A parietal memory network revealed by multiple MRI methods

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The manner by which the human brain learns and recognizes stimuli is a matter of ongoing investigation. Through examination of meta-analyses of task-based functional MRI and resting state functional connectivity MRI, we identified a novel network strongly related to learning and memory. Activity within this network at encoding predicts subsequent item memory, and at retrieval differs for recognized and unrecognized items. The direction of activity flips as a function of recent history: from deactivation for novel stimuli to activation for stimuli that are familiar due to recent exposure. We term this network the ‘parietal memory network’ (PMN) to reflect its broad involvement in human memory processing. We provide a preliminary framework for understanding the key functional properties of the network.

Parietal cortex contributes to memory processing in multiple ways

Since the earliest days of functional neuroimaging, researchers have sought to discover how the brain builds, and later accesses, memories. How one might predict whether a given experience would be remembered or forgotten [1,2], and how successful and unsuccessful retrieval differed in their neural signatures [3], were among the first questions asked by scientists when it became possible to isolate activity to single events or classes of events. Many of the answers, it turns out, are a rather unsatisfying ‘it depends’. The neural correlates of successful encoding vary as a function of the type of initial study [4] or later retrieval task [5], while the correlates of successful retrieval differ as a function of how one’s memory is tested, and typically appear in regions distinct from those implicated in encoding (e.g., [6–9]). In this review we identify a network of brain regions that demonstrates both encoding- and retrieval-related signals that appear to generalize across task conditions. We review evidence suggesting that the activity of this network reflects a continuum of how novel or how familiar a stimulus is perceived to be, and we discuss the importance of this network in advancing understanding of neural mechanisms related to learning and memory.

Although early neuroimaging studies focused on the medial temporal and frontal lobes, parietal cortex has consistently been linked to human memory processing [10,11]. Numerous studies have associated parietal cortex with retrieval-success effects (see Glossary [12–15]), but regions of parietal cortex also show differential activity for: (i) subsequently forgotten, relative to subsequently remembered, items during memory encoding [16,17]; (ii) intentional retrieval tasks relative to intentional encoding tasks [18]; (iii) items that have been encoded multiple times relative to items that are encoded for the first time [19,20]; (iv) false alarms (new items judged as old) relative to misses (old items judged to be new) [21]; (v) more confidently, relative to less confidently, retrieved items [6]; and (vi) items for which rich, relative to sparse, contextual information is accessible at retrieval [7,22].

Hypotheses have been forwarded to explain these different patterns of data (see [10,23] for reviews), but no single hypothesis can account for all of the patterns

Glossary

Encoding-retrieval flip: a regional BOLD response pattern in which the direction of evoked activity, relative to resting baseline, flips between encoding and retrieval. Typically this pattern is observed in encoding-induced deactivations and retrieval-induced activations.

Functional network: a group of brain regions that coactivate during particular types of task or task conditions and that show highly correlated deactivations and activations in the absence of explicit task conditions (i.e., during the ‘resting-state’).

Repetition enhancement: repetition enhancement involves an increase in neural activity across multiple presentations of an item. Such effects have been observed in several studies, typically in the context of encoding-induced deactivations and retrieval-induced activations.

Resting-state functional connectivity MRI: an fMRI-based technique to assess the functional relatedness of different regions of cortex, in the absence of any explicit task conditions; that is, the participant lies still and passively stares at a fixation cross or closes their eyes. High correlations between regions are thought to reflect a history of coactivation across one’s lifetime.

Retrieval-success effect: regional differences in average activity, during retrieval, for items that are successfully retrieved as compared to those that are not. Within the realm of recognition memory, retrieval-success effects take the form of greater activity for correctly recognized old items (‘hits’) as compared to correctly identified new items (‘correct rejects’) or less frequently, incorrectly classified old items (‘misses’).

