bore, which the participants viewed through a mirror attached to the coil (field of view = 21.5° of visual angle). Ear plugs were provided to participants to protect their hearing. In-scanner responses were made via button press on a fiber-optic (MRI compatible) keypad.

Structural images were acquired using a high-resolution sagittal, T1-weighted MP-RAGE sequence (TE = 2.22ms, TR = 2.4s, TI = 1000ms, flip angle = 8°, 208 frames with 0.8 x 0.8 x 0.8 mm voxels); these images were used for between-participant registration and anatomic localization. Functional (BOLD) (including functional connectivity) images were collected using an asymmetric spin-echo, echo-planar sequence sensitive to T2\* contrast. In each functional run, whole brain coverage had in-plane resolution of 3 x 3mm isotropic voxels (48 contiguous slices), acquired in an interleaved fashion parallel to the anterior-posterior commissure plane. Frames were collected every 1.1 s (TE = 27ms, flip angle = 50°) with a multiband factor of 4. The first 4 images of each run were discarded automatically by the scanner to allow for longitudinal magnetization stabilization and would not be included in functional analyses. Temporal jitters were introduced into each scan run in order to maximize design efficiency.

## **2.5 Task-based data pre-processing**

Preprocessing was performed using AFNI (Analysis of Functional NeuroImages) (Cox, 1996, 2012) to remove noise and artifacts in imaging data. In the order of analysis steps, outlier censoring was applied to TRs (frames) when more than 10% of voxels were outliers. Despiking was performed using AFNI's 3dDespike algorithm. After despiking, the anatomical T1 scan was skullstripped. For each subject, individual BOLD runs and the anatomical T1's centers were first aligned to the center of the template, the 2009c nonlinear asymmetric version of the MNI152 template (Fonov et al., 2011; Fonov, Evans, McKinstry, Alml, & Collins, 2009). The BOLD runs were then aligned to the anatomical T1 image using affine transformation. Next, the anatomical T1 image was warped to standard space using non-linear transformation. The same non-linear transformation was then applied to each BOLD run. Each functional run was blurred with a fwhm of 4.0mm. The voxel time series were scaled to have a mean of 100.

## **2.6 Task-based fMRI data analysis overview**

Three analysis approaches were taken to analyze task-based fMRI data: whole-brain univariate analysis, linear-mixed effects (LME) analysis, and multivariate pattern analysis (MVPA). The whole-brain univariate analysis (contrasting the magnitudes of BOLD activation between different levels of processing) served mostly as manipulation checks, offering us a way to qualitatively compare our results with previous studies examining level of processing and subsequent memory effects. For analyses on subsequent memory effects, the dissertation focused on subsequent hits versus subsequent misses. Even though remember and know judgments were collected, these data were not essential to the primary research questions mentioned here. Hence,

aside from reporting univariate tests, remember and know trials were collapsed for further analyses.

The primary analyses of this study employed linear mixed-effect models to examine the role of PMN regions at encoding. Linear mixed effect models were used for the levels of processing analysis and subsequent memory analysis, examining if a deeper level of processing leads to greater deactivation in PMN and whether variability in trial-by-trial activity in PMN regions predicts subsequent memory. LME analysis has the benefit of taking individual differences between participants into account, by assigning each participant a separate intercept in the model while taking account of trials that are nested within the same individual (Chen, Saad, Britton, Pine, & Cox, 2013; St. Jacques, Szpunar, & Schacter, 2017). This approach contrasts with the usual analysis approach, in which variability across trials is removed by averaging first within participants.

Multivariate pattern analysis was used alongside LME because it can take advantage of differences in spatial patterns of activation to aid in classification, something neither the standard univariate analysis nor LME analysis can do. For instance, in a hypothetical case where only some voxels in a region are predictive of subsequent memory, MVPA can still take advantage of the information in those voxels and make accurate predictions. The LME analysis, in its current form in this study, averaged across voxels within a region; as a result, the LME analysis would find significant results only if the average across the entire region differs across conditions.

To independently define PMN regions for LME and MVPA analysis, resting-state functional connectivity was used. More specifically, PMN regions were identified from a seed correlation map from the full sample of subjects (24 in total, see section 2.8 for more details),

which is a map consisting of each voxel's correlation to a region of interest over the span of resting state scans (discussed in more detail later).

## **2.7 Task-based fMRI data analysis: General linear models and *t*-tests**

Image processing was performed using AFNI as well. The BOLD signal for each participant was analyzed using a general linear model (GLM) approach that estimated beta for each trial type with the assumption that the hemodynamic response had a gamma shape (AFNI default for gamma function: height of 1, duration of approximately 12 seconds).

Three sets of GLMs were built, with one coding for the level of processing (orthographic, phonological and semantic), another coding for the subsequent memory effect (subsequent hits and subsequent misses, with subsequent hits including remember and know judgments coded separately), and a last set following the beta series regression (Rissman, Gazzaley, & D'Esposito, 2004) approach to obtain individual beta estimates for each trial for linear mixed effect analysis and MVPA analysis.. The biggest difference between the beta series regression approach and regular GLM approach is that in the beta series regression, each individual trial was modeled using a separate regressor (whereas trial types were used for the standard GLMs). It is worth mentioning that Mumford and colleagues (2012) argued that building a separate GLM for each trial was associated with higher classification accuracy with higher signal-to-noise ratio. Nevertheless, Abdulrahman and Henson (2016) suggested that depending on the actual ratio of trial-to-trial variability to scan noise, the beta series regression approach can be better when the ratio is high.

For the first two sets of GLMs, analysis was conducted initially for each participant, and group maps were generated by averaging beta coefficients from each participant. Specific



univariate contrasts were performed by conducting  $t$ -tests (paired samples, 2-tailed) between conditions. These contrasts include: Semantic versus orthographic processing, phonological versus orthographic processing, semantic versus phonological processing, and subsequent hits (remember) versus subsequent misses, subsequent hits (know) versus subsequent misses, and subsequent hits (remember) versus subsequent hits (know) and subsequent hits (average of remember and know) versus subsequent misses.

The  $t$ -test images were thresholded to  $p < .001$  at the voxel level, using a cluster size threshold yielding  $\alpha < .05$ . The minimum number of contiguous voxels for surviving clusters was determined using AFNI's `-Clustsim` option in the program `3dttest++`, which simulates 1000 null results to control for the false positive rate. This new procedure was designed to remediate the issues described in Eklund, Nichols, and Knutsson (2016), addressing incorrect assumptions regarding the shape of the spatial auto-correlation function. Although all analyses were done on the volumetric data, for visualization purposes the resulting statistical maps were projected onto a partially inflated surface representation of the human brain using Connectome Workbench software (Marcus et al., 2011).

## **2.8 Resting-state functional connectivity analysis: Defining PMN regions for further analyses in an unbiased manner**

Resting-state scans were collected for 24 participants (one dropped due to excessive motion in the task-based data). The scans consisted of two separate runs of 382 frames (764 frames in total). Preprocessing was conducted in the same manner as the task-evoked data described above, with the exception that the voxel time series were not scaled to have a mean of 100. Global signal regression was not used in processing, as considerable amount of debate still centers around its use (Gotts et al., 2013; Murphy, Birn, Handwerker, Jones, & Bandettini, 2009;

Murphy & Fox, 2017; Jonathan D. Power et al., 2014; Jonathan D. Power, Schlaggar, & Petersen, 2015; Saad et al., 2012). While global signal regression offered several benefits, such as better removal of motion and cardiac and respiratory signals, it can also introduce artefactual anti-correlations and lead to biases when comparing groups with different noise characteristics and network structures (Murphy & Fox, 2017; Jonathan D. Power et al., 2015). Below, specific steps used to identify the regions within the PMN for this specific set of subjects using their resting state data are described. Once the PMN was defined, the remaining analyses examine the task-related responses within the network.

PMN regions were defined from clusters that emerged from a seed correlation map. After initial preprocessing, a seed correlation map was obtained for the mid cingulate observed in the paper by Nelson and colleagues (Nelson et al., 2013). The choice of using mid cingulate (rather than precuneus) as the seed was an arbitrary one. However, the specific seed from the Nelson paper was chosen due to the concern that extracting correlation from a seed more posterior would risk picking up regions correlated with posterior cingulate, a major hub in the default mode network (Buckner et al., 2009). The seed was created centering around coordinates 1, -24, 33, with radius of 5 mm. Temporal fluctuation of BOLD during wakeful rest within the mid cingulate seed was averaged across all included voxels and then correlated with the temporal fluctuation of every other voxel in the brain for each subject. The subject-level correlation map was then averaged across subjects to produce a single group connectivity map.

Clusters within the single group connectivity map were then used for LME and MVPA analyses, testing if PMN activity was modulated by the levels of processing and whether PMN activity predicted subsequent memory. The mid cingulate and precuneus cluster masks used for linear-mixed effect modeling and MVPA analysis were arbitrarily defined by thresholding the

correlation map to Pearson's  $r$  of .6 threshold (**Figure 2.3**). As Figure 2.3 illustrates, even though a spherical mask was used to generate the seed correlation map, the mid cingulate cluster from the correlation map followed the shape of the cingulate gyrus more closely. As a result, the cluster from the correlation map rather than the initial sphere was used for further analyses. The mid cingulate cluster contained voxels from both hemispheres. Left and right precuneus, however, emerged as two separate clusters and were analyzed separately for further analyses. Bilateral PIPL did not emerge at correlation of 0.6 and required lowering the correlation to 0.4 (**Figure 2.4**). The resultant functional connectivity map at the 0.4 threshold resembled the medial parietal system identified by Gordon and colleagues (2017) as well as the Cluster 2 identified by Cha and colleagues (2017), which both included ACC as well as PMN regions.

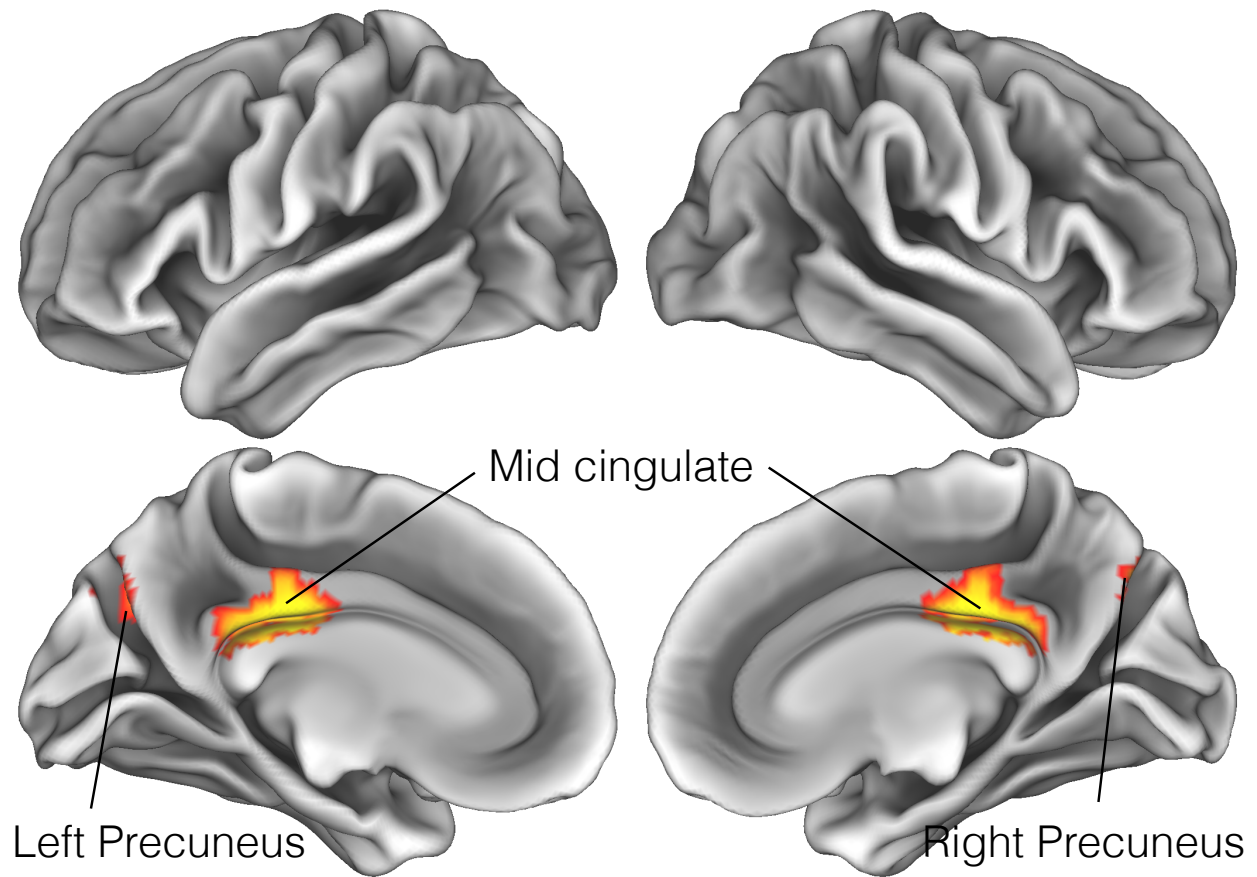


Figure 2.3. Functional connectivity map at the correlation of 0.6 level when mid cingulate coordinates (-1, -24, 33) from Nelson and colleagues (2013) was used as the seed. The mid cingulate cluster and the precuneus clusters were used as masks for the LME and MVPA analysis. The center of mass coordinates for left precuneus were -9, -73, 36; the center of mass coordinates for right precuneus was 12, -68, 36.7; the center of mass coordinates for mid cingulate were 0, -29, 30.

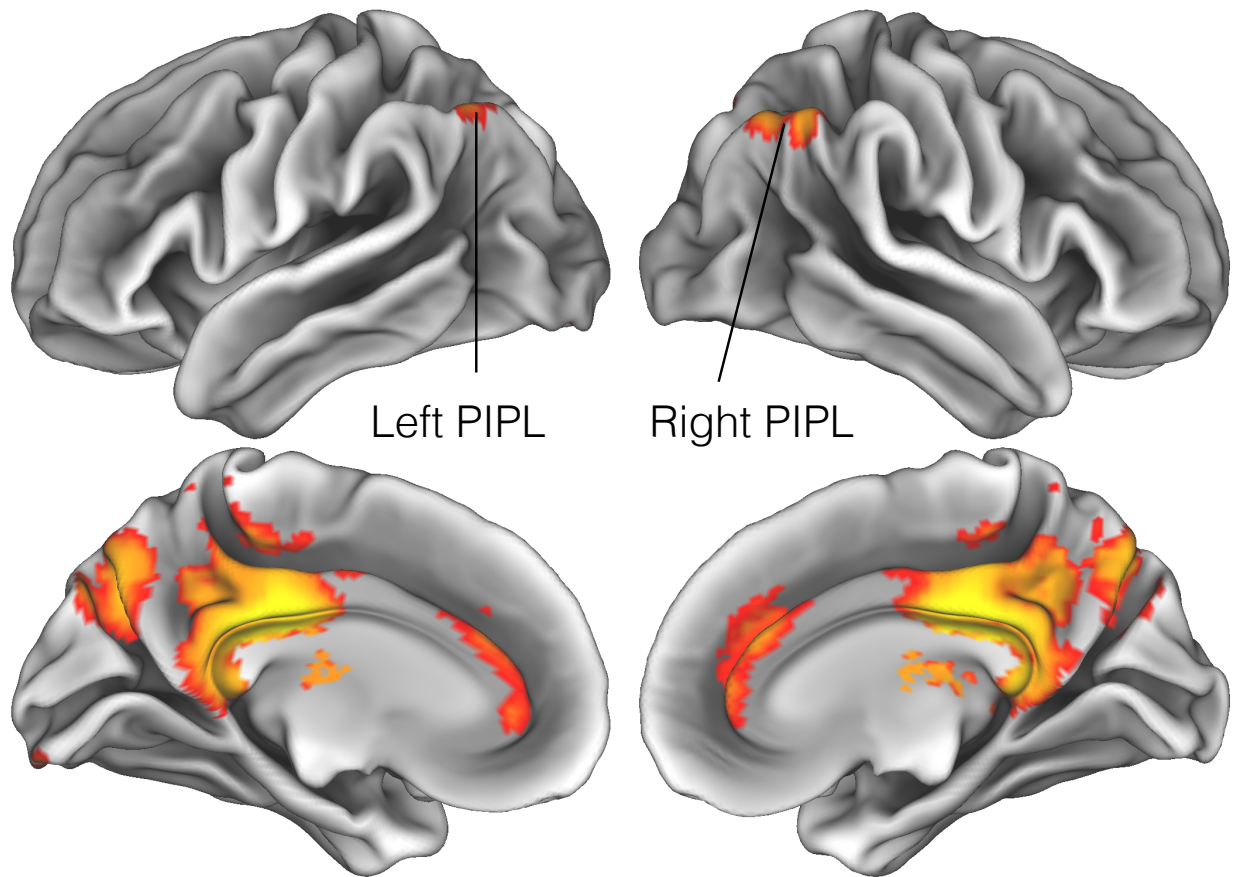


Figure 2.4. Functional connectivity map at the correlation of 0.4 level when mid cingulate coordinates (-1, -24, 33) from Nelson and colleagues (2013) was used as the seed. The bilateral PIPL clusters were used as masks, separately, for the LME and MVPA analysis. The center of mass coordinates for left PIPL were -40, -63, 52. The center of mass coordinates for right PIPL were 47, -58, 48.

