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Article in *Trends in Cognitive Sciences* · May 2017

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Review

Neurobiology of Schemas and Schema-Mediated Memory

Asaf Gilboa^{1,2,3,*} and Hannah Marlatte^{1,2}

Schemas are superordinate knowledge structures that reflect abstracted commonalities across multiple experiences, exerting powerful influences over how events are perceived, interpreted, and remembered. Activated schema templates modulate early perceptual processing, as they get populated with specific informational instances (schema instantiation). Instantiated schemas, in turn, can enhance or distort mnemonic processing from the outset (at encoding), impact offline memory transformation and accelerate neocortical integration. Recent studies demonstrate distinctive neurobiological processes underlying schema-related learning. Interactions between the ventromedial prefrontal cortex (vmPFC), hippocampus, angular gyrus (AG), and unimodal associative cortices support context-relevant schema instantiation and schema mnemonic effects. The vmPFC and hippocampus may compete (as suggested by some models) or synchronize (as suggested by others) to optimize schema-related learning depending on the specific operationalization of schema memory. This highlights the need for more precise definitions of memory schemas.

What Is a Memory Schema?

During development humans establish large-scale knowledge systems that continue to develop throughout life [1,2]. These knowledge structures are intuitively drawn on to interpret ongoing reality and to determine appropriate actions, so much so that it has been argued that children see only what they already know, projecting their thought schemas into things [1]. Schemas also greatly influence how new information is encoded, retained, and later retrieved. The idea that cognitive schemas influence how memory is constructed and reconstructed has a long history in cognitive psychology [3]. Curiously, however, only recently has the neurobiology of memory schemas been tackled systematically [4–10].

Schemas are higher-level knowledge structures that organize lower-level representations from long-term memory. They serve as general-form reference templates against which new information can be compared, binding multiple features that consistently co-occur; their elements are nonspecific, reflecting commonalities among experiences, and have considerable overlap and interconnectedness [1,3,10]. Importantly, schemas are dynamic structures constantly evolving with new experiences and memories [3] through processes dubbed **assimilation** (see [Glossary](#)) and **accommodation** [1,10].

The recent neuroscience literature has used the term schema rather loosely to refer to relevant mental and neurobiological prior associative networks that influence new information processing [8,9], a definition that matches multiple forms of prior knowledge ([Box 1](#)). The present review therefore adopts an inclusive approach to schema definition, also because many of these forms of prior knowledge are important components of schemas as classically defined ([Figure 1](#)). These subcomponents are likely to share neurobiological processes with richer, more complex

Trends

Similar but discernible neural networks mediate schema instantiation and schematic influences on mnemonic functions, be it enhancement of or interference with accurate memory acquisition.

Schema networks include the ventromedial prefrontal cortex (vmPFC), hippocampus, angular gyrus, and posterior cortical regions, although schema instantiation may engage more ventral parts of the vmPFC and more widespread cortical structures.

Schema instantiation appears to involve earlier processes than schema-mediated mnemonics and possibly sustained activity across the network.

Mutual inhibition may exist between vmPFC-centered and hippocampus-centered mnemonic processes under conditions of very strong schematic influences or no prior knowledge, respectively.

Moderate degrees of prior knowledge may lead to vmPFC–hippocampal interaction to resolve overlapping associations and their relevant contexts.

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Box 1. Types of Prior Knowledge

Multiple forms of prior knowledge bear substantial resemblance to schemas. Certain definitions equate these forms with schemas [8,9]; others consider them the building blocks of schemas and highlight important distinctions that arise from schemas' superordinate properties [10].

Narratives and Event Gists

Narratives are accounts of connected events that unfold over time, often according to causal principles. Like schemas they are organized as associative networks. Unlike schemas narratives can be encoded in a single episode rather than extracted over multiple experiences and have (see Figure 1C in main text) relatively fixed, rather than adaptable, structure and unit details [75]. Event gist is a related term referring to high-level central elements that are critical to the overall storyline coherence, as opposed to low-level details whose omission would not alter the event essence [23,76]. Neural networks of narrative comprehension and gist extraction are similar and involve the dorsal (but not the ventral) mPFC, the left IFG, the posterior STS/TPJ, the bilateral anterior temporal cortex, and midline posterior cortices [75,77]. vmPFC recruitment during gist extraction could reflect schema reinstatement when relevant preexisting schemas serve as scaffolds for interpretation of the gist of specific events (e.g., for highly typical events; see Figure 1B in main text).