Subsequent memory effect: regional differences in average activity, during encoding, for items that are later retrieved on a memory test relative to those that are forgotten. This pattern typically emerges as greater activity for items that are later recognized. Negative subsequent memory (nSM) effects show the reverse of this pattern, with less activity for items that are later recognized relative to those later missed; specifically, this latter pattern is often revealed in greater deactivation for items later recognized relative to those later missed. nSM effects are sometimes called ‘subsequent forgetting’ effects.
described above. In part, this is because these hypotheses focus primarily on retrieval [17]. In addition, they mainly focus on lateral parietal cortex, with less consideration of medial parietal cortex, which is also strongly linked to memory (e.g., [18,24,25]). Further, lateral parietal cortex is heterogeneous, composed of a mosaic of distinct functional areas, each with its own pattern of connectivity and each with its own functional response profile during memory tasks ([26–29], but see also [11,30]). The network we highlight in this report consists of both medial and lateral parietal regions that are involved in multiple stages of memory processing. Identification of this small collection of regions, and the claim that they form a functional network, emerged from two distinct analysis approaches, described below.

### Three parietal regions consistently support memory functioning

Meta-analyses identify regions most consistently associated with a condition of interest, and allow trends across many studies to emerge over the peculiarities specific to any individual dataset. Meta-analyses of encoding- and retrieval-related effects have each implicated the precuneus (PCU), the mid-cingulate cortex (MCC), and the posterior inferior parietal lobule/dorsal angular gyrus (pIPL/dAG; Figure 1). The MCC region would be characterized by some as ‘posterior cingulate cortex’, but we use the term MCC to help differentiate it from the adjacent, well-known posterior cingulate regions reported in other contexts (e.g., [31,32]). The three regions are among those most consistently associated with retrieval success.

![Figure 1. Task-based and functional connectivity descriptions of a parietal memory network.](image)

Task-based meta-analytic descriptions

- Kim (2013) - 48 studies
- Nelson et al. (2010) - 7 studies
- McDermott et al. (2009) - 18 studies
- Kim (2011) - 11 studies
- Otten and Rugg (2001) - 2 studies

Connectivity-based network descriptions

- Human connectome project (2013)
- Shirer et al. (2012)
- Yeo et al. (2011)
- Power et al. (2011)
- Doucet et al. (2011)

Remaining maps are adapted from [33,36-38] with permission from Elsevier and the American Physiological Society.
They also exhibit negative subsequent memory (nSM) effects [16,33,34]. In summary, these three regions reflect mnemonic processing during both initial encoding and later retrieval. They are distinct from other regions in this regard.

A converging stream of analysis leads to the conclusion that these three regions form a functional network. Researchers have begun to uncover the functional network structure of the human brain using resting-state functional connectivity MRI (RSFC MRI) (e.g., [35–39]). RSFC MRI represents a paradigm shift in neuroimaging; instead of manipulating variables during a cognitive task, RSFC MRI permits the subject to engage in undirected thought. Analyses utilize low-frequency (<0.1 Hz) correlations across the cortex, present even in the absence of explicit task conditions, to estimate functional relationships between cortical regions [35,40]. Numerous RSFC analyses converge on a network consisting of PCU, MCC, and pIPL/dAG that is distinct from nearby networks (Figure 1, right), such as the default mode network (DMN), which sits adjacent to all of the regions of this novel network. The PCU, MCC, and pIPL/dAG network and adjacent DMN also show different connectivity profiles across the human lifespan, reinforcing the distinction between these adjacent networks (41); see Box 1 for further discussion). One recent RSFC MRI analysis highlighted this network as one of unknown function [37], although it was tentatively linked to memory (see also [40]).

To reiterate, meta-analyses of the memory literature point to the contribution of these three regions in memory encoding and retrieval, and RSFC analyses demonstrate that the regions form a functional network. We will refer to the network as the ‘parietal memory network’ (PMN). Below we consider other recent task-based memory studies to highlight the characteristic patterns of this network that speak to its distinct functional profile.

**nSM effects**

nSM effects are observed at encoding when less activity within a region is associated with a higher probability of later item recognition or recall. Such effects tend to come in two forms: regions are either more active, relative to baseline, for subsequently forgotten items than for subsequently remembered items, or else they show greater deactivation, relative to baseline, for the successfully remembered items. PMN regions, as well as some DMN regions, show the latter pattern [42–44].

What can be made of nSM effects? Several resource-allocation accounts have been forwarded. Regions displaying greater positive activity for forgotten items may reflect inefficient stimulus processing for those items [33]. Regions that show greater deactivation for remembered items than for forgotten items may reflect more effective neural resource allocation for the subsequently remembered items elsewhere in the brain [42]. The latter hypothesis was specifically proposed to explain the nSM effect in DMN regions because many of its member regions show nSM effects [45,46].