## 2.9 Motion censoring for mixed effect modeling analysis

Frames with excessive motion were detected in AFNI when more than 10% of voxels were outliers for that frame (outlier censoring). Outliers were determined using AFNI's *3dToutcount* function, which took into account the trend of each voxel time series as well as the median absolute deviation (median absolute value of time series minus trend). Values that were too many median absolute deviations from the trend were considered outliers. The exact cutoff for

the number of median absolute deviation depends on the number of TRs, and it was calculated with the following formula:  $\text{Cutoff} = qginv(0.001/\text{Number of TRs}) * \text{sqrt}(\text{PI}/2) * \text{median absolute deviation}$  (Note: *qginv* is an AFNI function that takes the inverse of the reversed Gaussian CDF). For a given TR number between 50 and 500, the cutoff for the number of median absolute deviation falls between 5.15 and 5.78. Trials were discarded if an outlier frame was detected during the trial, or within 10 TR (11 seconds) after the trial. The reasoning for choosing 11 seconds was because motion within that duration after the trial could impact the measurement of that trial. Among the total of 4176 trials, 3670 trials remained and were later used in linear mixed effect and MVPA analysis.

## **2.10 Exploratory factor analysis for mixed effect modeling analysis**

The high correlations among PMN regions will likely lead to multicollinearity and suppression issues when multiple highly-correlated predictors are in the same linear-mixed effect models. For instance, multicollinearity could lead to parameters that make little sense (e.g., sign changes) when activity of all PMN regions are in the same model to predict subsequent memory. Building one model for each PMN region to predict subsequent memory solves the multicollinearity issue, but is not parsimonious. To mitigate the multicollinearity concern, an exploratory factor analysis was performed. While forming an average of all PMN regions was another option, an exploratory factor analysis provides an objective way of determining the number of factors in the data. The exploratory factor analysis was performed using the *psych* 1.7.8 (Revelle, 2016) package in *R* 3.4.0 (R Core Team, 2017) on the extracted beta values for each region for each trial, across all encoding runs. One recommended technique for identifying the number of factors is a parallel analysis (Courtney, 2013), which was first conducted with the

*fa.parallel* function. After arriving at a probable number of factors, the *fa* function of the *psych* package was used to perform the factor analysis with maximum likelihood estimation. The *oblimin* option was chosen for rotation, as there was good reason to believe that the factors were correlated. The resultant factors scores were extracted for further analysis.

## **2.11 Linear mixed effect modeling analysis**

*R* and the *lme4* 1.1-13 package in *R* (Bates, Mächler, Bolker, & Walker, 2015) were used to perform linear mixed effect (LME) analyses examining if PMN activity predicted later memory performance (hit or miss) and how levels of processing influenced activity in PMN regions on a trial-by-trial basis. The “top-down strategy” outlined by West, Welch and Gałecki (2014) was applied: fixed effects were first loaded in the model, then random intercepts and slopes were evaluated for their significance; testing for statistical significance was prioritized over model selection, so non-significant fixed effects were not dropped.

The first LME model was created to investigate whether neural activity within the PMN could predict whether items would be recognized (hit) or not (miss). Specifically, a mixed effects logistic regression model assessed if activity in PMN regions could predict later recognition success when other predictors such as levels of processing and response time (RT) were also entered the model. The *glmer* function in the *lme4* package of *R* was used. Later memory performance was coded as hits or misses. Fixed effects for the initial model included the factor scores from performing exploratory analysis on PMN regions, levels of processing (semantic, phonological and orthographic, with semantic processing as the reference level so that contrast of semantic versus phonological and semantic versus orthographic could be set up) and response time at encoding. Participant was entered as a random effect. Grand-mean centering was performed on response time (Enders & Tofighi, 2007). Centering was not performed for levels of

processing, a categorical variable. Centering was also not performed on the factor scores because they were already centered at 0. In a related model, the level of processing effect was modeled as a random slope to allow the level of processing to vary for different participants. To further test PMN regions' unique contribution to subsequent memory, another related model added activity from left IFG to the above model, assessing if factor scores of PMN regions still predicted subsequent memory, above and beyond the contribution of left IFG. The left IFG region was defined by drawing a 5-mm radius sphere around the coordinates from Kim's meta-analysis (2011) on subsequent memory (Talairach: -46, 26, 16; MNI: -49, 31, 11).

The next few linear mixed effect models assessed if levels of processing influenced activity of PMN regions and left IFG, separately. The procedure was similar to the first model, with a few exceptions. The dependent variable for each of these models was activity of PMN regions or left IFG, in the form of beta coefficients, rather than factor scores. Factor scores were not used here because multicollinearity was no longer a concern when only one PMN region appeared in each model, and PMN activity was the dependent variable. Another difference from the previous model was that the *lmer* function in the *lme4* package was used because the dependent variables were continuous. The predictors (levels of processing, reaction time) were coded and centered similarly; PMN activity was centered as well; and the other predictor was subsequent memory performance (coded as hits or misses).

## **2.12 Multivariate pattern analysis (MVPA)**

Multivariate pattern analysis was used to determine whether brain activity permitted decoding of the level of processing and subsequent memory (semantic processing versus orthographic processing, semantic processing versus phonological processing, phonological processing versus orthographic processing and subsequent hits versus misses). Because the levels



of processing manipulation would likely lead to different subsequent memory performance for different levels of processing (e.g., semantic processing would lead to a higher number of hits than orthographic processing), classification was performed for semantic versus phonological processing, but only for hits (the number of orthographic hits was much lower, so phonological processing was chosen); similarly, classification was performed for subsequent hits versus misses, but only for phonological processing (the choice was somewhat arbitrary, but semantic processing would lead to too few subsequent miss trials).

Only classification across participants was performed due to the relatively low number of items in some conditions within each run (for example, a low number of misses within a run for some participants). In addition, imbalance in the number of trials in different levels of processing could be caused by dropping trials flagged with excessive motion. Classification was performed for the clusters from the resting state seed map (bilateral precuneus, mid cingulate and bilateral IPL), as well as the left IFG region used in the LME analysis. An additional control region was created by drawing a 5-mm radius sphere centering at corpus callosum. The reason for choosing corpus callosum was to provide a control region at chance-level classification performance. Classification was performed using the linear support vector machine (SVM) in PyMVPA (Hanke et al., 2009).

The input for MVPA analysis consisted of *t*-maps from the beta-series analysis in AFNI that went into the LME analysis; the only difference was that rather than raw betas, the beta estimates for each trial underwent a *t* transform according to Misaki and colleagues' finding that *t*-maps led to better classification performance (Misaki, Kim, Bandettini, & Kriegeskorte, 2010).

For each classification, data were divided into 29 partitions (29 participants). Trials from one participant were only trained using trials from the other 28 participants (leave-one-subject-

out). For each training set, the number of trials in each category was matched to make sure the trained algorithm was not biased; for instance, if there were more hit than miss trials in the training set, hit trials were randomly dropped until the numbers of hit and miss trials were equal. Statistical significance was determined using permutation testing; the null distribution was generated by permuting category labels 1000 times for the training set, then classifying on the actual data. To make sure dropping trials did not lead to non-representative samples, each classification was performed 10 times, and median classification accuracies and median  $p$ -values were reported.

## **Chapter 3: Results**

### **3.1 Outline**

The results section will begin with behavioral results. Next, whole-brain maps examining the subsequent memory effect as well as the level processing effects serve as manipulation checks to ensure the data quality is sound. The heart of the imaging analysis using linear mixed effect models to predict subsequent memory and assess the level of processing manipulation then follows. Last but not the least, multivariate pattern analysis complements the linear mixed effect analysis in informing the readers about the ability of using PMN activity to infer subsequent memory status and the level of processing.

### **3.2 Behavioral results**

The levels of processing manipulation significantly influenced memory performance, as expected ( Craik & Lockhart, 1972; Craik & Tulving, 1975). As **Figure 3.1** shows, semantic processing, a deep level of processing, led to a higher hit rate (adding both remember and know

hit rates) ( $M = 0.83$ ,  $SD = 0.10$ ) than phonological processing ( $M = 0.70$ ,  $SD = 0.13$ ),  $t(28) = 8.15$ ,  $p < .001$ . In addition, phonological processing led to a higher a hit rate than orthographic processing ( $M = 0.48$ ,  $SD = 0.11$ ),  $t(28) = 8.89$ ,  $p < .001$ . It is worth noting that all of the trials from each participant, regardless of motion during scanning, went into the analysis (and the graph in **Figure 3.1**). In addition to behavioral results for old items, the results for new items are also shown in the figure, with the caveat that levels of processing were not applicable for new items. The false alarm rate is quite low, at 15.35% of the trials ( $d' = 1.399$  when using the average of all encoding conditions for the hit rate to calculate  $d'$ ).

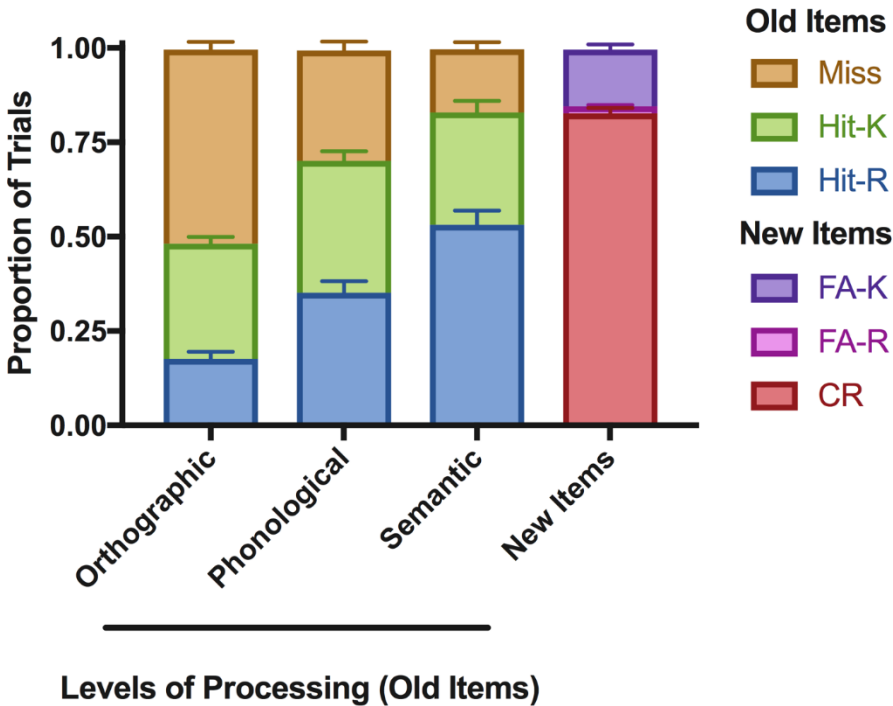


Figure 3.1. Behavioral performance. Error bars represent standard error of the mean across the participants. CR = correct rejection; FA = false alarm; R = remember; and K = know. The specific proportions are listed below: Orthographic Miss: 0.51; Orthographic Hit-K: 0.31; Orthographic Hit-R: 0.18; Phonological Miss: 0.29; Phonological Hit-K: 0.35; Phonological Hit-R: 0.35; Semantic Miss: 0.17; Semantic Hit-K: 0.30; Semantic Hit-R: 0.53.

### 3.3 Univariate analysis

*Manipulation check 1: Are the whole-brain subsequent memory and negative subsequent memory effects replicated?*

Before proceeding with the focused analysis of primary interest, I report two manipulation checks designed to ensure that the data quality is sound and that well-known (whole-brain) results with respect to subsequent memory and levels of processing are replicated in this dataset.

The subsequent hits (collapsing across remember and know judgments) versus subsequent misses map (**Figure 3.2; Table 3.1**) qualitatively replicated Kim's meta-analysis (Kim, 2011), shown in **Figure 3.3**. Regions that showed a positive subsequent memory effect (greater activity for subsequent hits than misses) effect in Kim's meta-analysis as well as in this study (warmer colors in **Figure 3.2**) included left inferior frontal gyrus, right inferior occipital gyrus and left middle occipital gyrus. In addition, regions that showed negative subsequent memory (less activity for subsequent hits than misses), the opposite effect (cooler colors in **Figure 3.2**), included PMN regions: bilateral precuneus, mid cingulate and right PIPL (whose cluster also includes right angular gyrus). The similarity of the of the subsequent memory maps gave us confidence that the quality of the dataset is sound.

The whole-brain map contrasting subsequent hits (remember judgments) and subsequent misses is shown in **Figure 3.4 (Table 3.2)**. The figure resembles the map contrasting subsequent hits (collapsing across remember and know judgments) and subsequent misses.

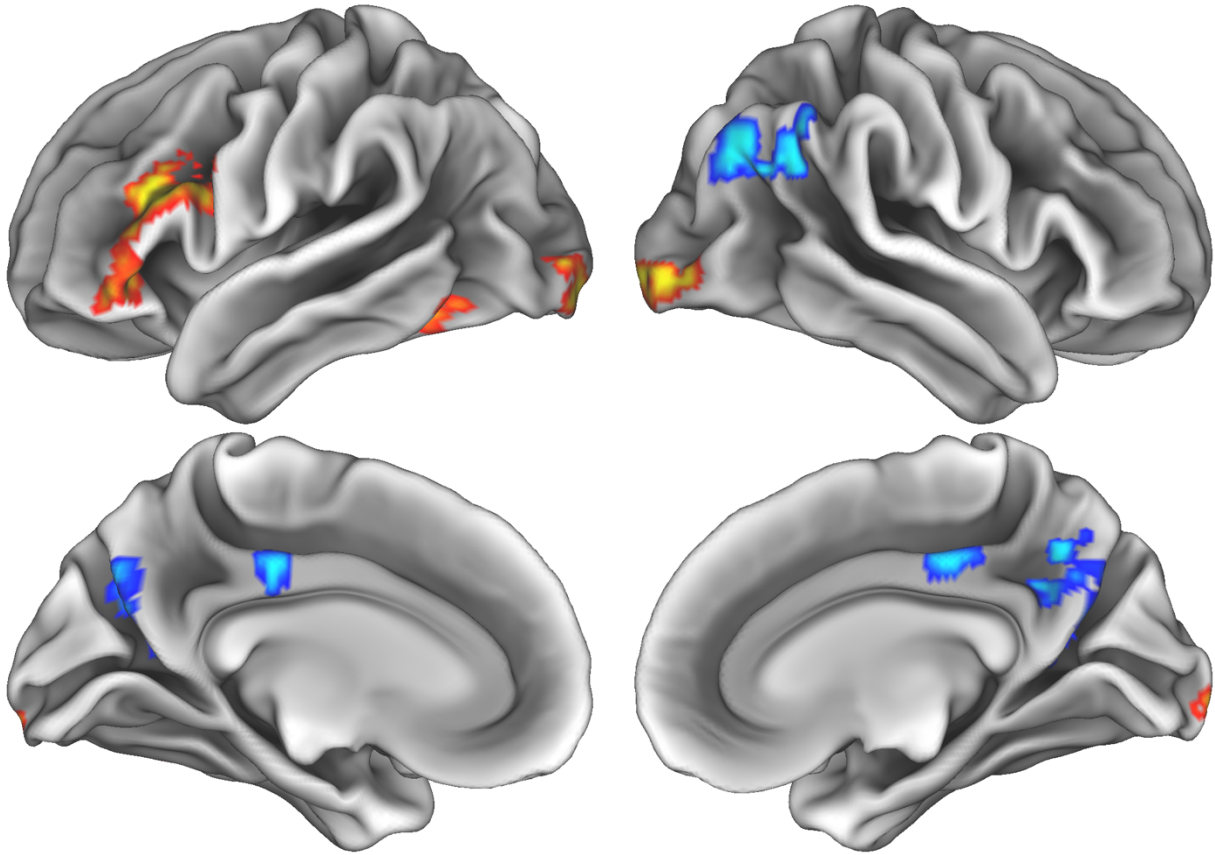


Figure 3.2. Two-tailed  $t$ -test map contrasting subsequent hits (collapsing across remember and know judgments) and subsequent misses at encoding. Warmer colors represent regions showing greater activity during encoding for items that are subsequent than subsequent misses (i.e. a positive subsequent memory effect). Cooler colors represent the opposite pattern, less activity for subsequent hits than subsequent misses (i.e. a negative subsequent memory effect). Clusters survive correction at the 0.05 level, with a minimum cluster size of 17 voxels and Z score of 3.291 ( $p$  of 0.001 at the voxel level).

Table 3.1. Center-of-mass coordinates for regions exhibiting differential activity at encoding for subsequent hits (collapsing across remember and know judgments) versus subsequent misses. PMN regions are highlighted in **bold**.