Concepts and Categories

Categories have an associative network structure of related concepts and their linked defining features that determine a concept's membership of a category [26,27,78,79]. Defining features, rather than the associative relationships between the nodes of the network, are what determines memberships (e.g., that mammals have fur) and therefore categories tend to be less flexible and adaptable than schemas [10], although they can hold exceptions as anomalies (e.g., the naked mole-rat). Conceptual knowledge is a critical part of most schemas and they are likely to share posterior neocortical structures, but the ATL and TPJ are considered conceptual knowledge hubs [26,27] and critically support the integration of new information into conceptual knowledge networks [67,68,71,80,81].

Statistical Regularities

This often-implicit knowledge involves the detection and extraction of recurrent patterns of stimuli and their interrelationships [82–86]. Like schemas they possess an associative network structure, are based on multiple episodes, and are sensitive to chronological organization. Most **statistical-learning** studies focus on repetition within a limited perceptual dimension and require a simple motor response, limiting the capacity of the information to be updated in response to environmental changes. However, enriching the learning context by varying stimulus characteristics and their associated motor outputs results in dynamic knowledge structures that allow the correct interplay between specificity and flexibility [87]. Learning statistical regularities involves local computations in modality-specific cortices coupled with multidomain contributions from the MTL/hippocampus, basal ganglia, and thalamus [86].

superordinate cognitive structures; whether the difference between these is qualitative or merely quantitative is currently unknown.

How Prior Knowledge Is Organized into Schemas in the Brain

Most neuroscientific studies of memory schemas focus on the way their presence influences the acquisition of new information. Much less direct attention has been devoted to schema representations themselves, how they are acquired, stored, and retrieved or **instantiated** to support the multitude cognitive processes for which they are required, and how they are modified as a result of new learning.

Acquisition

Controlled experimental investigation of acquisition or accommodation [1] of large-scale knowledge systems is challenging because constructing these schemas can take years [2]. Some studies attempted schema acquisition designs to examine the influence of pretrained knowledge on the learning of new associations in controlled settings. Several studies extensively trained participants on experimental stimuli (e.g. [11–13]) or followed the acquisition of large-scale knowledge in naturalistic academic environments [14,15]; these studies, however,

Glossary

Accommodation: occurs in conjunction with assimilation; involves adapting existing schemas to take into account new related information and is at the heart of the idea that schemas are essentially active knowledge structures.

Angular gyrus (AG): located in the inferior lateral parietal lobe, posterior to the supramarginal gyrus; a heteromodal part of the TPJ surrounding the parietal extension of the STS corresponding to Brodmann area (BA) 39. Within semantic memory the AG supports the integration and retrieval of supramodal complex knowledge, such as the integration of single concepts into large wholes, consistent with schemas. It is highly developed in humans and almost missing in other primates. The AG is connected almost entirely with other associative areas.

Assimilation: the active process of adapting new external information to fit with internal cognitive structures or schemas. Individuals may apply any mental structure available to them to assimilate a new event.

Concept: a mental representation denoting a class of items or entities that belong to a particular category; often conceived as a hierarchy with superordinate, basic-level, and subordinate levels of specificity.

Gist: refers to high-order elements of a narrative or a memory that if omitted or changed would substantially alter the meaning of the storyline. Note that while schemas are typically detail-rich and highly elaborate cognitive structures, a gist is a representation of a single episode that is stripped of much of its detailed information.

Schema instantiation: the process of matching input from ongoing reality into activated schema 'variables', reflecting the manner in which activated schemas may bias information processing from the input stream.

Schema-linked interactions between medial prefrontal and medial temporal regions (SLIMM): a competition-based model accounting for the roles of the vmPFC and MTL in schema-mediated mnemonic functions.