In this review we suggest that the degree of deactivation within the PMN is indicative of the relative novelty of a stimulus within the experimental setting (rather than its absolute novelty or familiarity across the lifespan). As we

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**Box 1. Resting-state functional connectivity (RSFC) MRI**

Task-evoked fMRI measures changes in the blood oxygen level dependent (BOLD) signal as a result of discrete, task-induced events (e.g., reading a word, remembering an event). Nonetheless, much of the variability in the BOLD signal remains unaccounted for by such task-manipulations. RSFC MRI takes advantage of this variability, previously considered to be noise, as a source of information relating to functional brain organization [75,76].

For example, examination of the time course of task-independent spontaneous BOLD fluctuations has revealed that, as left motor cortex activity spontaneously waxes and wanes, so does activity in right motor cortex [35]. That is, brain regions that tend to coactivate during directed tasks exhibit synchrony in their spontaneous firing.

Consider the following scenario, which describes an RSFC analysis at its most basic level. A person lies still for a 15-min period of ‘rest’ while undergoing MRI (i.e., without any overt task, other than to lie still and remain awake). We now choose a region of interest and plot the BOLD signal across the 15-min period. Using that temporal pattern as a regressor reveals other brain regions that exhibit similar temporal activity patterns.

Variations of this method have been utilized to map out the network structure of the entire brain (e.g., [36–38,71]). The methods have been validated in part by the observation that known brain networks are revealed with these methods (e.g., the motor system). Another prominent example is the default mode network (DMN), a set of regions first defined by the observation that they deactivate when participants are engaged in externally oriented, attention-demanding tasks of many types [77]. The same regions (located within medial and superior frontal cortex, ventral angular gyrus, posterior cingulate, and lateral temporal cortex) exhibit synchrony in their resting-state signals [36–38,46,78]. As discussed in this review, PMN regions deactivate during initial encoding. Because deactivation is a prominent characteristic of the DMN, one might wonder if the PMN is a part of the DMN. RSFC analyses (and, as we will discuss, other types of task-related activity) reveal that the two networks are distinct. In Figure I in this box we plot the PMN and DMN on a common surface [74], as defined by task-induced fMRI [20] and by RSFC, from a dataset analyzed using an independent components analysis [39]. Regions of the PMN flank members of the DMN, but the networks are distinct.

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**Figure I.** (A) RSFC MRI consists of tracking the BOLD signal within a specified brain region across a period of awake rest, and then identifying other regions with temporally correlated spontaneous activity. (B,C) Both task-based and RSFC MRI analyses demonstrate that the DMN (cool colors) and the PMN (warm colors) form distinct networks. Task data were originally reported in [76] (DMN) and [20] (PMN), and RSFC data were reported in [39]. Maps were generated by projecting original data onto Connectome Workbench surfaces.
shall discuss, greater novelty may elicit more extensive and elaborative processing (and thus, on average, better subsequent memory) of particular items as compared to other items. This hypothesis has the additional benefit of providing a putative mechanism by which the resource-allocation accounts might operate.

**Repetition enhancement and the encoding/retrieval flip**

As stimuli are experienced repeatedly, regions of the PMN show repetition enhancement, which refers to an increase in neural activity with repetition of a stimulus or set of stimulus features [47]. Repetition enhancement is the reverse of the more commonly discussed repetition suppression (also termed neural priming) in which activity attenuation occurs in response to repeated stimulus presentations [48–50].

One example of PMN regions exhibiting repetition enhancement is depicted in Figure 2. During a paired associate learning task, activity increased in each of the PMN regions between an initial and a subsequent encoding period [20]. Further, the degree of enhancement was moderated by specific item history. At the time of final encoding, items that had been studied twice by participants exhibited less of an increase than did items that had been studied three times, and these in turn demonstrated less of an increase than did items for which the participants had practiced retrieval between encoding sessions. Thus, factors other than mere re-exposure can affect repetition enhancement in the PMN.

Several hypotheses have been proposed to account for repetition enhancement effects, but different causes may exist for the effect in different regions of cortex [47], and no consensus has emerged. Notably, some have argued that repetition enhancement may reflect the formation of a memory representation [51]. The repetition enhancement observed within PMN regions may thus be viewed as an indication of the progression of an item from novel to familiar.