Region	Voxels	CM x	CM y	CM z	alpha
<i>Positive subsequent memory</i>					
Left inferior frontal gyrus	197	-48	18	25	<.01
Right inferior occipital gyrus	61	31	-93	-3	<.01
Left middle occipital gyrus	49	-27	-99	-3	<.01
Left inferior frontal gyrus	45	-46	33	-3	<.01
Left inferior temporal gyrus	33	-46	-57	-14	<.05
<i>Negative subsequent memory</i>					
<b>Right precuneus</b>	112	13	-60	29	<.01
<b>Left precuneus</b>	94	-11	-66	27	<.01
<b>Right angular gyrus/PIPL</b>	86	48	-65	36	<.01
<b>Mid cingulate</b>	34	1	-25	39	<.05

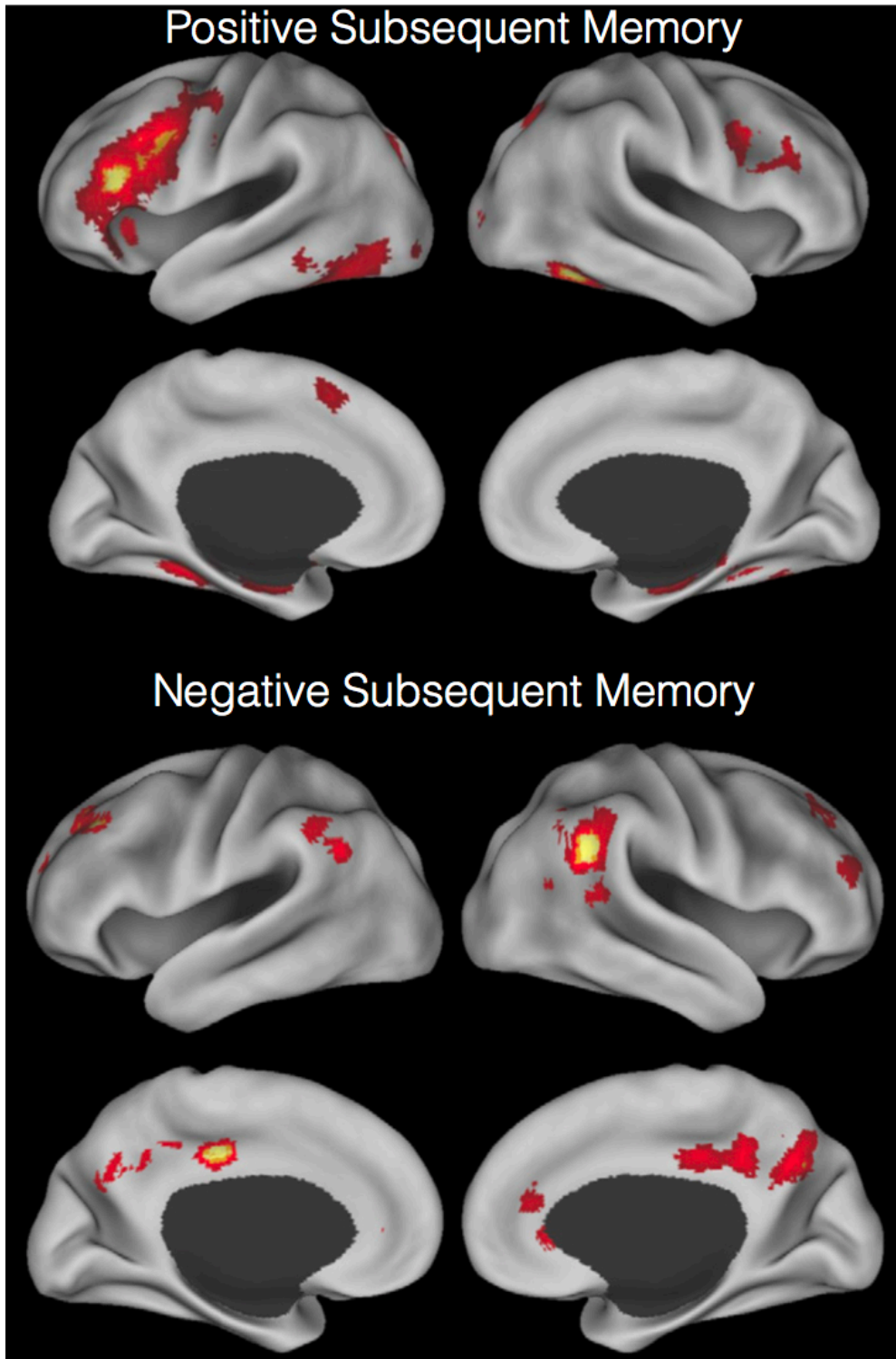


Figure 3.3. Positive and negative subsequent memory maps adapted from the meta-analysis conducted by Kim (2011).

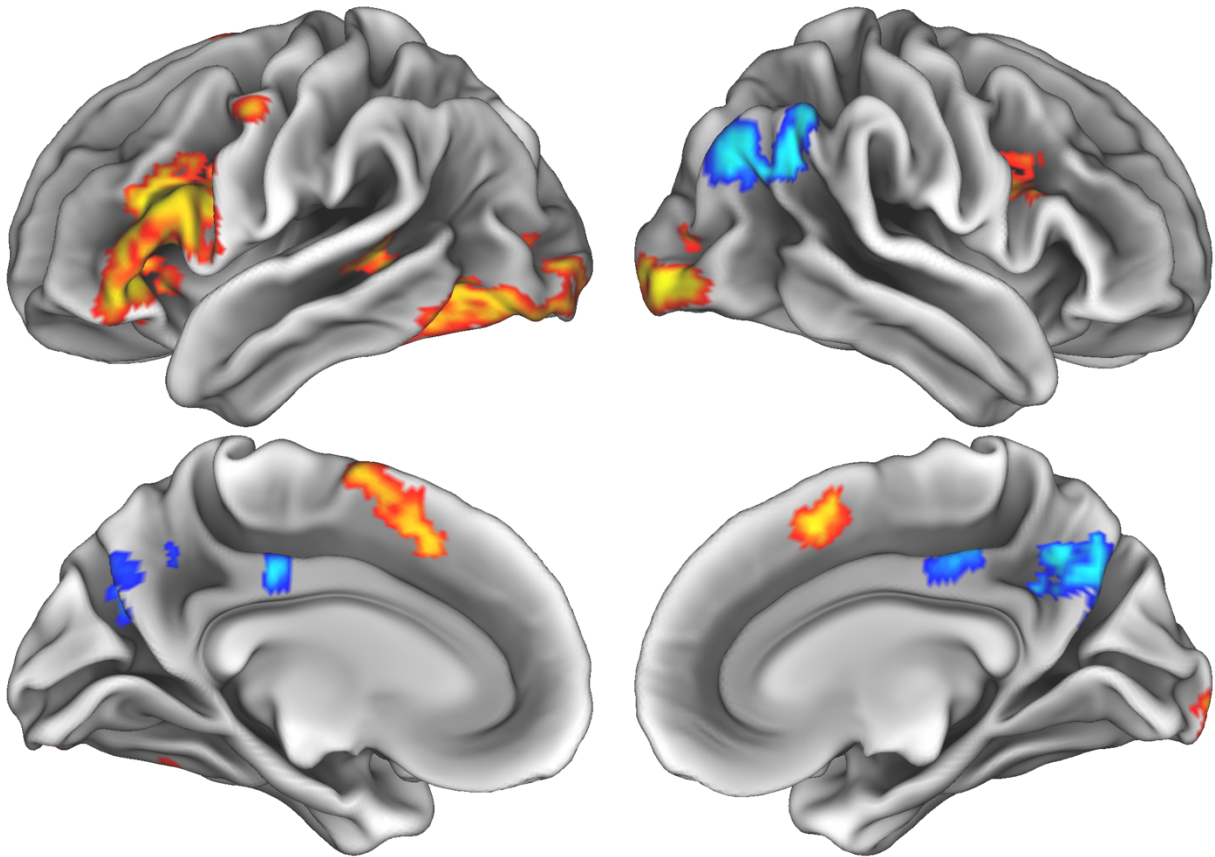


Figure 3.4. Two-tailed  $t$ -test map contrasting subsequent hits (remember judgments) and subsequent misses at encoding. Warmer colors represent regions showing greater activity during encoding for items that are subsequent hits (remember) than subsequent misses. Cooler colors represent the opposite pattern, less activity for subsequent hits (remember judgments) than subsequent misses. Clusters survive correction at the 0.05 level, with a minimum cluster size of 19 voxels and Z score of 3.291 ( $p$  of 0.001 at the voxel level).



Table 3.2. Center-of-mass coordinates for regions exhibiting differential activity at encoding for subsequent hits (remember judgments) versus subsequent misses. PMN regions are highlighted in **bold**.

Region	Voxels	CM x	CM y	CM z	alpha
<i>Positive subsequent memory</i>					
Left inferior frontal gyrus	566	-48	19	19	< 0.01
Left inferior occipital gyrus	227	-37	-82	-8	< 0.01
Right middle occipital gyrus	122	32	-93	-3	< 0.01
Left superior frontal gyrus	90	-1	11	56	< 0.01
Right middle frontal gyrus	52	44	12	29	< 0.01
Left superior temporal gyrus	25	-52	-39	5	< 0.05
<i>Negative subsequent memory</i>					
<b>Right inferior parietal lobule</b>	136	49	-65	35	< 0.01
<b>Right precuneus</b>	112	10	-63	34	< 0.01
<b>Left precuneus</b>	75	-12	-66	29	< 0.01
<b>Bilateral cingulate gyrus</b>	26	2	-26	39	< 0.05

The whole-brain map contrasting subsequent hits (remember judgments) and subsequent hits (know judgments) is shown in **Figure 3.5 (Table 3.3)**. The map contrasting subsequent hits (know judgments) and subsequent misses is shown in **Figure 3.6 (Table 3.4)**. Both maps are quite sparse.

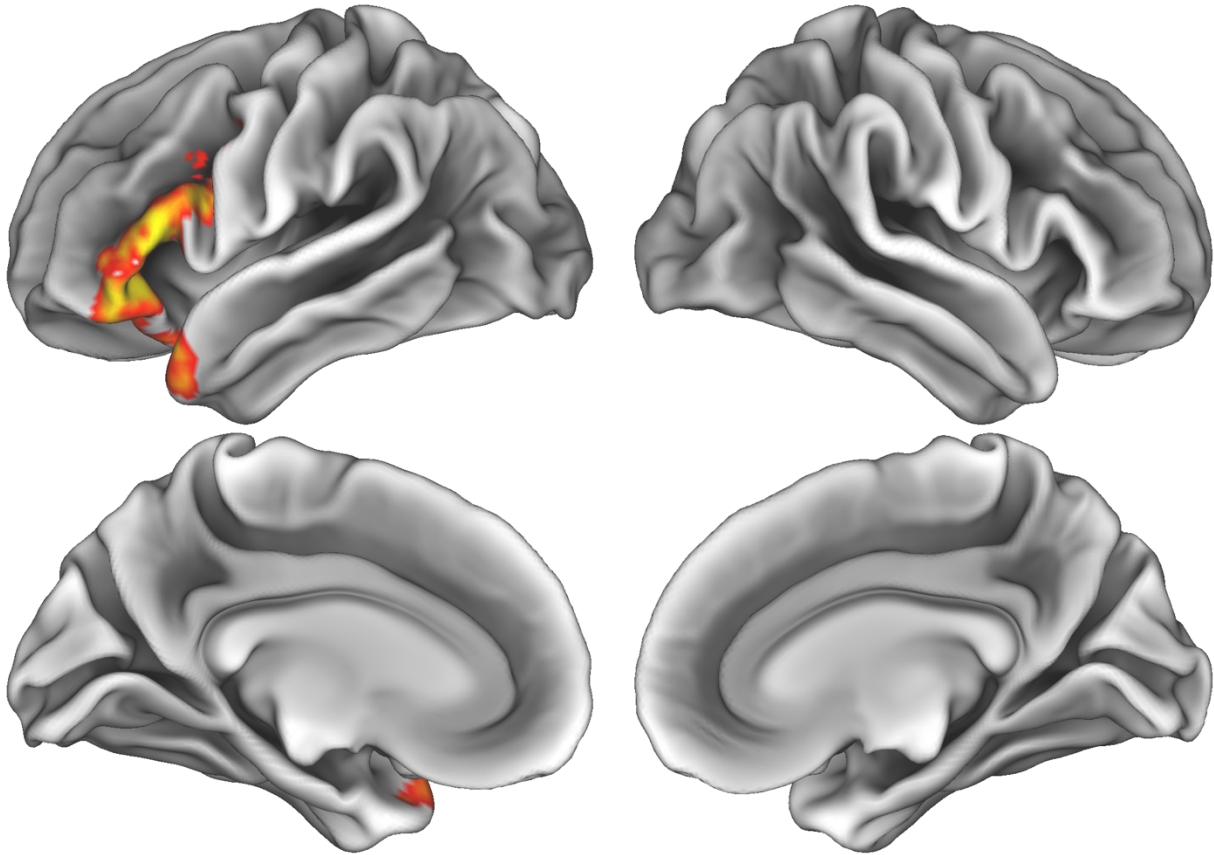


Figure 3.5. Two-tailed  $t$ -test map contrasting subsequent hits (remember judgments) and subsequent hits (know judgments) at encoding. Warmer colors represent greater activity for subsequent remembering than subsequent knowing. No region showed the opposite pattern. Clusters survive correction at the 0.05 level, with a minimum cluster size of 17 voxels and Z score of 3.291 ( $p$  of 0.001 at the voxel level).

Table 3.3. Center-of-mass coordinates for regions exhibiting differential activity at encoding for subsequent hits (remember judgments) versus subsequent hits (know judgments).

Region	Voxels	CM x	CM y	CM z	alpha
<i>Subsequent hits (remember) &gt; Subsequent hits (know)</i>					
Left inferior frontal gyrus	396	-47	25	4	< 0.01

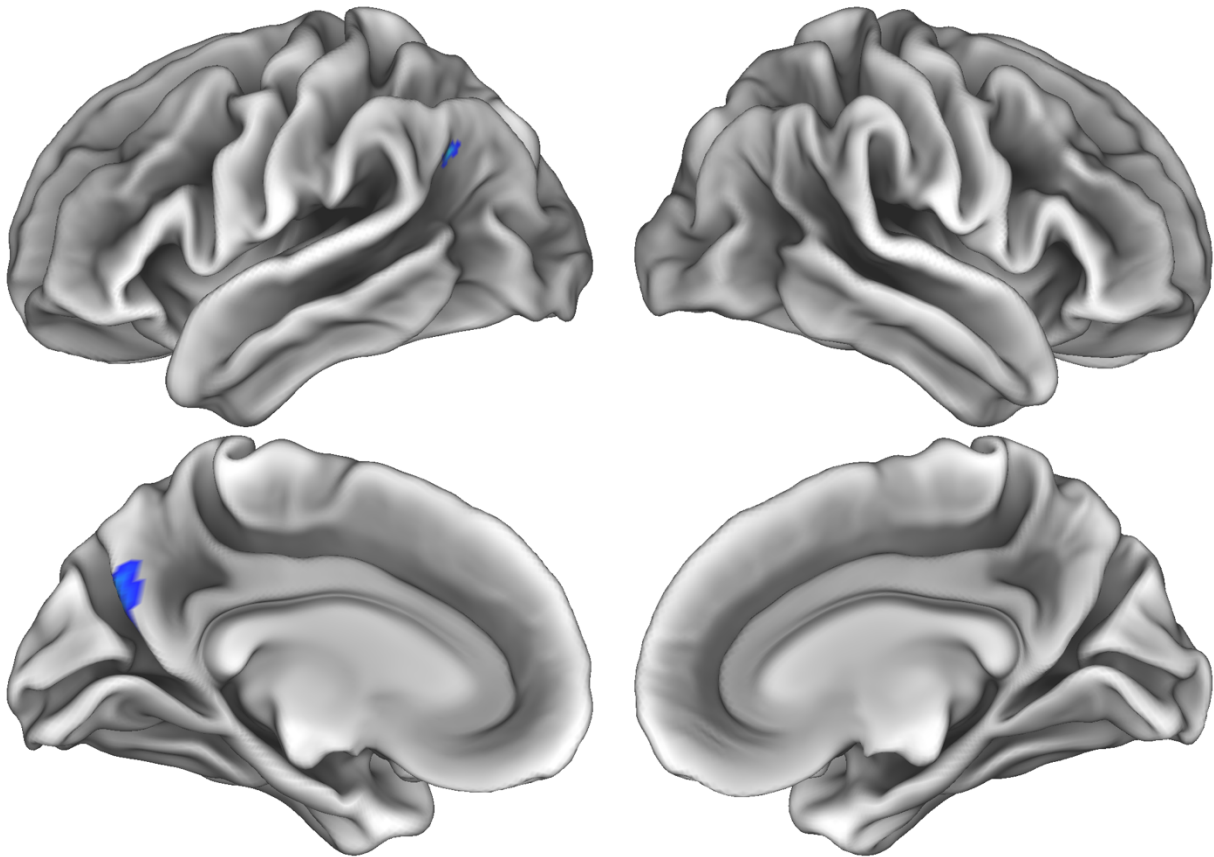


Figure 3.6. Two-tailed  $t$ -test map contrasting subsequent hits (know judgments) and subsequent misses at encoding. Cooler colors represent regions showing greater activity for subsequent misses than subsequent hits (know judgments). No region showed the opposite pattern. Clusters survive correction at the 0.05 level, with a minimum cluster size of 18 voxels and Z score of 3.291 ( $p$  of .001 at the voxel level).