Schema reinstatement: the process of activating and sustaining a prototypical, abstracted 'template'

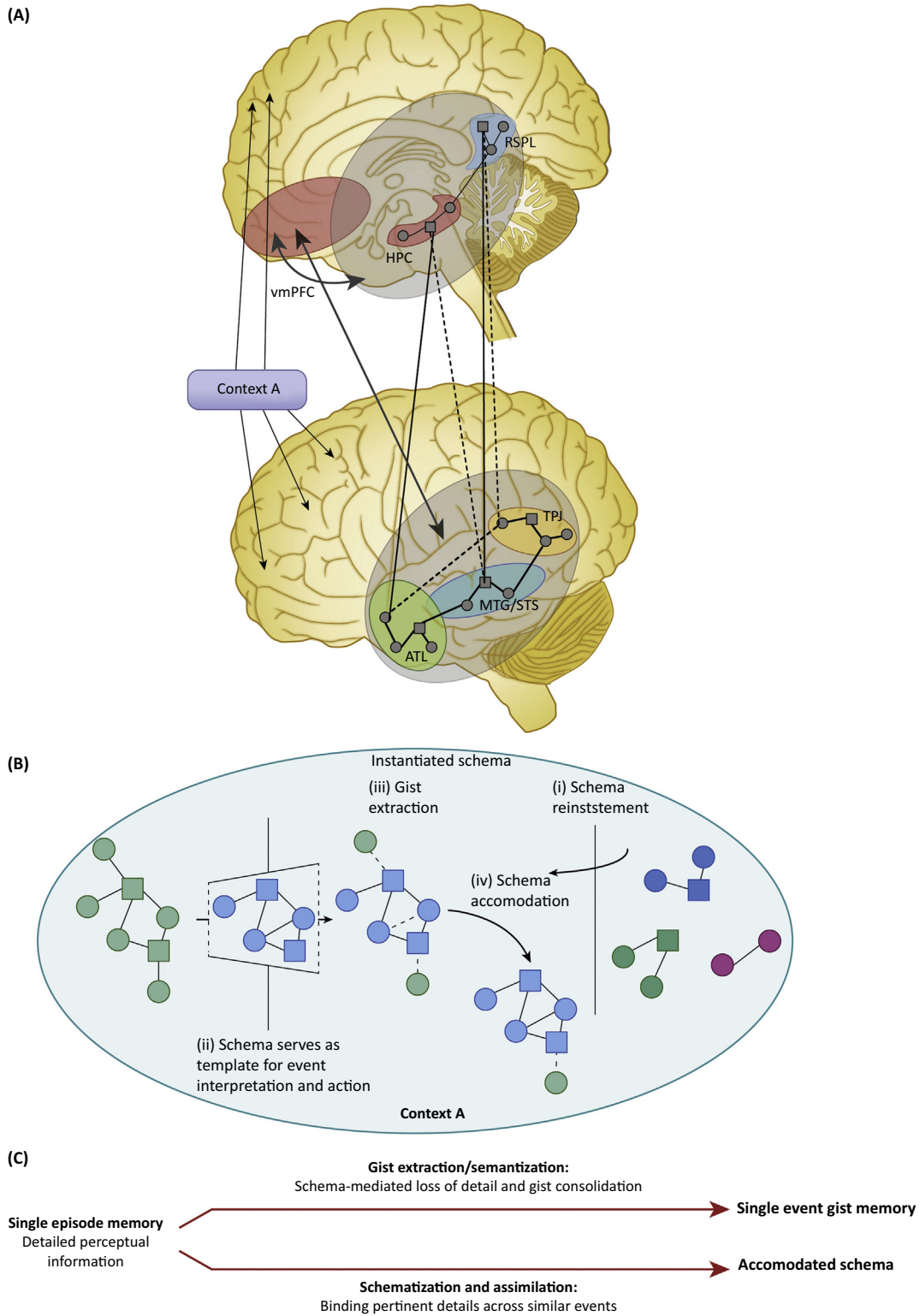


Figure 1. Hypothetical Functional Neuroanatomical Model of Memory Schemas. (A) Memory schemas are coactivated long-term representations in the posterior neocortex [e.g., retrosplenial cortex (RSPL), middle temporal gyrus (MTG)/superior temporal sulcus (STS), anterior temporal lobe (ATL), temporoparietal junction (TPJ)]

(Figure legend continued on the bottom of the next page.)