The repetition enhancement effect observed within PMN regions shows a distinctive property: a change from deactivation during initial encoding conditions to above-baseline activation after repeated exposure to a stimulus [i.e., a flip in the direction of the BOLD (blood oxygen level dependent) response]. This ‘encoding/retrieval flip’ about baseline has been reported across multiple studies that focus on lateral and medial parietal cortex [52–55], although some uses of the term refer to a pattern different than that discussed here [43] (Box 2). Several factors appear to modulate the degree of deactivation and activation during encoding and retrieval (alternatively, during initial study and re-exposure to specific stimuli). One factor, already discussed, is the experiential history of an item–retrieval practice, and increasing repetitions can increase the positive activation levels observed (Figure 2). In addition, encoding/retrieval flips have been observed even within a single trial [17]. While viewing scenes, participants showed encoding-related deactivation of the regions similar to those in the PMN; after each encoded scene, subjects were cued to remember or forget the previously viewed item. When cued to remember, a within-trial flip was observed in PMN-like regions, whereas those cued to be forgotten did not demonstrate such a

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**Figure 2.** Regions within the parietal memory network (PMN) show trialwise repetition enhancement effects, and ‘flip’ about baseline. BOLD activity within PMN regions increases across multiple presentations of an item, and flips from initial deactivation to subsequent activation. Figure labels: ‘Initial encoding’ represents initial exposure to an item; ‘Final encoding without restudy’ indicates a second item exposure; ‘Final Encoding with Restudy’ indicates a third item exposure; and ‘Final Encoding after test’ indicates that participants initially studied an item, had their memory for it tested, and were given a restudy opportunity. Figure adapted from [20] with permission from the Society for Neuroscience.
Box 2. Disambiguating the ‘encoding/retrieval flip’

The term ‘encoding/retrieval flip’ has been used to describe several different trialwise effects in lateral parietal and posteromedial cortex. Different meanings of the phrase constrain it to different regions of parietal cortex. Both the proximity of the neuroanatomy associated with distinct meanings of the term, and the similarity with which they are discussed (and even plotted), can lead to confusion between, or conflation of, the definitions. We spotlight here the differences that exist between meanings of the term in the literature.

One definition of encoding/retrieval flip (adopted in the present manuscript) refers to the direction of the BOLD response relative to resting baseline [52,54,55]. In the PMN, deactivation occurs during encoding trials, and activation occurs during retrieval trials. Although the use of resting baseline remains a matter of ongoing debate (we refer readers to [79–83] for in-depth treatment of the subject), we note that this definition has an advantage over the one discussed below, in that it better distinguishes the PMN from the DMN. Both networks show encoding-related deactivations, but the retrieval-related response properties within PMN regions are distinct from those observed in the posterior cingulate cortex or AG (Figure 1, top). Instead, the regions showing this form of the encoding/retrieval flip are fairly limited, and they align very closely with the PMN as defined using other methods (cf. Figure 1 and Figure I).

An alternative meaning of the encoding/retrieval flip, forwarded by Daselaar and colleagues [43], describes regions that show different relationships between hits and misses at encoding and retrieval. Specifically, Daselaar and colleagues used the term to describe regions showing more trialwise activity for hits than for misses during retrieval, but less activity for items subsequently remembered (hits) than for those subsequently forgotten (misses) during encoding. That is, this definition relies on the direction of the relative difference between hits and misses (which flips between encoding and retrieval), without respect to the direction of the BOLD response relative to baseline (Figure I, bottom). The functional neuroanatomy of this effect appears to shift across task conditions, and is associated with a much broader expanse of cortex than is the alternative definition of the encoding/retrieval flip.

Each of the definitions of the encoding/retrieval flip is therefore distinct. We look forward to future research being conducted in which the relative merits of each definition can be better understood and appreciated.