Table 3.4. Center-of-mass coordinates for regions exhibiting differential activity at encoding for subsequent hits (know judgments) versus subsequent misses. PMN region is highlighted in **bold**.

Region	Voxels	CM x	CM y	CM z	alpha
<i>Subsequent misses &gt; Subsequent hits (know)</i>					
<b>Left precuneus</b>	41	-11	-63	24	< 0.01
Left supramarginal gyrus	22	-53	-64	32	< 0.05

*Manipulation check 2: Is the whole-brain semantic versus non-semantic processing map replicated?*

Here, a whole-brain contrast of deep (semantic judgment) versus shallow (orthographic) was conducted (**Figure 3.7; Table 3.5**). The goal of examining the whole-brain univariate deep versus shallow processing map was to compare the current data's map to Wagner and colleagues' (1998) map of semantic versus non-semantic processing. Our resulting map is qualitatively similar to that of Wagner and colleagues. Wagner and colleagues found that left frontal cortex, parahippocampal cortex, and fusiform cortex showed greater activity during semantic processing, relative to non-semantic processing.

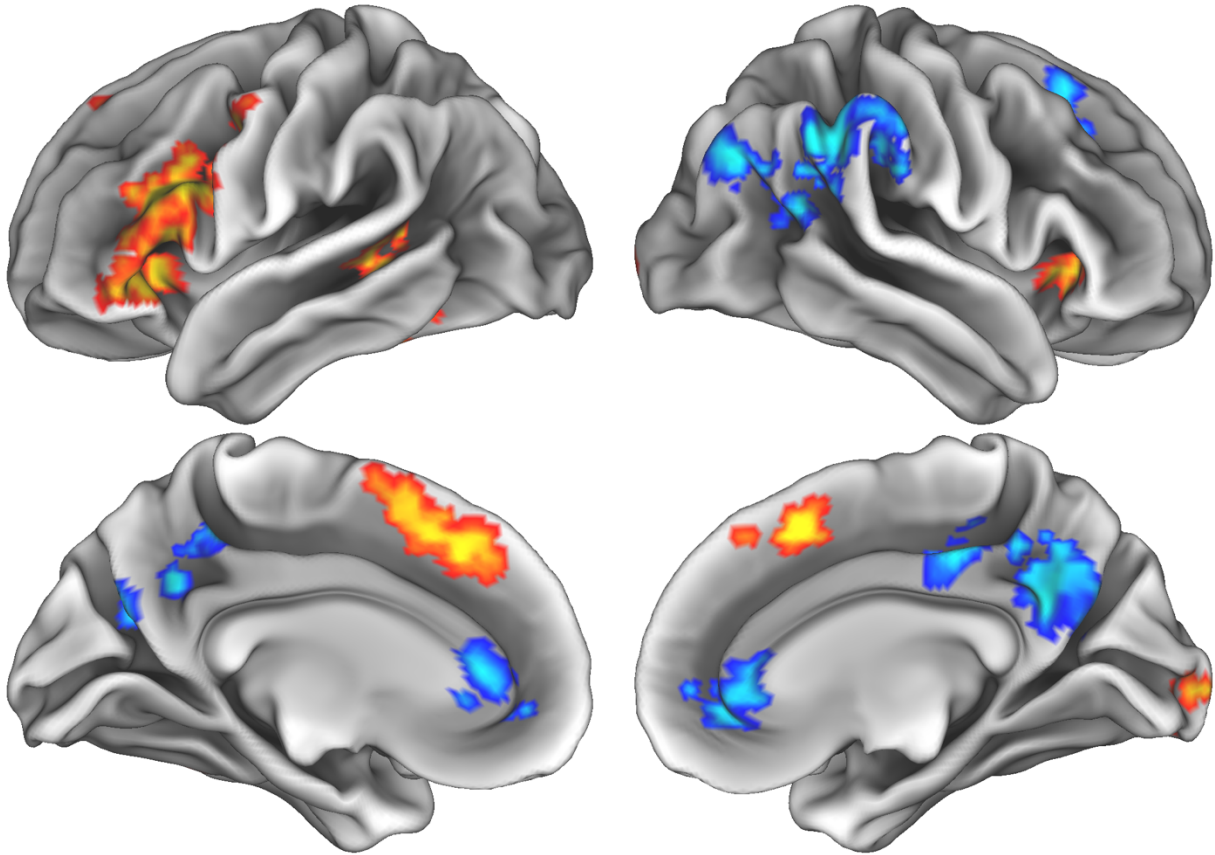


Figure 3.7. Two-tailed  $t$ -test map contrasting semantic processing and orthographic processing at encoding. Warmer colors represent regions showing greater activity for semantic processing than orthographic processing. Cooler regions represent the opposite pattern. Clusters survive correction at the 0.05 level, with a minimum cluster size of 19 voxels and Z score of 3.291 ( $p$  of 0.001 at the voxel level).

Table 3.5. Center-of-mass coordinates for regions exhibiting differential activity at encoding for semantic processing versus orthographic processing. PMN regions are shown in **bold**.

Region	Voxels	CM x	CM y	CM z	alpha
<i>Semantic processing &gt; Orthographic processing</i>					
Left inferior frontal gyrus	501	-48	23	14	< .01
Left medial frontal gyrus	154	-3	22	49	< .01
Right cerebellum (Crus 1)	90	13	-80	-29	< .01
Right inferior frontal gyrus	35	37	26	-2	< .05
Left superior temporal gyrus	33	-52	-40	3	< .05
Left fusiform gyrus	26	-45	-52	-15	< .05
Right cuneus	25	15	-94	-1	< .05
<i>Orthographic Processing &gt; Semantic processing</i>					
Right supramarginal gyrus	254	55	-42	35	< .01
<b>Right precuneus</b>	186	9	-56	32	< .01
Right anterior cingulate	121	2	41	01	< .01
Right angular gyrus	49	45	-72	32	< .01
<b>Left precuneus</b>	48	-12	-67	26	< .01
<b>Right mid cingulate gyrus</b>	43	6	-27	42	< .01
Left posterior cingulate gyrus	39	-10	-51	40	< .01
Right superior frontal gyrus	23	23	26	49	< .05

Wagner and colleagues reported 5 regions (coordinates converted to MNI) in left frontal cortex, one in parahippocampal cortex and another in fusiform. Two regions in left middle frontal gyrus (-45, 14, 33 and -42, 27, 17) and two regions in left inferior frontal gyrus (-45, 18, 26 and -29, 25, 0) fell within the large inferior frontal gyrus cluster in **Table 3.5**. The fourth left frontal region (-42, 36, 6), however, was slightly beyond the cluster reported here. The fusiform gyrus cluster reported in the table (center of mass at -45, -52, -15) is fairly close to the fusiform region reported by Wagner and colleagues (-36, -42, -13). The parahippocampal region was not obtained here.

*Bilateral precuneus and right mid cingulate showed lower activity for semantic processing than orthographic processing*

Now that the manipulation checks have shown results in line with previous research, the attention is turned to how the level of processing influenced activity in PMN regions. While more in-depth analyses focusing on only PMN regions using linear mixed effect models are shown below, the whole-brain map of semantic versus orthographic processing offered a quick look of the effect of the manipulation. **Figure 3.7** and **Table 3.5** showed that bilateral precuneus and right mid cingulate (but not PIPL) showed lower activity for the deepest level of processing (semantic processing) than the shallowest level of processing (orthographic processing) in our study. This finding agreed with our hypothesis that if deactivation in PMN regions signals the quality of encoding process, PMN regions should show lower activity for deeper levels of processing.

Before moving to the linear-mixed effect analysis, the whole brain contrast of phonological processing against orthographic processing (**Figure 3.8; Table 3.6**) and the contrast of semantic and phonological processing (**Figure 3.9; Table 3.7**) have also been included here. The only PMN region that survived cluster correction was left precuneus, which showed greater deactivation for semantic processing than orthographic processing.

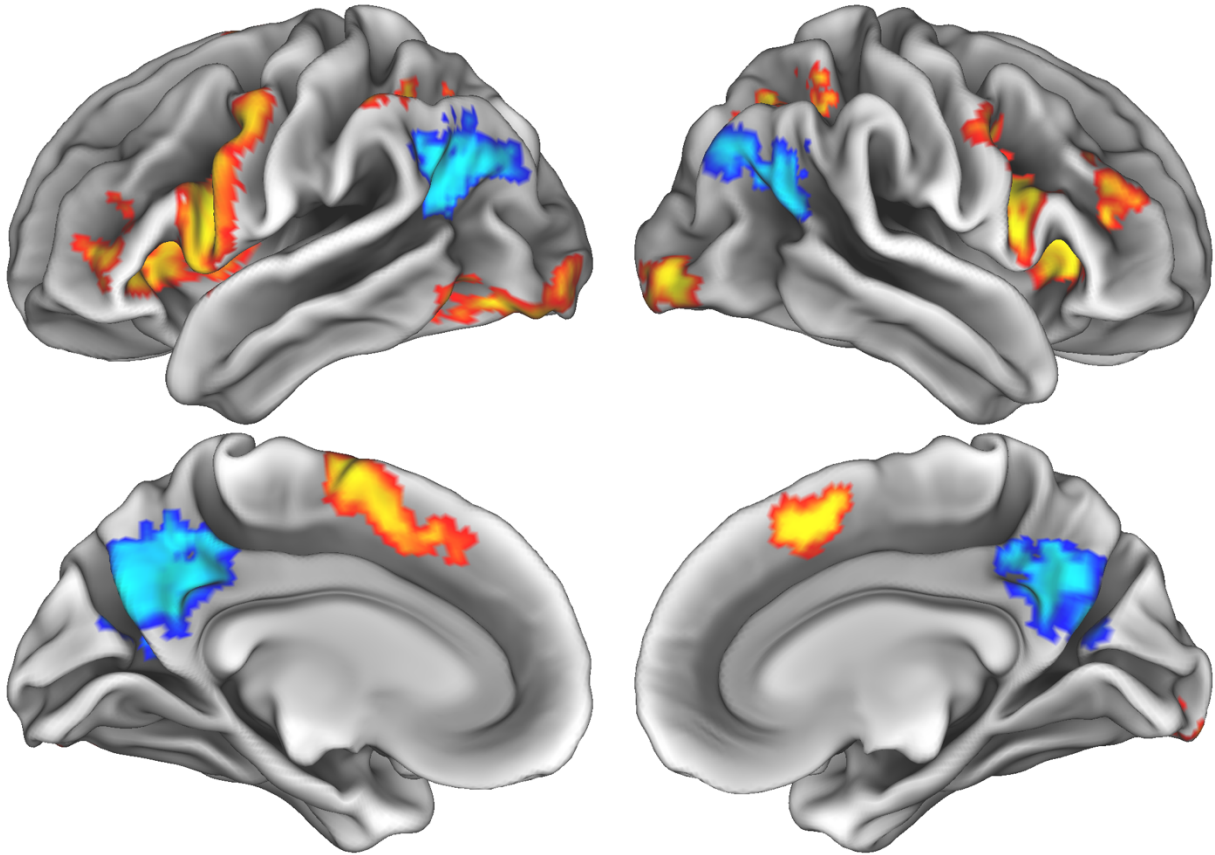


Figure 3.8. Two-tailed  $t$ -test map contrasting phonological processing and orthographic processing at encoding. Warmer colors represent regions showing greater activity for phonological processing than orthographic processing. Cooler colors represent the opposite pattern. Clusters survive correction at the 0.05 level, with a minimum cluster size of 20 voxels and Z score of 3.291 ( $p$  of .001 at the voxel level).



Table 3.6. Center-of-mass coordinates for regions exhibiting differential activity at encoding for phonological processing versus orthographic processing. PMN region is highlighted in **bold**.

Region	Voxels	CM x	CM y	CM z	alpha
<i>Phonological processing &gt; Orthographic processing</i>					
Left inferior frontal gyrus	685	-47	12	18	< .01
Right insula	302	45	14	20	< .01
Left superior frontal gyrus	252	-2	8	57	< .01
Left inferior parietal lobule	123	-42	-47	46	< .01
Left inferior occipital gyrus	113	-39	-82	-8	< .01
Right inferior parietal lobule	95	37	-53	59	< .01
Right middle occipital gyrus	62	31	-92	-6	< .01
Right pallidum	32	22	8	1	< .05
Left cerebellum (Crus 1)	31	-37	-68	-26	< .05
Right middle frontal gyrus	31	42	39	22	< .05
Left precuneus	25	-26	-68	38	< .05
Left cerebellum (VII)	24	-27	-70	-48	< .05
Right cerebellum (VIII)	22	24	-67	-50	< .05
Right cerebellum (VI)	22	30	-72	-23	< .05
Left cerebellum (Crus 2)	20	-6	-80	-28	< .05
<i>Orthographic processing &gt; Phonological processing</i>					
<b>Left precuneus</b>	611	-2	-58	34	< .01
Left angular gyrus	339	-50	-66	32	< .01
Right middle temporal gyrus	186	52	-64	29	< .01

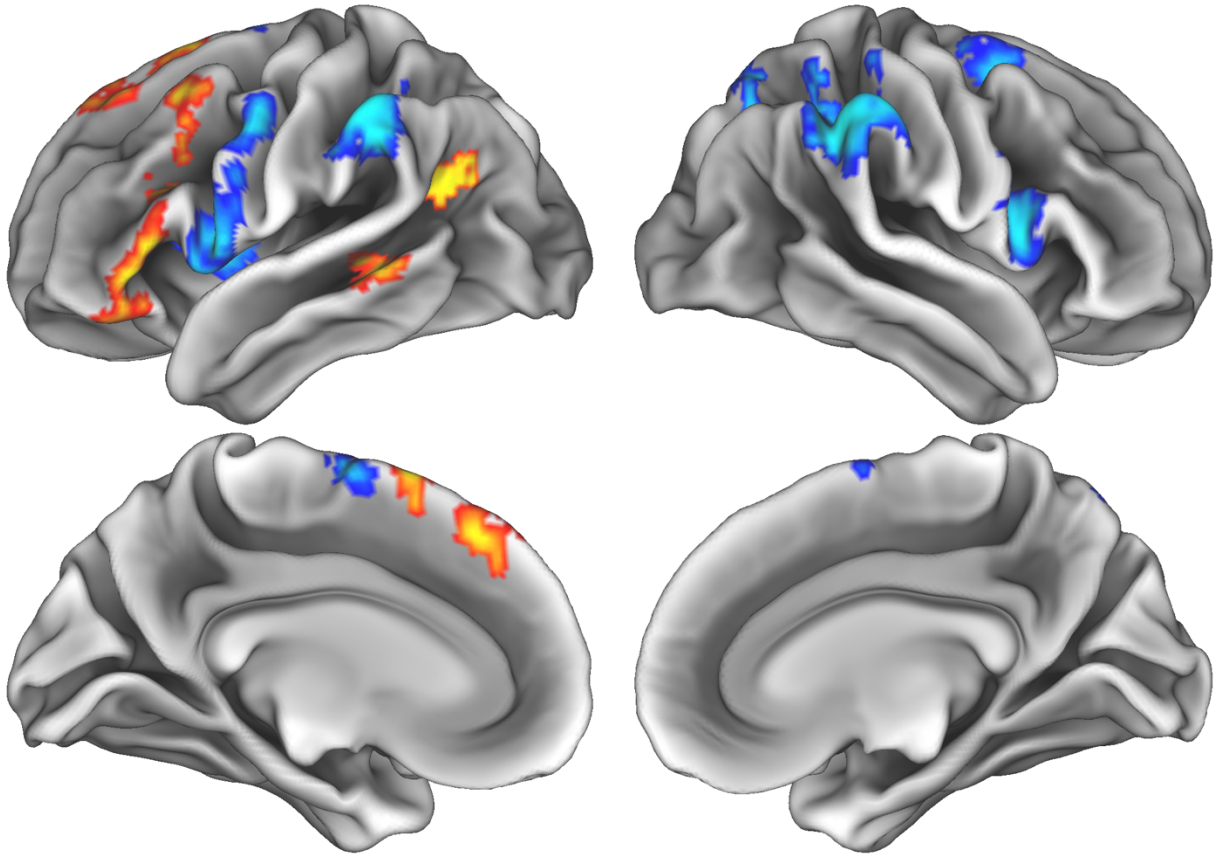


Figure 3.9. Two-tailed  $t$ -test map contrasting semantic processing and phonological processing at encoding. Warmer colors represent regions showing greater activity for semantic processing than phonological processing. Cooler colors represent the opposite pattern. Clusters survive correction at the 0.05 level, with a minimum cluster size of 20 voxels and Z score of 3.291 ( $p$  of .001 at the voxel level).