Box 2. Animal Studies

Human studies on the neurobiology of schemas were inspired by animal work that either directly or indirectly addressed similar questions [4–6,17,54–57]. In a series of landmark studies, rats were exhaustively trained on a set of flavor–place PAs within an ‘event arena’ that was accessed from various directions [4–6,17]. The schema comprised the shared spatial set of trained PAs. Novel schema-congruent PAs could be acquired rapidly and, surprisingly, became hippocampal-independent within 48 h [4], much faster than typical learning, suggesting that rapid learning-induced neocortical plasticity is possible when new information is embedded within an existing schema [4,6,17,88]. The nature of schematic representations within the hippocampus was highlighted by a second approach probing how related memories are represented electrophysiologically [41]. Rats learned to associate locations with rewarded and unrewarded objects, but reward contingencies for the same objects were context dependent and no single location within a context predicted reward. Using representational similarity analysis of neural activity, a hierarchical structure emerged, with context demonstrating anticorrelated activity patterns (suggesting pattern separation) while position, valance, and item identity showed increasing similarity (overlapping) of patterns [41]. Interestingly, when new items were learned within previously learned contexts, the hierarchical schema structure was immediately evident, demonstrating how prior knowledge rapidly influences hippocampal neural code during new learning. According to this view, neural networks within the hippocampus are critical for initial schema encoding and for integrating related features of distinct memories into an organized context-sensitive representation. This integration involves persistent recruitment and modification of widespread synaptic circuits [89] and of firing patterns [62] with the addition of new information and depends on hippocampal dopamine receptor activation [5] and NMDA-dependent plasticity [88] at encoding. Once consolidated, schema storage and updating relies on neocortical areas like the anterior cingulate cortex (ACC) [6] and mPFC [17,85]. Specifically, NMDA and AMPA receptors in the ACC [6] (but not the hippocampus [88]) are required for schema updating and AMPA receptors for schema expression. Updating also involves the upregulation of immediate-early genes in prefrontal regions of the mPFC [17], which is critical for conflict resolution when incoming information is schema incongruent [85]. The consolidation process itself relies on the hippocampus supporting the rapid generation of an immature prefrontal memory trace during encoding that undergoes functional maturation with time [90]. Finally, the orbitofrontal cortex can also support schema-based learning by linking events based on reward value [91]; thus, different networks are involved depending on whether schemas are ‘context based’ or ‘value based’.

of the constituent properties and the interrelationships that define a typical instance of the knowledge structure it represents.

Statistical learning: the ability of an individual to detect environmental regularities and extract and retain these recurring environmental patterns.

Ventromedial prefrontal cortex (vmPFC): an ill-defined swath of cortex along the ventral medial part of the prefrontal cortex; typically refers to the subcallosal gyrus (BA25), the posterior medial orbitofrontal cortex (BA14, medial parts of BA11), and BA12 leading into medial parts of BA10. It has mostly been described with relation to decision-making, affective processing, and extinction learning but more recently also as a critical node in schema memory and memory monitoring.

typically do not track the neural signature associated with the acquisition and accommodation of the premise information itself.

Studies that have directly examined the dynamics of schema acquisition have: (i) trained participants on specific spatial arrays of object–location paired associates (PAs) [16] inspired by influential rodent studies of memory schema [4–6,17] (Box 2; cf. [12]); (ii) taught participants rule-based relationships [18] based on weather-prediction tasks; or (iii) had participants learn overlapping paired associations that allowed inference of an unlearned pair during the test [19–22] (we discuss these in the next section).