![Trialwise activity relative to baseline](image)

**Figure 1.** Two distinct ‘encoding/retrieval flips’. (Top) In one definition, the direction of encoding- and retrieval-related activity is relative to a resting baseline. Deactivations are present at encoding, and activations are present at retrieval (e.g., [54]). (Bottom) The alternative definition relates to the direction of the difference in activity between hits and misses. At the time of encoding, items later recognized (hits) are accompanied by less activity than are items that are later forgotten (misses) (e.g., [43]), whereas during retrieval hits are associated with more activity than are misses. The two definitions isolate different parts of cortex, and should not be confused across different empirical studies or reviews. Figures are adapted from [43,52] and [43], respectively, with permission from Frontiers and Elsevier.

flip. Further research will need to clarify the relation, if any, between these flips and those observed in experiments with distinct encoding and retrieval phases (e.g., [20,52–55]). Finally, age-related attenuations in the level of initial deactivation and later activation have been observed across regions in posteromedial and lateral parietal cortex, which appear to coincide with the PMN described here [55].

**Retrieval-success effects as a form of repetition enhancement**

PMN regions activate more for hits than for correctly rejected lures in recognition memory. This pattern can be considered a form of repetition enhancement in that the hits, which are repeated items, show greater activity than do novel lures, which are seen for the first time.
Although other brain regions can show retrieval-success effects, the PMN appears to be unique in that its retrieval-success effects show this pattern of repetition enhancement largely irrespective of task conditions. Retrieval-success effects in other brain regions appear to be sensitive to experimental manipulations, and can disappear with some task demands [56,57]. In addition to consistently showing enhancement effects, it appears that the response in PMN regions scales with the familiarity of the items and with confidence of one’s decision during retrieval, rather than being a single, static response [6,8,58].

A preliminary functional account of the PMN

Based on extant data, we forward a preliminary hypothesis of the functional role of the PMN. Many theories have been proposed to explain parietal lobe contributions to memory, and we consider how the PMN may fit with these explanations in Box 3. We offer an alternative hypothesis below, specific to the PMN, which we argue best captures that which is presently known about the network.

Deactivations within the PMN signal novelty.

A parsimonious account of the response properties we have highlighted in PMN regions is that they reflect the perceived familiarity of a stimulus (Figure 3). During initial stimulus presentation, deactivations are indicative of the novelty of a specific stimulus within the context of the experimental setting. In this account we consider novelty to be the same as a lack of familiarity, although we recognize that there is some discussion as to whether novelty and familiarity represent a single continuum or are distinct from one another [59–61].

Further, the amount of deactivation is predictive of later memory performance for a given stimulus. As mentioned previously, nSM effects are typically couched in terms of resource allocation, and here we hypothesize that differential resource allocation may be driven, at least in part, by the degree to which a stimulus is perceived as novel. It is not clear what properties of a stimulus are responsible for making it more or less novel (e.g., if specific perceptual features are important), or if factors external to a given stimulus may influence this perception (e.g., the task set for the participant). This issue will need to be addressed in later work.

Activations during retrieval reflect previous experience with a stimulus

In the same way as deactivations are hypothesized to reflect a lack of perceived familiarity with a stimulus, activations indicate that an item is subjectively

Box 3. Do other prominent theories of parietal function speak to PMN processing?

Numerous hypotheses link parietal cortex to memory functions, but none of them predict the pattern of activity observed within PMN regions, nor do they predict the specific regions comprising the PMN. In Table I below, prominent hypotheses and their relation to the PMN are reviewed. It cannot be overstated how crucial it is to define the anatomical space in which these theories are explored because it is likely that different descriptions arise from distinct brain regions within a cortical expanse [84].