Table 3.7. Center-of-mass coordinates for regions exhibiting differential activity at encoding for semantic processing versus phonological processing.

Region	Voxels	CM x	CM y	CM z	alpha
<i>Semantic processing &gt; Phonological processing</i>					
Right cerebellum (Crus 2)	148	21	-81	-33	< .01
Left superior frontal gyrus	97	-10	34	55	< .01
Left inferior frontal gyrus	77	-52	34	-3	< .01
Left precentral gyrus	54	-44	18	37	< .01
Left superior temporal gyrus	49	-44	-61	26	< .01
Left middle temporal gyrus	38	-57	-39	0	< .01
Right cerebellum (IX)	28	3	-55	-46	< .05
<i>Phonological processing &gt; Semantic processing</i>					
Right parietal inferior lobule	356	52	-39	50	< .01
Left parietal inferior lobule	207	-56	-39	47	< .01
Left precentral gyrus	174	-49	8	9	< .01
Right inferior frontal gyrus	79	51	12	18	< .01
Right superior frontal gyrus	46	25	5	59	< .01
Left precentral gyrus	36	-55	-5	44	< .05
Left middle frontal gyrus	31	-4	-2	68	< .05
Right precuneus	29	19	-67	49	< .05

### 3.5 Exploratory factor analysis

An exploratory factor analysis was performed on the beta-series regression data of encoding trials to mitigate potential multicollinearity and suppression issues in LME models predicting subsequent memory. The parallel analysis suggested that the appropriate number of factors was two. Precuneus and mid cingulate mostly loaded onto the first factor score, whereas bilateral PIPL mostly loaded onto the second factor score. The path diagram is shown in **Figure 3.10**. For reference, the Tucker-Lewis index (TLK) of 0.978 suggested that the fit was good. The root mean square error of approximation (RMSEA) of 0.088 suggested the fit was neither good or bad and the standardized root mean square residual (SRMR) of 0.028 suggested the fit was

good (Cangur & Ercan, 2015; L. T. Hu & Bentler, 1999).

### Factor Analysis

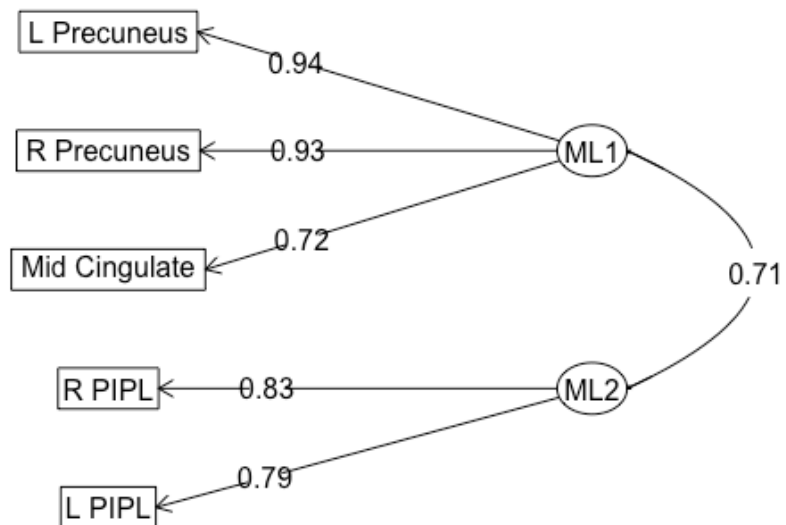


Figure 3.10. Path diagram of the factor analysis. For brain regions, L stands for left and R stands for right. Values represent correlation. ML1 is a latent factor of precuneus and mid cingulate activity; whereas ML2 is a latent factor of PIPL activity. The values are standardized solutions so the values between the manifest variables (in squares) and the latent variables (in circles) can be interpreted as standardized regression coefficients (i.e. beta weights). The value between the latent variables is standardized covariance (i.e. correlation).

## 3.6 Linear mixed effect analysis

### 3.6.1 Trial-by-trial variation of activity in precuneus and mid cingulate predicted subsequent memory

The first two models examined if encoding-related activity in PMN regions predicted the likelihood of a subsequent hit, when the variables of levels of processing and response time (RT) were both in the model (**Table 3.8**). As a reminder, the PMN regions were identified from the resting-state seed analysis whereas the spherical left IFG ROI was defined from coordinates; activity from each PMN region is shown in **Figure 3.11**. Activity from left IFG is shown in **Figure 3.12**. Subsequent memory refers to whether the studied item was subsequently a hit, which could be accompanied by either remember or know judgment, or a miss. A quick glance at the figure reveals that left precuneus, right precuneus and mid cingulate show similar activity pattern across different conditions. Response times for each condition are shown in **Figure 3.13**, and it can be seen that orthographic processing led to shorter response time than semantic and phonological processing. It is worth mentioning again that the two factor scores (one corresponding to precuneus and mid cingulate, the other corresponding to bilateral PIPL) from the exploratory factor analysis, rather than actual activity from each region were entered into the subsequent memory models.

Table 3.8. Parameters of the random intercept and random slope models predicting subsequent memory (hits versus misses). Levels of processing and the factor scores representing precuneus and mid cingulate activity significantly predicted subsequent memory. The fixed parts of the model include the intercept, levels of processing (semantic processing as the reference class), factor scores representing precuneus and mid cingulate activity, factor scores representing bilateral PIPL and encoding RT). Odds ratio greater than 1 suggests that the predictor is associated with better subsequent memory (more likely a hit than a miss). Odds ratio less than 1 (not negative) suggests that the predictor is associated with worse subsequent memory. CI refers to confidence interval, and  $p$ -values indicate the significance of the fixed effects. Random parts of the model are not the focus of the analysis. For reference,  $\tau_{00}$  refers to the random intercept variance for participants and  $\rho_{01}$  refers to slope-intercept correlation. ICC refers to the intraclass correlation, or correlation among items within the same participant.

	Subsequent Memory (Random Intercept model)			Subsequent Memory (Random Slope Model)		
	<i>Odds Ratio</i>	<i>CI</i>	<i>p</i>	<i>Odds Ratio</i>	<i>CI</i>	<i>p</i>
<b>Fixed Parameters</b>						
(Intercept)	5.51	4.42 – 6.87	< .001	5.81	4.45 – 7.60	< .001
LOP (Orthographic)	0.17	0.14 – 0.21	< .001	0.16	0.12 – 0.21	< .001
LOP (Phonological)	0.47	0.38 – 0.57	< .001	0.45	0.36 – 0.56	< .001
Factor Scores (Precuneus & Mid Cingulate)	0.82	0.72 – 0.93	0.003	0.83	0.73 – 0.94	0.004
Factor Scores (Bilateral PIPL)	1.08	0.94 – 1.23	0.271	1.09	0.95 – 1.25	0.202
Encoding RT	0.94	0.81 – 1.09	0.4	0.92	0.79 – 1.07	0.277
<b>Random Parameters</b>						
$\tau_{00}$ , Participant		0.179			0.318	
$\rho_{01}$		N/A			-0.755	

$N_{\text{Participant}}$	29	29
$ICC_{\text{Participant}}$	0.052	0.088
Observations	3670	3670
Deviance	4106.672	4056.242

Table 3.9. Parameters of the random slope models predicting subsequent memory (hits versus misses), with left IFG added to the model. Levels of processing and the factor scores representing precuneus and mid cingulate activity significantly predicted subsequent memory. The fixed parts of the model include the intercept, levels of processing (semantic processing as the reference class), left IFG, factor scores representing precuneus and mid cingulate activity, factor scores representing bilateral PIPL and encoding RT). Odds ratio greater than 1 suggests that the predictor is associated with better subsequent memory (more likely a hit than a miss). Odds ratio less than 1 (not negative) suggests that the predictor is associated with worse subsequent memory. CI refers to confidence interval, and  $p$ -values indicate the significance of the fixed effects. Random parts of the model are not the focus of the analysis. For reference,  $\tau_{00}$  refers to the random intercept variance for participants and  $\rho_{01}$  refers to slope-intercept correlation. ICC refers to the intraclass correlation, or correlation among items within the same participant.

	Subsequent Memory (Random Slope Model with left IFG)		
	<i>Odds Ratio</i>	<i>CI</i>	<i>p</i>
<b>Fixed Parameters</b>			
(Intercept)	5.78	4.41 – 7.56	<.001
LOP (Orthographic)	0.16	0.12 – 0.22	<.001
LOP (Phonological)	0.46	0.37 – 0.57	<.001
Factor Scores (Precuneus & Mid Cingulate)	0.86	0.75 – 0.98	.022
Factor Scores (Bilateral PIPL)	0.99	0.86 – 1.15	.917
Left IFG	1.42	1.20 – 1.69	<.001
Encoding RT	0.90	0.78 – 1.05	.177
<b>Random Parameters</b>			
$\tau_{00, \text{Participant}}$		0.323	
$\rho_{01}$		-0.756	
$N_{\text{Participant}}$		29	
$ICC_{\text{Participant}}$		0.089	
Observations		3670	





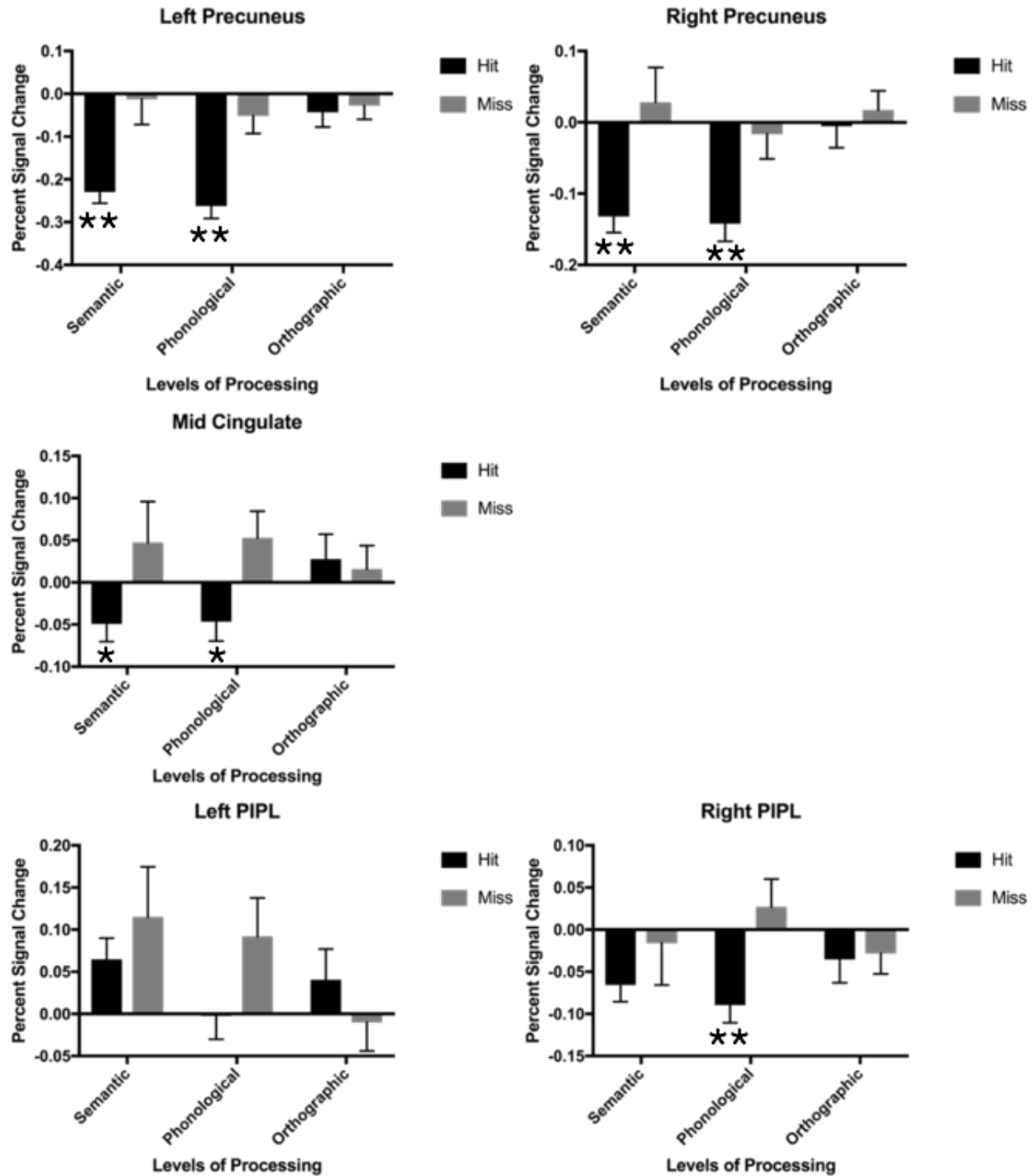


Figure 3.11. Percent signal change for each of the PMN regions. Error bars represent standard error of the mean across all the trials that survived motion correction for the LME and MVPA analysis. LME models reveal that left precuneus, right precuneus and mid cingulate showed less activity subsequent hits than misses. Also, these three regions displayed lower activity for semantic than orthographic processing. Right PIPL also showed the subsequent memory effect. \*\* indicates significance against the baseline at the .001 level using *t* tests; \* indicates significance at the .05 level and would not survive multiple comparison.

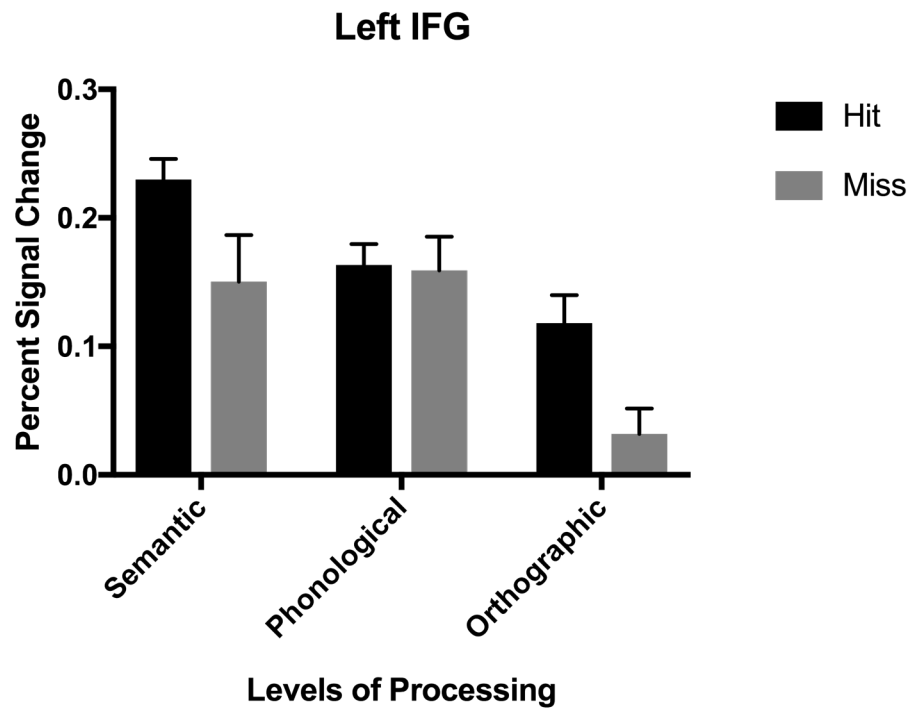


Figure 3.12. Percent signal change for left IFG. Error bars represent standard error of the mean across all the trials that survived motion correction for the LME and MVPA analysis. Linear mixed effect models reveal that left IFG activated more for subsequent hits than misses. In addition, left IFG activated more for semantic processing than both phonological and orthographic processing.

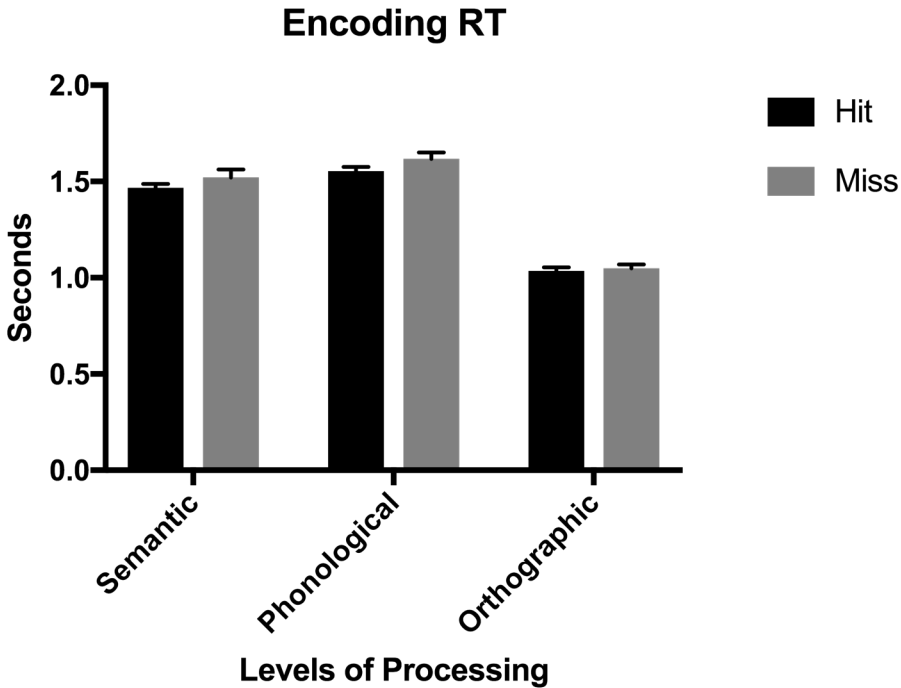


Figure 3.13. Response time for trials used in LME analysis. Errors bars indicate standard error of the mean across all the trials that survived motion correction for the LME and MVPA analysis. A two-way ANOVA revealed significant main effects of levels of processing and subsequent memory status but no significant interaction. Planned comparisons revealed that orthographic processing led to shorter RT than phonological processing ( $p < .001$ ) and semantic processing ( $p < .001$ ).