In one of the most intensive attempts to teach experimentally controlled new schemas, participants were followed over 9 months as they learned ten distinctive arrays of object–location PAs. Only some of the potential locations in each array were associated with objects, so that empty locations could later be trained in the context of old knowledge [16]. Tracking changes in representations of the premise PA structure took place on training days 1 and 2 and again after ~3 and ~6 months of training [16]. Consistent with prior research on time-

that are temporarily bound together by the ventromedial prefrontal cortex (vmPFC) to form a superordinate knowledge template. The schematic structure activated is context sensitive: specific associative pathways (unbroken lines) biased by the vmPFC reflect context-relevant information while other potential but contextually irrelevant associations (broken lines) are not activated or even inhibited. The hippocampus may interact with the vmPFC during schema instantiation or its activity could reflect memory assimilation and schema adaptation processes. (B) Schemas comprise prototypical sets of variables such as general concepts (represented by circles) and associated action scripts (represented by squares). (i) When a schema is reinstated or activated, these variables and their interrelationships serve as a template (ii) for the interpretation of incoming information that populates the schema nodes (instantiated schema). (iii) From the onset of encoding, schemas drive the process of gist extraction, in which inconsequential unique details or schema-incongruent components are weakened and eventually lost while connections for schema-congruent components are strengthened and the event gist is retained. Reiterative processes of gist extraction can ultimately lead to concept abstraction. (iv) Schemas themselves are not static: relevant schema-incongruent components can lead to a process of schema adaptation, and with repeated experiences new components can become assimilated into the existing schema or the existing connections can shift to accommodate the new information. (C) Memory transformation processes can lead to multiple forms of long-term representations such as gist (detail-poor) memory for a single event or a schematic representation that results from multiple similar experiences and that can be highly detailed but not unique.

dependent trace transformation [23–25] a shift from hippocampal to **vmPFC** representation was observed over the first night of training. However, by 3 months there was no evidence of vmPFC activity; instead, the ventrolateral PFC (vlPFC) coupled with the anterior temporal lobe (ATL) and the **AG**/temporoparietal junction (TPJ) was associated with retrieval of these highly over-learned PAs. Another study trained premise information comprising simple rules studied over 2 days of training [18]. Similar to the short delay findings from the spatial schema [16], retrieval of the premise rules after 24 h was associated with increased activity in the vmPFC, posterior cingulate, and higher-level sensory cortices [18]. Based on multivoxel pattern analysis (MVPA), the AG was hypothesized to serve as a convergence zone for low-level visual features and high-level decision rules that comprised the schema in that paradigm.

There is clearly a need for more rigorous investigation of the dynamics of schema acquisition. The data suggest similar patterns of brain activity as those described in the rich literature on semantization and **gist** extraction [23]. However, there is some evidence that more intense exposure results in a different neural signature that involved the vlPFC and ATL rather than the vmPFC, bearing similarity to semantic networks [26,27]. As discussed below, however, **reinstatement** of even highly learned schemas strongly engages, and even requires, the vmPFC. Perhaps when training involves repeated encoding of specific associations it results in denotational semantic representations. Schemas, however, involve highly variable abstract representations of both the nodes and their interrelations, and under these conditions the vmPFC and its interactions with posterior cortices could be necessary even when no specific episodic information is retrieved. Training protocols that capture the abstraction of commonalities across variable encoding episodes in combination with previous knowledge may result in structured, flexible symbolic representations. That is, rather than specific PAs or formal rules, training could involve the detection of statistical regularities but also be constrained by rational inference of relationships based on prior abstract knowledge and assumptions [2].