Table I. Prominent hypotheses and their relation to the PMN

<table>
<thead>
<tr>
<th>Hypothesis</th>
<th>Nature and discussion of agreement and disagreement with our account of the PMN</th>
</tr>
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<tbody>
<tr>
<td>Attention to memory/ bottom-up attention (AtoM/BUA) [11,86]</td>
<td>(i) Both AtoM and BUA emphasize the importance of attention in activity related to parietal memory function. (ii) Our description of the PMN relies heavily on attentional capture by novel and familiar stimuli.</td>
</tr>
<tr>
<td>Primary difficulty: anatomy</td>
<td>(i) iPPL/dAG sits at the confluence of putative superior parietal (‘top-down’) and ventral parietal (‘bottom-up’) attention regions. AtoM/BUA do not offer clear predictions of the behavior of this region. (ii) AtoM explicitly considers PMC to be a ‘top-down’ region, but evidence we describe here suggests that it supports largely bottom-up processing. (iii) Neither AtoM nor BUA discuss MCC or make predictions as to its information processing role.</td>
</tr>
<tr>
<td>Attention to internal representations [10]</td>
<td>Emphasizes the importance of attending to internal memory representations, which our description of the PMN shares.</td>
</tr>
<tr>
<td>Primary difficulty: E/R flip</td>
<td>Does not easily accommodate deactivations present during encoding because these would presumably also require attentional shifts related to memory search processes.</td>
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<tr>
<td>Mnemonic accumulator [10]</td>
<td>(i) Assumes that recognition decisions, such as perceptual decisions, are based upon an accumulation of ‘evidence’ over time. (ii) As a familiarity signal becomes stronger across multiple repetitions, an accumulator would integrate the signal more quickly. (iii) This is consistent with the repetition enhancement effects observed in PMN regions. (iv) If novelty is processed as ‘negative evidence’ then this explanation could account for initial deactivation, although we acknowledge that this assumption would require explicit testing.</td>
</tr>
<tr>
<td>Primary difficulty: anatomy</td>
<td>This explanation is inspired by monkey area LIP. While iPPL/dAG sits adjacent to IPS (a potential homolog to LIP [86]), this hypothesis does not account for PCU or MCC activity.</td>
</tr>
<tr>
<td>Output buffer [10]</td>
<td>This account suggests that regions of parietal cortex may act as a ‘working memory’ buffer for mnemonic information. Does not readily predict any specific aspect of the data we have reviewed here.</td>
</tr>
<tr>
<td>Primary agreement: none</td>
<td>In the same way as this account does not anticipate the data discussed in this review, they are not disconfirmed either.</td>
</tr>
</tbody>
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Review

Hypothesized processing within the parietal memory network

Increasing novelty
Increasing familiarity
Greater attentional capture

Figure 3. A schematic model of parietal memory network functioning. Activity within parietal memory network regions is diagnostic of the perceived familiarity of a stimulus. Novel (unfamiliar) items elicit deactivations, whereas familiar items elicit activations above resting baseline. Stronger deviations from baseline are associated with items that are perceived to be more novel, more familiar, or that more strongly capture one’s attention.

experienced as familiar. If, during the encoding or processing of an item, its properties match a representation in memory, this familiarity signal is manifested as activation within PMN regions (PMN regions need not be directly involved in the decision-making process, but may be situated either upstream or downstream of it). By this account, greater activation is indicative of a stronger familiarity signal that more readily captures one’s attention. This suggestion is consistent with reports indicating that PMN regions show greater activity for high-confidence, relative to low-confidence, familiarity judgments [6], and show a fairly linear decrease in activity from items strongly perceived to be old, to those strongly perceived to be new [58]. It is also consistent with prior observations that regions associated with the processing of familiarity include the PMN (e.g., [62]).

PMN activation may not always involve an intentional retrieval attempt. Consider again Figure 2, depicting data from [20]. In this experiment robust activation was observed during a final restudy period. The authors noted in this paper that the time-courses of the BOLD response during initial study and restudy matched those observed for new and old items (respectively) in recognition memory studies. This finding is consistent with the account that it is the novelty or familiarity of an item, rather than the explicit task conditions, that elicit deactivations and activations in PMN regions. Of course, it is also possible that the strong familiarity of restudied items may have triggered a retrieval attempt or an involuntary recollection (possibilities raised by the authors); this finding exemplifies the difficulty in cleanly separating encoding and retrieval processes [17,20,63].

Other recent work has shown that activity in pIPL/dAG and other regions corresponding to the PMN can be influenced by the degree to which the familiarity of an item captures one’s attention. In situations where participants are cued to expect a new item during a recognition memory task, and are instead shown a studied (i.e., familiar) item, greater pIPL/dAG activity was observed than in situations in which participants were cued to expect a familiar item and were subsequently presented with one [64]. That is, expectation violations in the form of unexpected familiarity can increase activity. Future work will need to examine the generality of this effect.

Outstanding questions and future directions

We have offered a preliminary process-level account of the PMN, and many questions still exist regarding the specifics of its functional properties. We identify a few such questions below.