To improve model fit, a likelihood ratio test was then conducted to assess if adding random slopes for levels of processing associated with each participant would improve the model ( $p < .001$ ) (in other words, to test if modeling individual difference in their response to the levels of processing manipulation would improve the model). The test statistic was significant ( $p < .001$ ), so the null hypothesis was rejected and the random levels of processing effect was included in the model. **Table 3.8** (right side) summarizes the parameters of the random slope model, as well as the significance of the fixed effects via  $F$ -tests. The random slope model predicting subsequent memory can be represented with the following equations, where  $Y$  is subsequent memory:

$$\text{Level 1: } \text{logit}(\text{Subsequent Memory}_{ij}) = \beta_{0j} + \beta_{1j}(\text{LOP}_{ij}) + \beta_{2j}(\text{Precuneus and Mid Cingulate Factor}_{ij}) + \beta_{3j}(\text{PIPL Factor}_{ij}) + \beta_{4j}(\text{Encoding RT}_{ij}) + r_{ij}$$

$$\text{Level 2: } \beta_{0j} = \gamma_{00} + u_{0j}$$

$$\beta_{1j} = \gamma_{10} + u_{1j}$$

$$\beta_{2j} = \gamma_{20}$$

$$\beta_{3j} = \gamma_{30}$$

$$\beta_{4j} = \gamma_{40}$$

For Level 1, the subscript  $ij$  in  $\text{Subsequent Memory}_{ij}$  indicates that each item  $i$  is nested within each participant  $j$ . As the model is a logistic linear-mixed model, the logit of subsequent memory is a linear combination of the intercept for each participant, the effect of the level of processing, the effect of the first factor score (precuneus and mid cingulate), the effect of the second factor score (bilateral PIPL), the effect of encoding RT, and the random error  $r_{ij}$  associated with each trial for each participant. For Level 2,  $\gamma_{00}$  is the overall intercept,  $u_{0j}$  the deviation of a participant's intercept from the overall intercept,  $\gamma_{10}$ ,  $\gamma_{20}$ ,  $\gamma_{30}$  and  $\gamma_{40}$  the slopes associated with each predictors, and  $u_{1j}$  the deviation of a level of processing's slope associated with each participant. For the random intercept model,  $u_{1j}$  is omitted.

In both models, *the F-tests revealed that the latent factor of precuneus and mid cingulate activity, but not the latent factor of PIPL, predicted later memory performance on a trial-by-trial basis.* The  $F$ -tests'  $p$ -values are shown in **Table 3.8**  $p$ -value columns. Also, levels of processing significantly predicted later memory performance, with semantic processing leading to better subsequent memory than phonological and orthographic processing (supported by significant  $F$ -tests comparing phonological and orthographic processing to the reference class, semantic

processing). In addition, the two models showed that activity in precuneus and mid cingulate significantly predicted subsequent memory at the trial level (supported by the significant  $F$ -test associated with the factor scores for precuneus and mid cingulate, the factors scores are numeric). Critically, as levels of processing and encoding RT were both entered in the model simultaneously along with the factor scores for precuneus and mid cingulate, the result suggested that activity in precuneus and mid cingulate uniquely contributed to explaining variance in subsequent memory, above and beyond the levels of processing manipulation. It is likely that precuneus and mid cingulate activity reflects uncontrolled item effects or more global attentional processing at the item level, but further research is required.

As a further test of precuneus and mid cingulate's involvement in encoding, an additional model (**Table 3.9**), added left IFG as a fixed effect to the previous random slope model (**Table 3.8 right**). Including left IFG in the model allowed us to ask the question of whether precuneus and mid cingulate predicted subsequent memory above and beyond the contribution of left IFG. The model showed that even though left IFG activity also significantly predicted subsequent memory, precuneus and mid cingulate still contributed to explaining unique variance in subsequent memory. The result strongly supports precuneus and mid cingulate's involvement in memory at encoding.

### **3.6.2 Levels of processing partially influenced activity in precuneus and mid cingulate**

The next couple of linear mixed effect models assessed if levels of processing influenced activity of PMN regions. The result was mixed, with only precuneus and mid cingulate partially showing lower activity for deeper levels of processing. As a reminder, all the models below attempted to predict the activity for each region, rather than factor scores because

multicollinearity is no longer a concern for these models (note: multicollinearity was an issue for subsequent memory models because PMN regions were the predictors, and their activity was highly correlated). In addition, predicting factor scores does not inform us as much about each region. Adding random slopes for levels of processing associated with each participant improved the model fit for the left precuneus model ( $p < 0.001$ ) (**Table 3.10**), right precuneus model (**Table 3.11**) ( $p < 0.001$ ), right PIPL model ( $p < 0.001$ ) (**Table 3.12**). However, for the mid cingulate (**Table 3.13**) and left PIPL models (**Table 3.14**), adding the random effect of levels or processing for each participant led to the new models not converging, so the original models were kept. For brevity's sake, only the model with the best model fit for each region was reported. Statistical significance for all the factors of interest (levels of processing, subsequent memory performance and RT) did not change regardless of whether random slopes were modeled. The random slope models predicting activity of PMN regions can all be represented in the following equations, where Y is the activity in each region:

**Level 1:**  $Y_{ij} = \beta_{0j} + \beta_{1j}(\text{LOP}_{ij}) + \beta_{2j}(\text{Subsequent Memory}_{ij}) + \beta_{3j}(\text{Encoding RT}_{ij}) + r_{ij}$

**Level 2:**  $\beta_{0j} = \gamma_{00} + u_{0j}$

$$\beta_{1j} = \gamma_{10} + u_{1j}$$

$$\beta_{2j} = \gamma_{20}$$

$$\beta_{3j} = \gamma_{30}$$

For level 1, the subscript ij in  $Y_{ij}$  indicates that each item i is nested within each participant j. The activity for each region is represented as the linear combination of the intercept for each participant, the effect of the level of processing, the effect of subsequent memory, the effect of encoding RT, and the random error  $r_{ij}$  associated with each trial for each participant. For level 2,  $\gamma_{00}$  is the overall intercept,  $u_{0j}$  the deviation of a participant's intercept from the overall intercept,

$\gamma_{10}$ ,  $\gamma_{20}$  and  $\gamma_{30}$  the slopes associated with each predictors and  $u_{1j}$  the deviation of a level of processing's slope associated with each participant. For the random intercept model,  $u_{1j}$  is omitted.



Table 3.10. Parameters of the random slope model predicting activity in left precuneus. Semantic processing led to significantly lower activity than orthographic processing. Also, subsequent memory and encoding RT both significantly explained variance in left precuneus: subsequently remembered items were associated with lower activity, and longer RT was associated with greater activity. The fixed parts of the model include the intercept, encoding RT, subsequent memory (misses as the reference class), levels of processing (semantic processing as the reference class). CI refers to confidence interval, and p values indicate the significance of the fixed effects. Random parts of the model are not the focus of the analysis. For reference,  $\sigma^2$  refers to the estimated residual variance,  $\tau_{00}$  the random intercept variance for participants and ICC the intraclass correlation, or correlation among items within the same participant.

Left Precuneus (Random Slope Model)			
	<i>B</i>	<i>CI</i>	<i>p</i>
<b>Fixed Parameters</b>			
(Intercept)	0.01	-0.12 – 0.14	.886
Encoding_RT	0.13	0.08 – 0.18	< .001
Subsequent Memory (Hit)	-0.11	-0.17 – -0.05	< .001
LOP (Orthographic)	0.19	0.06 – 0.31	.006
LOP (Phonological)	-0.02	-0.10 – 0.05	.549
<b>Random Parameters</b>			
$\sigma^2$		0.634	
$\tau_{00, \text{Participant}}$		0.089	
$\rho_{01}$		-0.848	
$N_{\text{Participant}}$		29	
$ICC_{\text{Participant}}$		0.123	
Observations		3670	
$R^2 / \Omega_0^2$		.109 / .107	

Table 3.11. Parameters of the random slope model predicting activity in right precuneus. Similar to the model for left precuneus, semantic processing led to significantly lower activity than orthographic processing. Also, subsequent memory and encoding RT both significantly explained variance in left precuneus: subsequently remembered items were associated with lower activity, and longer RT was associated with greater activity. The fixed parts of the model include the intercept, encoding RT, subsequent memory (misses as the reference class), levels of processing (semantic processing as the reference class). CI refers to confidence interval, and p values indicate the significance of the fixed effects. Random parts of the model are not the focus of the analysis. For reference,  $\sigma^2$  refers to the estimated residual variance,  $\tau_{00}$  the random intercept variance for participants and ICC the intraclass correlation, or correlation among items within the same participant.

Right Precuneus (Random Slope Model)			
	<i>B</i>	<i>CI</i>	<i>p</i>
<b>Fixed Parameters</b>			
(Intercept)	0.01	-0.07 – 0.10	.756
Encoding_RT	0.11	0.06 – 0.15	< .001
Subsequent Memory (Hit)	-0.08	-0.13 – -0.03	.003
LOP (Orthographic)	0.13	0.04 – 0.22	.007
LOP (Phonological)	-0.02	-0.08 – 0.05	.583
<b>Random Parameters</b>			
$\sigma^2$		0.476	
$\tau_{00, \text{Participant}}$		0.028	
$\rho_{01}$		-0.666	
$N_{\text{Participant}}$		29	
$ICC_{\text{Participant}}$		0.056	
Observations		3670	
$R^2 / \Omega_0^2$		.077 / .074	

Table 3.12. Parameters of the random slope model predicting activity in right PIPL. Subsequently remembered items were associated with lower activity in right PIPL. Longer RT at encoding was associated with greater right PIPL activity. The fixed parts of the model include the intercept, encoding RT, subsequent memory (misses as the reference class), levels of processing (semantic processing as the reference class). CI refers to confidence interval, and p values indicate the significance of the fixed effects. Random parts of the model are not the focus of the analysis. For reference,  $\sigma^2$  refers to the estimated residual variance,  $\tau_{00}$  the random intercept variance for participants and ICC the intraclass correlation, or correlation among items within the same participant.

Right PIPL (Random Slope Model)			
	<i>B</i>	<i>CI</i>	<i>p</i>
<b>Fixed Parameters</b>			
(Intercept)	0.02	-0.07 – 0.11	.640
Encoding_RT	0.07	0.03 – 0.11	< .001
Subsequent Memory (Hit)	-0.05	-0.09 – -0.00	.040
LOP (Orthographic)	0.04	-0.06 – 0.14	.457
LOP (Phonological)	-0.01	-0.08 – 0.07	.826
<b>Random Parameters</b>			
$\sigma^2$		0.382	
$\tau_{00, \text{Participant}}$		0.038	
$\rho_{01}$		-0.868	
$N_{\text{Participant}}$		29	
$ICC_{\text{Participant}}$		0.089	
Observations		3670	
$R^2 / \Omega_0^2$		.076 / .072	

Table 3.13. Parameters of the random intercept model predicting activity in mid cingulate. Similar to the models for left and right precuneus, semantic processing led to significantly lower activity than orthographic processing. Also, subsequent memory and encoding RT both significantly explained variance in left precuneus: subsequently remembered items were associated with lower activity, and longer RT was associated with greater activity. The fixed parts of the model include the intercept, encoding RT, subsequent memory (misses as the reference class), levels of processing (semantic processing as the reference class). CI refers to confidence interval, and p values indicate the significance of the fixed effects. Random parts of the model are not the focus of the analysis. For reference,  $\sigma^2$  refers to the estimated residual variance,  $\tau_{00}$  the random intercept variance for participants and ICC the intraclass correlation, or correlation among items within the same participant.

Mid Cingulate (Random Intercept Model)			
	<i>B</i>	<i>CI</i>	<i>p</i>
<b>Fixed Parameters</b>			
(Intercept)	0.01	-0.06 – 0.08	.831
Encoding_RT	0.09	0.04 – 0.13	< .001
Subsequent Memory (Hit)	-0.05	-0.10 – -0.00	.040
LOP (Orthographic)	0.08	0.02 – 0.14	.012
LOP (Phonological)	0.00	-0.05 – 0.06	.891
<b>Random Parameters</b>			
$\sigma^2$		0.449	
$\tau_{00, \text{Participant}}$		0.015	
$N_{\text{Participant}}$		29	
$ICC_{\text{Participant}}$		0.033	
Observations		3670	
$R^2 / \Omega_0^2$		.043 / .042	

Table 3.14. Parameters of the random intercept model predicting activity in left PIPL. Longer RT at encoding was associated with greater right PIPL activity. The fixed parts of the model include the intercept, encoding RT, subsequent memory (misses as the reference class), levels of processing (semantic processing as the reference class). CI refers to confidence interval, and p values indicate the significance of the fixed effects. Random parts of the model are not the focus of the analysis. For reference,  $\sigma^2$  refers to the estimated residual variance,  $\tau_{00}$  the random intercept variance for participants and ICC the intraclass correlation, or correlation among items within the same participant.

Left PIPL (Random Intercept Model)			
	<i>B</i>	<i>CI</i>	<i>p</i>
<b>Fixed Parts</b>			
(Intercept)	0.03	-0.07 – 0.12	.555
Encoding_RT	0.19	0.14 – 0.24	<.001
Subsequent Memory (Hit)	-0.01	-0.08 – 0.05	.644
LOP (Orthographic)	0.02	-0.05 – 0.09	.579
LOP (Phonological)	-0.07	-0.13 – 0.00	.051
<b>Random Parts</b>			
$\sigma^2$		0.676	
$\tau_{00, \text{Participant}}$		0.032	
$N_{\text{Participant}}$		29	
$ICC_{\text{Participant}}$		0.045	
Observations		3670	
$R^2 / \Omega_0^2$		.064 / .063	

Table 3.15. Parameters of the random slope model predicting activity in left IFG. Subsequently remembered items were associated with greater activation in left PIPL. Longer RT at encoding was associated with greater left IFG activity. The fixed parts of the model include the intercept, encoding RT, subsequent memory (misses as the reference class), levels of processing (semantic processing as the reference class). CI refers to confidence interval, and p values indicate the significance of the fixed effects. Random parts of the model are not the focus of the analysis. For reference,  $\sigma^2$  refers to the estimated residual variance,  $\tau_{00}$  the random intercept variance for participants and ICC the intraclass correlation, or correlation among items within the same participant.

	LIFG		
	<i>B</i>	<i>CI</i>	<i>p</i>
<b>Fixed Parameters</b>			
(Intercept)	0.00	-0.07 – 0.07	.954
Encoding RT	0.10	0.06 – 0.13	<.001
Subsequent Memory (Hit)	0.06	0.03 – 0.10	<.001
LOP (Orthographic)	-0.08	-0.14 – -0.02	.014
LOP (Phonological)	-0.06	-0.12 – -0.00	.047
<b>Random Parameters</b>			
$\sigma^2$		0.224	
$\tau_{00, \text{Participant}}$		0.024	
$\rho_{01}$		-0.506	
$N_{\text{Participant}}$		29	
$ICC_{\text{Participant}}$		0.097	
Observations		3670	
$R^2 / \Omega_0^2$		.143 / .141	

The random slope models for left and right precuneus (**Table 3.10; Table 3.11**) both revealed that semantic processing led to lower precuneus activity than orthographic processing,

supporting the hypothesis that a deeper level of processing would lead to greater deactivation in PMN regions (Note: as Figure 3.11 illustrates, orthographic processing did not lead to deactivation). However, bilateral precuneus activity did not differentiate between semantic and phonological processing, suggesting a limit of deactivation. It is also worth mentioning that subsequent memory (not surprisingly from the models examining subsequent memory) and RT were both significant in the two models. The Subsequent hits were associated with lower precuneus activity. The significant subsequent memory effect despite controlling for the levels of processing manipulation suggests that precuneus activity might index uncontrolled item effects or more global attentional processing at the item level. After controlling for other variables, greater RT was associated with higher precuneus activity.