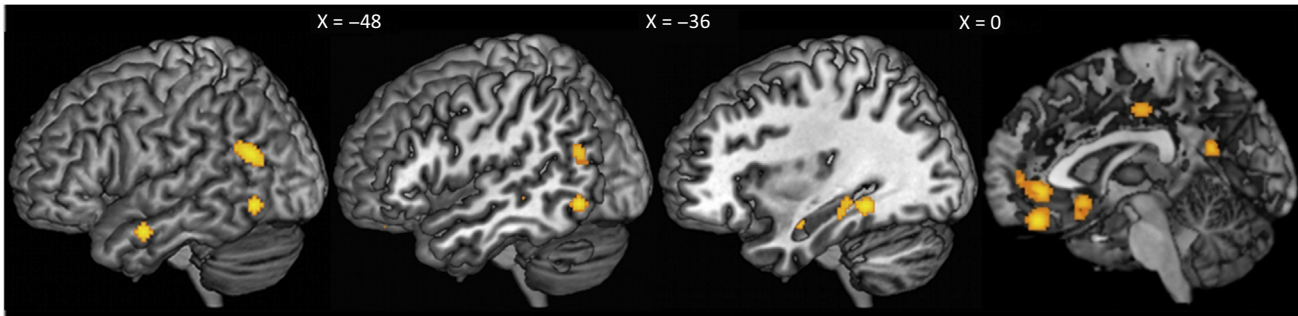
Schema Reinstatement and Instantiation

Cognitive and neurocognitive models suggest that schema reinstatement and instantiation [10,28–31]: (i) are mediated by interactions between the vmPFC and posterior neocortical structures with possible hippocampal contributions; (ii) influence processing of incoming information; (iii) exert their influence rapidly; and (iv) are sustained within a defined context (Figure 1). Several studies broadly support these ideas.

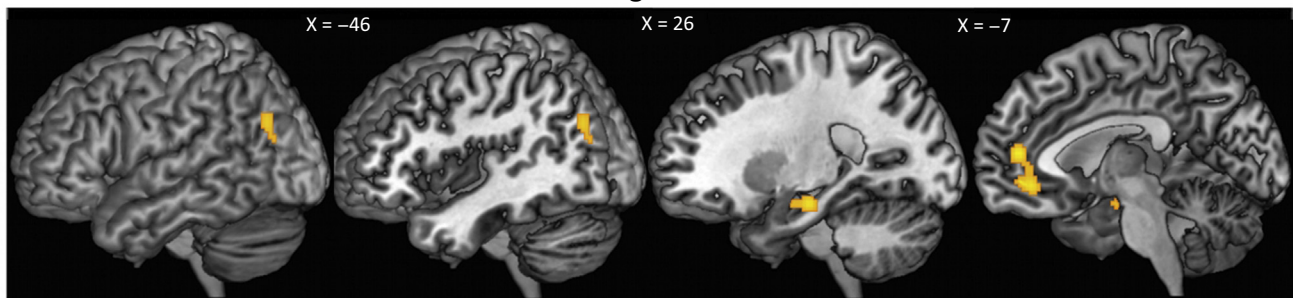
Human lesion studies have been central in demonstrating the critical roles of the parietal lobes and vmPFC in memory generally and schema memory in particular [32]. For example, lesion studies demonstrated that the right TPJ/AG is critical for extracting language-independent schematic iconic spatial relationships from richly textured visual representations in which they are embedded [33]. Similarly, a patient with severe perceptual deficits (simultanagnosia) following bilateral occipital damage (sparing the TPJ/AG) was better at matching concrete exemplars of spatial relations only when they could be directly compared with schematic iconic representations (abstracted analog forms) but not when compared with prepositions or with other exemplars [34]. Together these studies point to the TPJ/AG as critical for online processing of superordinate abstracted (visual) relationships.

Deficits in processing schema-related information online have more often been observed following vmPFC damage [35–37]. Patients with vmPFC damage and confabulation were impaired in making simple decisions on whether words (e.g., ‘receptionist’) were associated with common everyday schemas (e.g., ‘visit to doctor’s office’). Thus, even when memory is not challenged vmPFC lesions impair the process of maintaining an active schema as a template for processing incoming information [35]. Conversely, on the Deese–Roediger–McDermott false-memory paradigm [36,37] damage to the vmPFC protects against the normal false-memory