To what extent is PMN activity reflective of bottom-up processing?

Although PMN activity is related to item familiarity, the extent to which external factors can influence activity within the network is unclear. Do the patterns we have reviewed here reflect bottom-up processing, top-down processing, or both? Beyond the effects of item cuing during explicit retrieval conditions [64], the evidence we have reviewed suggests that PMN processing is largely bottom-up in nature. One might address this question by determining if PMN regions show their signature encoding/retrieval flip when stimuli are experienced subliminally. Observation of the flip in response to stimuli that are perceived at a level below conscious awareness would speak strongly to ‘automatic’ processing driving activity in PMN regions (admittedly, implementation of this idea would be challenging). Alternatively, one could observe PMN activity in tasks that involve repeated presentation of stimuli in an orthogonal task, as might be done in a standard repetition priming paradigm. In either case, bottom-up and top-down processes likely interact, and a clean separation of these issues will therefore be difficult.

Does degree of initial deactivation predict degree of later activation?

We have reviewed evidence that PMN regions show nSM effects and retrieval-success effects. Further, across groups of people who differ in memory performance (e.g., younger and older adults), better memory performance is associated with greater initial deactivation and greater subsequent activation [55]. However, we do not yet know how tightly linked the degree of initial deactivation at encoding is to the level of later activation upon re-exposure to an item. Based on the nSM effects we have described, one might expect that (other factors being equal) greater deactivations for a specific item should lead to greater activity for the same item at a later time. Alternatively, one might posit that the probability of an item being recalled may be reflected in (though not necessarily causally driven by) the difference between activity related to the encoding of the item and activity observed for the same item during a later retrieval attempt. This latter case does not require reference to any specific baseline, and simply asks if the interaction between presentations carries predictive utility. To
our knowledge, no published data speaks to this issue at either the item level or across individuals. A similar question might be asked (even within existing datasets) by comparing the differences between encoding- and retrieval-related activity for deeply and shallowly encoded items (i.e., one could manipulate the depth of processing across items [65,66]). Prior literature suggests that parietal regions can show different activation patterns at retrieval based upon the encoding history of an item (e.g., [67]), but to our knowledge no experiment has specifically examined the regions we highlight here.

**How susceptible are PMN regions to false memory effects?**

Given the hypothesized PMN functions we have forwarded here, one may ask how PMN regions behave in false memory situations. For instance, the DRM paradigm [68] is known to elicit very strong illusions of having seen specific words (e.g., ‘sleep’) when people are presented with lists of highly associated items (e.g., bed, rest, awake, etc.). Similarly, after studying categorized lists, people are very likely to false alarm to highly typical, but unstudied, exemplars from that category (e.g., one may falsely, yet confidently, recognize ‘carrot’ after studying a list of vegetables, even though that word was not presented [69,70]). How do PMN regions respond in these cases? Because the target stimulus has not been presented, one might expect deactivations within PMN regions (particularly if they operate on perceptual information). However, given that the lure items are typically perceived to be old, we can hypothesize that PMN regions show robust activations rather than deactivations. Knowledge of how PMN regions respond in DRM-like conditions would provide important insights into the information being processed in these regions [21,68].

**Are laterality effects present in PMN?**

We have focused on PMN regions within the left hemisphere. However, functional connectivity descriptions suggest that the PMN is bilaterally present (e.g., [36–38,71]). The MCC region falls along the midline, but the PCU appears to sit far enough from the midline to potentially show laterality effects, and certainly effects might be observed in the pIPL/dAG region. Given the robust left/right hemisphere differences that are known to exist for verbal and non-verbal materials [72,73], one might ask if hemispheric differences exist within the PMN as well, and, if so, to what degree.

**Concluding remarks**

Investigation of the network structure of the human brain is moving at a rapid pace, and the identification of the PMN represents one especially exciting outcome of this research. Its characteristic flip about baseline for novel and familiar items suggests that it has a unique role in learning and memory. Despite showing task-induced deactivations in particular contexts, it is a sparse but reliably observed network that is distinct from the adjacent DMN, with distinct functional properties. Improved knowledge of the PMN will provide us with several pieces to the puzzle that is the role of parietal cortex in human memory function, and to the broader question of how we can readily distinguish between novel and familiar objects in our local environments.

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