The random intercept model for mid cingulate (**Table 3.13**) showed almost the same pattern as the models for bilateral precuneus above. Semantic processing led to lower mid cingulate activity than orthographic processing, similarly supporting mid cingulate's role in effective encoding. However, mid cingulate activity, like precuneus, did not differentiate between semantic processing and phonological processing. Subsequent memory and RT were both significant in the model, as well. Subsequent hits were associated with lower mid cingulate activity. Longer RT was associated with higher mid cingulate activity.

The random slope model for right PIPL (**Table 3.12**), however, showed that manipulating levels of processing did not lead to changes in right PIPL activity. In addition, Right PIPL barely showed the subsequent memory effect. Longer RT was associated with higher right PIPL activity.

Left PIPL, similar to right PIPL, was not influenced by levels of processing manipulation (**Table 3.14**). Left PIPL, however, did not show the subsequent memory effect in this model.

Also, semantic processing was associated with marginally *higher* activity than phonological processing, the opposite of the hypothesis. The only pattern consistent with the other regions was that longer RT was associated with higher left PIPL activity.

While the left IFG region is not the primary focus of the analysis, it nonetheless serves as a good comparison to PMN regions. As opposed to precuneus and mid cingulate (which differentiated between semantic and orthographic processing but not between semantic and phonological processing), left IFG activity showed greater activation for semantic than phonological processing and orthographic processing (**Table 3.15**), after controlling for RT and subsequent memory. Left IFG also showed significantly greater activity for subsequent hits than misses. Longer RT was associated with greater left IFG activity.

In summary, the LME analysis examining if PMN activity was influenced by the level of processing manipulation showed mixed results. Only precuneus and mid cingulate showed lower activity for semantic than orthographic processing. However, precuneus and mid cingulate did not differentiate between semantic than phonological processing. Bilateral PIPL, on the other hand, did not show lower activity for semantic processing compared to orthographic or phonological processing.

### **3.7 Multivariate pattern analysis**

Multivariate pattern analysis was used alongside LME analysis because the MVPA analysis was able to take advantage of spatial differences in the pattern of activation within a region, something LME analysis was not able to do. For instance, it is possible that some voxels in precuneus and mid cingulate differentiated between semantic and phonological processing, but their signal gets washed out when all voxels in each region's mask are averaged. In addition, the



leave-one-subject-out cross validation procedure employed in the MVPA analysis more rigorously tests the predictive power of PMN regions as well as left IFG and corpus callosum in subsequent memory, using only other participants' data to form the training set. In other words, all the training sets are blind to the data in the classification set. Hence, successful classification of subsequent memory using MVPA would imply that it is possible to predict whether someone would later remember an item by only examining PMN regions and without relying on any data from that person.

### **3.7.1 Subsequent memory classification was successful using individual trial estimates from each of the PMN regions, further supporting PMN role in memory**

Decoding subsequent memory (hits versus misses) was above chance level for all of the PMN regions: left precuneus (54.24%,  $p < .001$ ), right precuneus (54.02%,  $p < .001$ ), mid cingulate (53.19%,  $p = .002$ ), right PIPL (53.46%,  $p < .001$ ) and left PIPL (52.78%,  $p = .009$ ) (**Figure 3.14**). Decoding subsequent memory was also above chance for left IFG (53.46%,  $p = .005$ ), but not corpus callosum (50.48%,  $p = .461$ )

### Subsequent Memory: Hits versus Misses

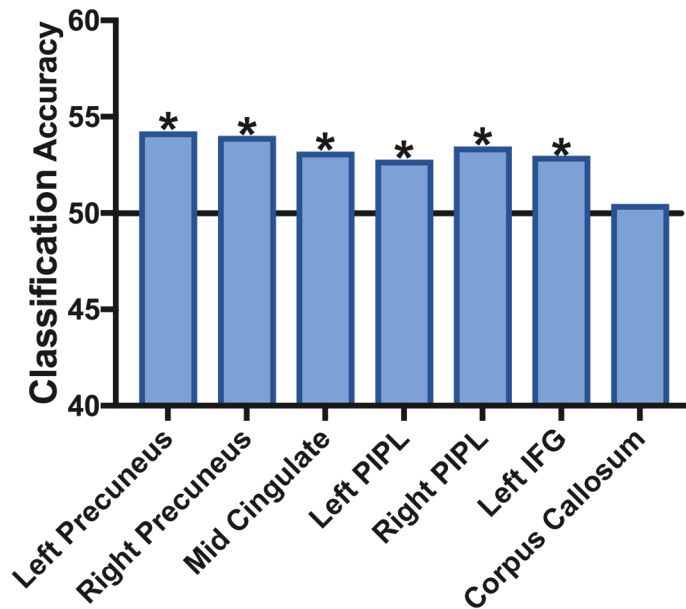


Figure 3.14. Classification for subsequent memory for PMN regions, left IFG and corpus callosum. Asterisk denotes statistical significance at the 0.05 level using permutation testing.

#### 3.7.2 Levels of processing classification: Accuracy in decoding semantic versus phonological processing was near chance for most PMN regions, with the exception of right PIPL

The LME models revealed that overall, mean activation magnitudes in PMN regions did not differentiate between semantic and phonological processing. Text step in the analysis was to assess whether spatial patterns of activation in PMN regions distinguish between different levels of processing, and especially between semantic and phonological processing. It was surprising that despite that semantic processing led to better subsequent memory than phonological processing, activity in PMN regions did not seem to differ. MVPA classification results otherwise aligned with univariate results from previous analyses reasonably well such that larger difference in magnitudes were more likely to lead to greater classification accuracy (this result

made sense, given that mean differences across conditions were not removed for the MVPA analysis)(**Figure 3.15; Table 3.16**), with the exception of right PIPL: decoding semantic processing from phonological processing was relatively high, at 59.29%, despite this region not showing an effect of levels of processing in the LME analysis. It is also worth noting that decoding semantic processing from phonological processing was statistically above chance for left precuneus, even though the accuracy of 51.89% was not that impressive. For left PIPL, the accuracy was 52.29%, but it just missed the  $p$  of 0.05 cutoff. Decoding semantic processing from phonological, however, was above chance for left IFG. Decoding semantic processing from orthographic processing was also above chance for left IFG. As for corpus callosum, decoding levels of processing was not significantly above chance.

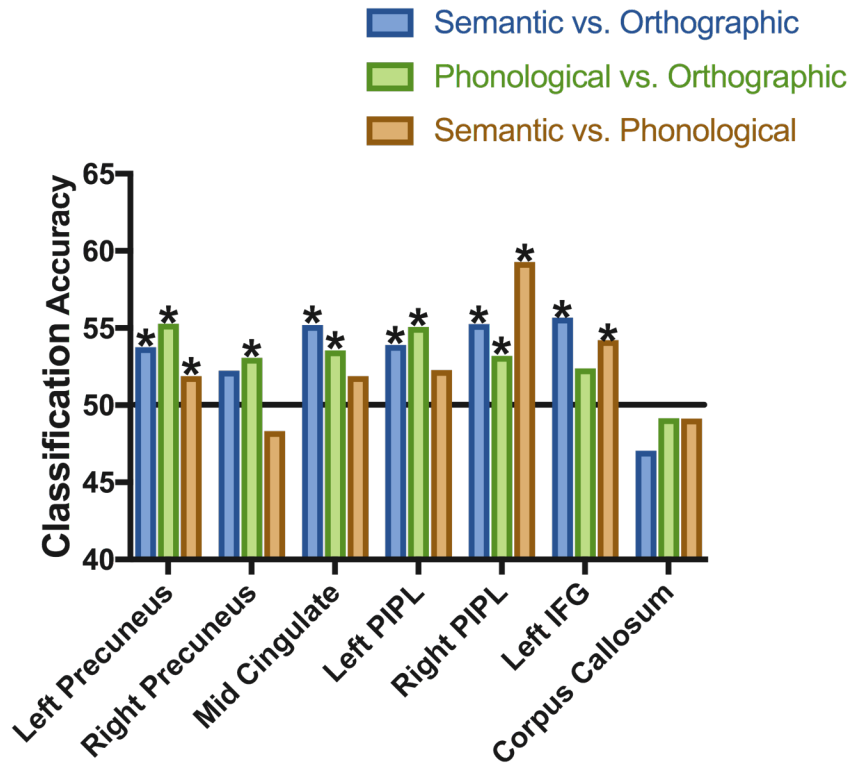


Figure 3.15. Classification accuracy for levels of processing (in pairs) in PMN regions. Asterisk denotes statistical significance at the 0.05 level using permutation testing.

Table 3.16. MVPA classification accuracy for levels of processing. Bold font indicates significance at the .05 level. *P* values are shown in parentheses.

Region	Classification accuracy		
	Semantic vs. Orthographic	Phonological vs. Orthographic	Semantic vs. Phonological
Left Precuneus	<b>53.77</b> (.002)	<b>55.29</b> (< .001)	<b>51.89</b> (.031)
Right precuneus	52.24 (.106)	53.08 (.021)	48.32 (.907)
Mid Cingulate	<b>55.2</b> (< .001)	<b>53.56</b> (.007)	51.89 (.074)
Left PIPL	<b>53.9</b> (.014)	<b>55.08</b> (< .001)	52.29 (.052)
Right PIPL	<b>55.27</b> (< .001)	<b>53.2</b> (.020)	<b>59.29</b> (< .001)
Left IFG	<b>55.67</b> (.001)	52.38 (0.078)	<b>54.21</b> (.009)
Corpus Callosum	47.25 (.97)	49.16 (.638)	49.14 (.757)

### **3.7.3 Semantic hits versus phonological hits classification: PIPL, but not precuneus and mid cingulate, differentiated between semantic and phonological processing**

Because different levels of processing were associated with different subsequent memory performance, two interesting questions arose: Is it possible to decode levels of processing when the classification is restricted to subsequent hits? In other words, do PMN regions contain information about different levels of processing when levels of processing no longer predict subsequent memory? On the other hand, is it still possible to decode subsequent memory when the classification is restricted to the same level of processing, such as phonological processing?

Restricting classification between semantic and phonological to only subsequent hit trials led to a dissociation in PMN regions: patterns in precuneus (51.56%,  $p = 0.077$ ) and mid cingulate (50.65%,  $p = 0.265$ ) did not offer clues to differentiate the two levels of processing (**Figure 3.16**). However, decoding between the two levels was possible in left PIPL (54.24%,  $p < 0.001$ ) and right PIPL (60.82%,  $p < 0.001$ ). The accuracy in left PIPL was slightly higher when classification was restricted to hits than when the classification was for hits and misses. The high accuracy in right PIPL was again surprising. As for left IFG, decoding semantic processing from phonological processing was still above chance even when the analysis was restricted to hits (54.18%,  $p = 0.014$ ). Finally, it was not possible to decode semantic processing from phonological processing for hits for corpus callosum, as expected (49.62%,  $p = 0.508$ ).

### **3.7.4 Decoding subsequent memory was still possible in left precuneus and to a lesser extent right precuneus when the classification was restricted to phonological processing**

Restricting classification of subsequent hits and misses to only phonological processing trials led to lower classification accuracy (**Figure 3.17**). Nevertheless, it was still above chance in left precuneus (55.81%,  $p = 0.003$ ), and marginally above chance in right precuneus (52.6%,  $p$

= 0.079). Classification accuracies in the other PMN regions were not above chance: mid cingulate (50.07%,  $p = 0.467$ ), left PIPL (52.67%,  $p = 0.101$ ), right PIPL (52.12%,  $p = 0.166$ ), left IFG (45.36%,  $p = 0.99$ ), and corpus callosum (51.45%,  $p = 0.225$ ).

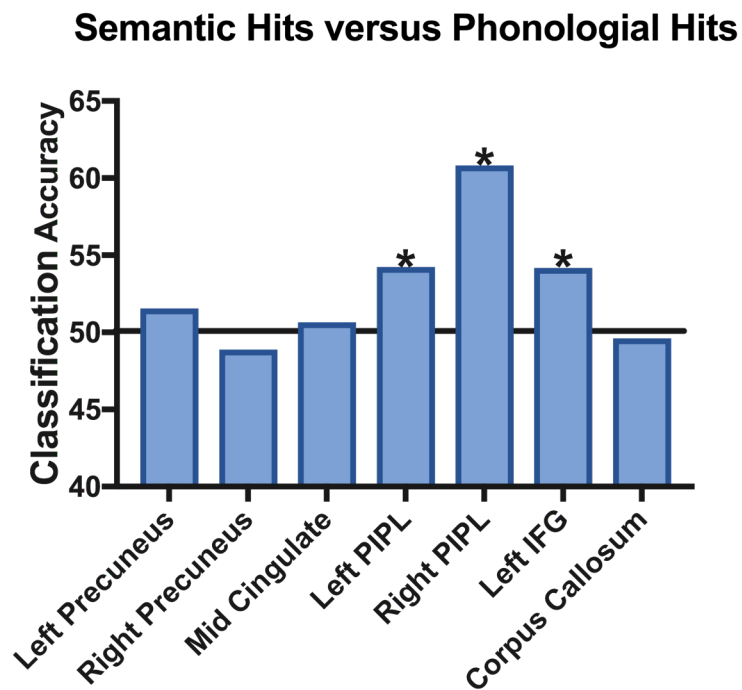


Figure 3.16. MVPA classification for semantic hits versus phonological hits. Asterisk indicates statistical significance at the 0.05 level using permutation testing.

### Phonological Hits versus Misses

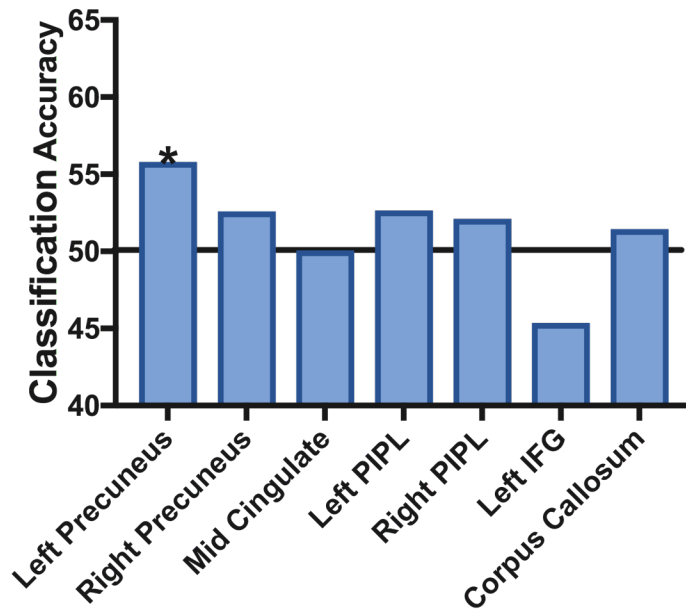


Figure 3.17. MVPA classification for phonological hits versus phonological misses. Asterisk indicates statistical significance at the 0.05 level using permutation testing.

In summary, the MVPA analysis showed that all PMN regions' patterns of activity could be used to predict subsequent memory above chance. In addition, the classifiers generalized across participants such that classifiers built using a subset of the data (in this case, all but one) could classify another subset of participants' data (one participant in our study). Restricting the subsequent memory classification to only phonological processing, however, reduced the classification accuracy such that only left precuneus was diagnostic of subsequent memory outcome. In addition, decoding level of processing in PMN regions was mostly above chance. However, decoding semantic from phonological processing in precuneus and mid cingulate still led to near chance or at chance classification accuracy, especially when the classification was restricted to subsequent hits.

## **Chapter 4: Discussion**

The study was designed to answer the questions of whether PMN regions deactivate more under deeper levels of processing—a more effective encoding condition—and whether trial-by-trial variation in PMN regions predict subsequent memory. The first research question led to mixed results: Precuneus and mid cingulate showed lower activity for semantic processing than orthographic processing but did not deactivate more for semantic processing than phonological processing. For the second question, precuneus and mid cingulate activity could be used to predict subsequent memory in a trial-by-trial manner, above and beyond the level of processing manipulation as well as contribution from left IFG. Finally, PIPL showed very different activity patterns compared to precuneus and mid cingulate. Bilateral PIPL did not show the level of processing effect and did not contribute to unique variance in predicting subsequent memory in the LME analysis (but mostly predicted levels of processing in the MVPA analyses).

### **4.1 Precuneus and mid cingulate deactivated for deeper levels of processing, but only to a certain extent**

Activity in bilateral precuneus and mid cingulate partially supported the hypothesis that PMN regions would deactivate more for deeper levels of processing, a more effective encoding condition: They showed the expected levels of processing effect in the LME analysis (deactivation for semantic processing but no deactivation for orthographic processing) yet did not differentiate between semantic and phonological processing. In the MVPA analysis, patterns of activity in bilateral precuneus and mid cingulate did not differentiate much between semantic and phonological processing either. After classification was restricted to subsequent hit trials, decoding between semantic and phonological processing in bilateral precuneus and mid cingulate was at chance. Further research will have to explore what the signals in precuneus and



mid cingulate represent. Currently, it is only possible to conclude that activity in precuneus and mid cingulate does not seem to represent semantic information or phonological information per se as they showed similar activity for both semantic and phonological processing.