(A) Schema reinstatement and instantiation



(B) Schema-mediated new information encoding



Trends in Cognitive Sciences

Figure 2. Activation Likelihood Estimates (ALEs) of the Convergence of Activated Foci Reported in fMRI Studies of Memory Schema ($P < 0.001$; $>100 \text{ mm}^3$). (A) ALE maps for contrasts that reflect schema reinstatement and instantiation derived from 132 foci from 12 experiments (Table S1 in the supplemental information online). Significant clusters include the ventromedial prefrontal cortex (vmPFC) (left posterior medial orbitofrontal cortex, right anterior cingulate, and bilateral subcallosal gyrus), the bilateral anterior temporal cortex, the temporoparietal junction including the angular gyrus ($R > L$), the bilateral hippocampus, the fusiform/parahippocampal gyrus, the posterior cingulate, and the left posterior cingulate/retrosplenial cortex. (B) ALE maps for contrasts that reflect schema-related encoding of new information derived from 96 foci from 15 experiments (Table S1). Significant clusters include the bilateral anterior cingulate ($L > R$), the left ventrolateral prefrontal cortex, superior and inferior parietal lobules, and angular gyrus ($R > L$), and the right anterior hippocampus and parahippocampal gyrus.

phenomenon of recalling non-presented target lures (e.g., ‘sleep’) after encoding thematically related word lists (e.g., dream, slumber, tired). Presumably, patients fail to construct a meta-mnemonic thematic representation that could bias encoding and therefore target lures are not activated and memory is paradoxically more accurate. Similar effects were found in healthy controls following transcranial magnetic stimulation (TMS) targeting the medial PFC (mPFC) [38].

Several fMRI studies have demonstrated similar activity patterns when schema information is brought online (Figure 2A). In a series of studies using simple associative learning, participants studied triads of stimuli (e.g., ABC) where only two of the possible three associations are explicitly learned (e.g., AB, BC), such that knowledge of the third (AC) reflects associative inference [19–21]. Spontaneous reactivation of pre-established AB pairs, and hippocampal interactions with content-relevant neocortical modules, predicted later BC learning as well as inferred AC knowledge and their neural signatures [19]. In a later study, representational similarity analysis on individual A and C items before and after triad training was used to index the reinstatement of these mini-associative networks [20]. Because A and C are never explicitly trained together, this provides insight on schema-based memory integration [20]. Patterns consistent with memory integration emerged in the anterior hippocampus and posterior vmPFC but only when new, overlapping representations (BC) were acquired in the context of well-established prior knowledge (AB). As discussed below, this is consistent with models that focus on the vmPFC and schema functions [8,10,39,40] and with those that highlight

hippocampal contributions to schema formation through the combination of overlapping information across episodes [9,41–44].

Neuroimaging studies have also highlighted the role of posterior cross-modal cortices such as the AG [12,45–48] and of modality-specific cortices [21,46–48] in schema instantiation (Figure 2A). For example, the inferior occipitotemporal cortex ('fusiform face area') is implicated in schema representation when faces are central components within newly acquired mini-schemas [21], are associated with domain expertise [14], or contain rich pre-experimental knowledge [47]. Connectivity analyses demonstrate coactivation of these posterior neocortical structures with the vmPFC and hippocampus.

Electrophysiological investigations have begun to uncover the temporal dynamics of schema instantiation, complementing the anatomical observations derived from lesion and fMRI studies. The influence of thematic contexts on processing of objects is very rapid [49–51], as predicted by schema theory. In one study, scenes with objects being handled (e.g., basketball game) were presented when the object was congruent (basketball) or incongruent (watermelon) with the scene [50]. Early frontally distributed event-related potentials (ERPs) (270–600 ms) discriminated congruent and incongruent scenes, interpreted as reflecting an overlap of perceptual (N300) and conceptual (N400) congruency effects instigated by context violation of activated schemas. Other studies [30,51,52] have reported schema-related effects as early as 170 ms. Cardiologists and pulmonologists performed a diagnosis-verification task by deciding whether an image (electrocardiogram or chest radiograph) matched a specific diagnosis (e.g., 'arterial fibrillation', 'tuberculosis'). Greater domain expertise predicted N170 amplitudes, suggesting that having an organized and accessible knowledge structure affects early perceptual processing of complex visual stimuli [52]. Similarly, when participants were required to activate their self-schema to endorse only personally known faces (and not famous or unknown faces), N170 amplitudes differentiated known from unknown faces [51]. Importantly, patients with vmPFC damage did not show the N170 familiarity modulation although it was source localized to the inferior posterior cortex (fusiform face area) [30][30]. This is consistent with the idea of rapid, top-down schema-mediated modulation of posterior representations. These studies demonstrate very early influences of schemas on the neural signatures of incoming information and that the vmPFC has causal influence over these posterior modulations.