If precuneus and mid cingulate activity does not differentiate between semantic and phonological processing, what regions might be responsible for the better subsequent memory for semantic processing? A good candidate is left inferior gyrus, which showed greater activity for semantic processing than phonological processing and perhaps relatedly, greater activity for subsequently remembered items than forgotten items in this study. Also, as mentioned before, Kim's meta-analysis (2011) found the subsequent memory effect in this region. In addition, left IFG had been implicated in a variety studies studying semantic processing. Also mentioned previously, Wagner and colleagues (1998) found that left inferior gyrus showed greater activity for semantic (abstract or concrete judgment) than non-semantic (upper or lower case judgment) processing; Gabrieli and colleagues (1996) found that left inferior gyrus displayed greater activity for semantic encoding of words (concrete or abstract judgment) than perceptual encoding of words (upper or lower case judgment); Roskies and colleagues (2001) found that left inferior frontal gyrus was more active during semantic judgments (synonym judgments) than rhyming judgments, and this region showed greater activity when a separate semantic categorization task was harder; McDermott and colleagues (2003) demonstrated that asking subjects to think about the relation between words that are semantically-related activated left IFG more than thinking about phonologically-related associates.

## **4.2 Magnitudes of PIPL activity did not differentiate between levels of processing, but MVPA analysis showed that spatial patterns of PIPL activity did**

Bilateral PIPL did not show the expected levels of processing effect in LME analyses and did not emerge in whole-brain univariate contrasts between levels of processing pairs either. In fact, left PIPL marginally showed the opposite effect in LME analysis: greater activity for semantic processing than phonological processing.

Decoding between different pairs of levels of processing in PIPL, however, was mostly above chance, suggesting that PIPL contained information about the three separate levels of processing. Nevertheless, the relatively high classification accuracy for semantic versus phonological processing in right PIPL could be due to the right PIPL mask including voxels from a different region and thus needs to be interpreted with caution. The average magnitudes of bilateral PIPL shown in **Figure 3.11** did not reveal any striking difference in magnitudes that would hint at high classification accuracy. Closer inspection of the whole-brain map contrasting semantic and phonological processing (**Figure 3.9**) revealed that there was a cluster slightly more anterior to the right PIPL defined using functional connectivity showing sensitivity to that contrast. While this cluster's center was not considered a part of the right PIPL in PMN, the right PIPL mask likely included voxels that were near the boundary of the two areas. It is possible that these voxels near the boundary drove the classification success. (Note: As linear SVM was used as the classifier, univariate difference could drive classification results.) More discussion on the dissociation between PIPL and the other PMN regions is below.

### **4.3 Trial-by-trial variation in PMN regions predicted subsequent memory**

Perhaps the most important finding is that the linear-mixed effect models on subsequent memory demonstrated that precuneus and mid cingulate activity could be used to predict subsequent memory on individual trials. PIPL, on the other hand, did not significantly explain significant variance for subsequent memory. MVPA analysis revealed that all PMN regions' activity led to above chance classification for subsequent memory. The ability to predict subsequent memory using only activity from these regions supported their involvement in memory and mnemonic processing (Gilmore et al., 2015; Rosen, Stern, Devaney, & Somers, 2017) at encoding. In addition, this was the first time activity from the PMN alone was successfully used to predict subsequent memory according to the author's knowledge. Impressively, activity in precuneus and mid cingulate from one set of participants could be used to predict other participants' subsequent memory performance with above chance accuracy.. Future research should collect more trials per person and assess if using each subject's own patterns to predict subsequent memory would lead to even higher accuracy.

### **4.4 Precuneus still predicted subsequent memory even after controlling for the level of processing**

Even though manipulating the level of processing is a strong way of influencing subsequent memory, precuneus activity (and to a certain extent, mid cingulate) still predicted subsequent memory even after controlling for levels of processing; data on the other regions were mixed. In the LME models predicting subsequent memory, the effect of the factor scores of precuneus and mid cingulate was significant even though the levels of processing were accounted for in the models. In addition, in the MVPA analysis, when restricting to the same

level of processing (phonological processing), decoding subsequent memory was still above chance using data from left precuneus, and marginally above chance for right precuneus ( $p = .079$ ). Future research should look at how other factors influence encoding and activity in PMN regions. For instance, it is possible that precuneus activity might be related to uncontrolled item effects, such as differences in imageability and word naming latency (Cortese et al., 2010, 2015; Yarkoni, Speer, Balota, McAvoy, & Zacks, 2008). It is also possible that precuneus activity indexed more global processes such as attention for each item at encoding, but the lack of measure of attention in this study makes directly testing the claim difficult.

#### **4.5 Is the PMN a memory network?**

When Gilmore and colleagues (2015) characterized the PMN as a memory network, their framework suggested that PMN activity represents perceived familiarity in the context of the experiment. For instance, at encoding, deactivations in PMN reflect the novelty (lack of familiarity) whereas at retrieval, activations in PMN reflect familiarity with the items. The framework applies to memory experiments quite well but poses challenges for non-memory studies (more discussion on this aspect later). Even though Gilmore and colleagues did not specifically predict how PMN deactivation at encoding would be influenced by deeper level of processing and whether subsequent memory can be predicted by using trial-wise PMN activity, it is still the case that our hypothesized function of the PMN was about memory. If we fail to observe the expected results, it would cast doubt on PMN as a memory network.

Our research question of using PMN activity to predict subsequent memory was supported with the LME analysis for precuneus and mid cingulate and in the MVPA analysis for all PMN regions. In addition, in the LME analysis, the contribution of precuneus and mid cingulate in predicting subsequent memory was above and beyond the level of processing

manipulation in addition to contribution from the left IFG region. Even though left IFG also predicted subsequent memory in the same model, the unique variance in subsequent memory explained by precuneus and cingulate supports precuneus and mid cingulate's role in encoding memory.

Nevertheless, the second research question was met with mixed results: semantic processing leading to lower activity in precuneus and mid cingulate was consistent with the prediction, but the lack of difference between PMN activity for semantic and phonological processing presents a challenge to account that PMN activity indexes the quality of processing probes at encoding. Deeper levels of processing seem to be effective in shifting the mean activation in precuneus and mid cingulate downward, but there appears to be a limit for how much deactivation can occur in PMN regions. The ability to use PMN activity to predict trial-by-trial subsequent memory in the LME analysis, however, suggests that so long as precuneus and mid cingulate are deactivated sufficiently, regardless of the levels of processing manipulation, successful encoding can occur. Nevertheless, it would appear that PMN is not the only set of regions mediating the difference in subsequent memory between semantic and phonological processing. As mentioned previously, perhaps the left inferior frontal region that showed greater activity for semantic processing than phonological processing and greater activity for subsequent hits than misses in our study mediated the behavioral difference between semantic and phonological processing.

As this study was designed to capture neural activity in response to a memory task, the study is not suitable to address PMN's function outside the context of a memory experiment. Nevertheless, this does not mean that PMN's possible role in non-memory tasks should be ignored. Recently, other researchers have raised the possibility that the PMN is not really a

memory network, at least not entirely. For instance, Rosen and colleagues (2017) suggested that precuneus, mid cingulate and PIPL are instead responsible for integrating information from mnemonic and external sources to guide attention. They showed that PMN (referred to as the parietal memory-attention network [PMAN] in their paper) regions activated more for long-term-memory-guided attention than long-term memory retrieval or stimulus-guided attention, when the stimulus familiarity was held constant. However, Rosen and colleagues did not provide an account for deactivation in PMN regions at encoding, so it is not clear what their prediction would be for the level of processing manipulation in PMN. In a prospective memory study, Lamichhane and colleagues (2018) found that PMN regions showed greater activity when participants responded to prospective memory targets as well predicted accuracy for prospective memory trials. They speculated that the PMN is engaged by familiarity-based capture of attention.

In addition to memory and attention, PMN regions likely subserve other cognitive control functions, such as tracking expectancy violation. For instance, in a memory experiment, O'Connor, Han and Dobbins (2010) found mid cingulate, PIPL and a region close to precuneus showing greater activity for invalidly cued than validly cued items (both successfully retrieved). Outside memory experiments, Waskom, Frank, and Wagner (2016) observed that precuneus and mid cingulate were strongly modulated by context prediction error, which expressed surprise about the trial in a task switching experiment judging the color or motion of dot stimuli. It is worth noting that other studies have also observed PMN regions showing greater activity for task switching trials, or trials that should be surprising to participants. For example, Reynolds and colleagues (2004) examined task switching and subsequent memory and found that while precuneus showed the task switching effect (switch > no-switch), it did not show a direct effect

of subsequent memory. Rather, they found an interaction between subsequent memory and the task-switching manipulation such that the subsequent memory effect was primarily found on task-switch trials. Piguet and colleagues (2013) and another study by De Baene and colleagues (2012) found mid cingulate and precuneus to be sensitive to task switching (switch > no-switch). Gerrits and colleagues (2015), on the other hand, found mid cingulate and PIPL to be sensitive to task switching (task > no-switch). Furthermore, a meta-analysis conducted by Kim (2014) examined the auditory and visual oddball studies to look for regions that showed the oddball pattern, i.e., oddball (less frequently repeated and more surprising stimuli) > standard (more frequently repeated stimuli). Mid cingulate and a region likely to be PIPL both showed greater activity for oddball than standard stimuli for auditory stimuli; precuneus was not revealed in the analysis. Last but not least, in line with the task switching and cognitive control account, Dosenbach and colleagues (2007) examined start-cue activity (color change of the fixation) across ten task conditions that ranged from semantic classification, visual classification, timing, naming, visual search to reading and found that precuneus and mid cingulate's activity was modulated by the start cues. Nevertheless, as much as expectancy violation explains this set of experiments, it is not clear how the expectancy violation account would explain the deactivation in PMN regions for encoding and the relationship between deactivation and subsequent memory. It is not obvious, for instance, how semantic processing, which led to lower activity in precuneus and mid cingulate, would be less surprising than orthographic processing.

What are the implications for PMN's sensitivity to the seemingly wide range of contrasts? Aside from acknowledging that the role of the PMN seems context-dependent, it is also possible that PMN regions are more heterogeneous than we thought. It is possible that the various

functions (memory, attention and cognitive control) suggested in different hypotheses are carried out by different populations of neurons; otherwise it would seem difficult to reconcile the differences in these hypotheses. Recently, Rutishauser and colleagues (2018) recorded single cell firing in left lateral parietal cortex and found memory-selective and confidence-selective cells. Even though their study measured firing rate in a location that was more superior to PIPL and hence not in the PMN, a similar study can measure single cell firing in PMN regions.

Is PMN a memory network? In light of studies supporting PMN's role in non-memory function, PMN is unlikely to be a memory-only network. What about the narrower question of whether PMN supports memory formation in the context of a memory experiment? Even though there are caveats (PIPL's dissociation from precuneus and mid cingulate, discussed below, and the lack of difference between semantic and phonological processing), the answer to that question appears to be "yes".

However, plenty of questions still remain regarding the role of parietal memory network in episodic memory. In particular, a concern is the lack of lesion studies showing severe episodic memory deficits aside from impaired subjective recollection following lesion to parietal regions (Cabeza et al., 2008; Simons, Peers, Mazuz, Berryhill, & Olson, 2010). This is in contrast to lesions to medial temporal lobe regions, which led to famous amnesic cases such as H.M.; lesions to the frontoparietal control network, also has been found to lead to attention deficits (Ptak, 2012). However, a lot of work assessing memory deficits following parietal lesions have focused on lateral parietal regions, whereas precuneus and mid cingulate are both much closer to the midline and precuneus is rarely lesioned in strokes or accidents (Cavanna & Trimble, 2006). Recently, Harroud and colleagues (2017) reported epilepsy patients who required surgical operations. Among the two patients with left precuneus resection, one of them showed poorer



recall in verbal memory after the operation. The two patients with right precuneus resection actually showed memory improvement following the procedure. As for mid cingulate, damage to parts of cingulate has been reported in patients with colloid cysts in the third ventricle, which often produce memory deficits. However, the patients with memory deficits usually have extensive damage to other brain areas. Whether fornix is damaged seems to be a good predictor of the presence of memory deficits (Aggleton et al., 2000; Desai, Nadkarni, Muzumdar, & Goel, 2002), but damage to mid cingulate was not extensively examined according to the author's knowledge. In short, there is not enough lesions studies on precuneus and mid cingulate to determine the impact on memory following damage to the two regions. Inhoff and Ranganath (2017) attempted to explain the lack of severe memory deficits following parietal lesions, arguing that perhaps medial temporal lobe regions are similar to the connector hubs in Warren's lesion study (Warren et al., 2014). In other words, lesions to medial temporal lobes leading to widespread damage was a result of the disruption of information flow from medial temporal lobe to others regions, but not a result of the information medial temporal lobe regions represent. Support for Inhoff and Ranganath's view came from patients suffering from Semantic Dementia and patients with Alzheimer's disease. Even though medial temporal lobe damage occurs in both Semantic Dementia and Alzheimer's disease, only Alzheimer's disease is associated with atrophy in medial and lateral parietal cortex as well as more pronounced episodic memory deficit (LaJoie et al., 2014). Inhoff and Ranganath argued that because medial temporal lobe damage was common in both Semantic Dementia and Alzheimer's disease, it was the additional atrophy in parietal cortex that was associated with episodic memory deficits. Nevertheless, it is worth pointing out that Inhoff and Ranganath mostly focused on parietal regions in the default mode despite those regions' close proximity to PMN regions.

Researchers have raised another concern about the role of PMN regions in memory, which is that PMN regions deactivate, rather than activate for subsequent hits (Daselaar et al., 2004; Otten & Rugg, 2001). Daselaar and colleagues argued that deactivation in posterior midline regions reflect a beneficial reallocation of neurocognitive resources, as deactivation is associated with subsequent hits. They also pointed out that compared to healthy young adults, older adults failed to show deactivation in mid cingulate and precuneus (Lustig et al., 2003); furthermore, patients with Alzheimer's disease showed activation in the two regions. Lustig and colleagues' finding is consistent with the idea that in deactivation in PMN regions is beneficial rather than detrimental. The results from this study is also consistent with the idea that deactivation in PMN regions is important for memory formation to occur. Nevertheless, future work has to assess what deactivation in PMN regions implies. If deactivation in the PMN is indeed associated with better resource reallocation, memory formation is unlikely to take place in the PMN.

#### **4.6 Dissociation between PIPL and the other two PMN regions (precuneus and mid cingulate) raises questions about PIPL's place in the PMN**

Several aspects of our findings raised questions about whether PIPL belongs in the PMN:

- 1) The inability to replicate the negative subsequent memory effect in left PIPL in the whole-brain analysis (right PIPL emerged in the whole-brain contrast of subsequent remember versus subsequent misses).
- 2) bilateral PIPL's lack of subsequent memory effect in the LME analysis.
- 3) The lower correlation between bilateral PIPL and mid cingulate (compared to precuneus).

Recently, Gordon et al.(2017) found that bilateral PIPL did not always belong to the same network as precuneus and mid cingulate based on functional connectivity. For example, in what Gordon and colleagues labeled as the medial parietal system, mid cingulate and precuneus were observed in 98 to 99% of subjects; the numbers went down to 72% and 73% for left and right

PIPL. Individual differences would also explain why in Yeo's 17-network parcellation (Yeo et al., 2011), PIPL did not get assigned to the same network as precuneus and mid cingulate. Similarly, Hu and colleagues (2016) did not find PIPL in the PMN using ICA. It would appear that using group-averaged functional connectivity maps to define bilateral PIPL carries the risk of defining PIPL at regions that serve different functions. Further research will have to examine whether these dissociations reflect true functional variability in this region, or a limit in our methodology. Perhaps the precision of the location of functional regions is the key to our understanding of functions in PMN, and collecting a greater amount of data (both resting-state and task-based) per participant will help us pinpoint the location of each region better.

## **4.7 Limitations**

This study is a start at looking at the functions of PMN. While it offers new ways of characterizing the behavior of this network, further research is necessary to answer the question of what PMN signals represent. Also, the inability to observe a subsequent memory effect in left PIPL and the lower correlation between bilateral PIPL and mid cingulate (compared to precuneus) highlighted the difficulty of consistently locating the PIPL and questioned its role in the PMN. In addition, the decision to perform between-subject subject classification in the MVPA analysis was driven by the relatively low number of trials available per person, given that classification with the event-related design is more difficult than the block design. In an ideal world with unlimited resources, we would have collected more trials to perform the within-subject classification.

## **4.8 Conclusions and implications**

In summary, with some caveats, this study supports the role of two members of the PMN, precuneus and mid cingulate, in indexing the quality of probe processing at encoding. Trial-wise

activity in precuneus and mid cingulate predicted subsequent memory, above and beyond the level of processing manipulation as well as contribution from left IFG. In addition, precuneus and mid cingulate showed lower activity for semantic processing than orthographic processing, a less effective encoding condition. Nevertheless, neither precuneus nor mid cingulate differentiated between semantic and phonological processing in the LME analysis. The finding suggests that there is a threshold for deactivation in the two regions; once the deactivation threshold is reached, regardless of the level of processing, successful encoding is likely to occur. Further research will have to examine if PIPL should be considered a member of the PMN.

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