How are such early top-down influences facilitated? According to schema theories, instantiation involves activating and sustaining a general 'template' (Figure 1) representing contextually relevant knowledge structures and biasing information processing from the input stream to be consistent with activated schema variables [10,28]. This should appear as protracted, tonic effects of interaction between the vmPFC and posterior cortical regions even before a stimulus is processed. One study found pre-stimulus sustained changes in low-frequency power (theta) and interregional coherence between the vmPFC and bilateral inferior and lateral temporal cortices [30], regions relevant to schema instantiation (Figure 1). Controls, but not patients with vmPFC lesions, demonstrated decreased interregional coherence before stimulus onset, a pattern that can support better expression of relevant neural codes during memory encoding and retrieval [53]. Thus, the vmPFC could bias processing of stimuli in a schema-consistent manner by maintaining tonic low-frequency desynchronization over schema-relevant posterior neural networks.

How Schemas Influence New Memory Formation

In addition to influencing how information is processed and interpreted online, prior knowledge also critically impacts what aspects of an experience would be encoded, what parts would be

retained, and what would be forgotten; it can also greatly impact the extent to which retained representations resemble the original events.

According to the **schema-linked interactions between medial prefrontal and medial temporal regions (SLIMM)** model [8], the mPFC signals the congruency between existing schematic representations and current experience, termed resonance (cf. [40] for similar ideas on vmPFC and memory monitoring). Greater resonance leads to a shift from memory processing driven by the medial temporal lobe (MTL) to vmPFC-based memory formation. The vmPFC is thought to activate relevant, and suppress irrelevant, schematic information to facilitate and constrain mnemonic processing. In situations that are congruent with prior knowledge, the vmPFC inhibits MTL-dependent binding of arbitrary event elements.

Other models, however, emphasize the central role of the hippocampus in relating new events to prior knowledge, in addition to its role in relational binding of arbitrary associations. These models argue that bidirectional hippocampus–mPFC interactions are required to support efficient memory encoding and context-dependent memory retrieval [9,41]. These latter models build on extensive animal work, predating current interest in memory schemas, that investigated associative inference and transitive inference in rodents [54–56] and primates [57] and that highlighted the complementary role of the hippocampal and prefrontal cortices in constructing flexible memory representations that allow abstraction of information. Together with more recent animal studies (Box 2), it is suggested that the hippocampus encodes hierarchical representations of feature overlaps of closely related events while differentiating the contexts in which these events occur. According to this view, context-defining information is relayed to the mPFC where distinguishable contextual ‘rules’ are encoded [9]. These rules are engaged when the same contextual information is again relayed from the hippocampus to the mPFC and that in turn determines the activation of appropriate hippocampal representations and suppression of context-inappropriate memories.

As we outline below, evidence for both models exists. It should be kept in mind, however, that events are never completely congruent or completely incongruent with existing schemas, and existing schemas may vary in strength. The current laboratory-based experimental data may emphasize more the joint contributions of the hippocampus and mPFC, while SLIMM might capture the interplay between them under conditions with particularly well-established, rich schemas.

New Learning: Encoding

Prior knowledge can enhance high-order evaluative, semantic, associative binding on the one hand and bias lower-level perceptual processing on the other hand. Depending on the encoding conditions, these influences can lead to reduced memory accuracy or enhance memory formation. For example, encoding information (e.g., cactus picture) in a schema-congruent (desert) versus -incongruent (ice rink) context leads to increased hits but also to increased false alarms when recognition involves perceptually similar items (similar cacti) [58] (cf. [59] for related findings). Thus, schema congruency boosts overall (conceptual) memory but undermines perceptual encoding of fine details and reduces recollection, as indexed by ERPs [59]. Interestingly, vmPFC lesions protect against this form of false alarms, but also eliminate the memory benefit for schema-congruent items [58]. These patterns are consistent with the SLIMM model as they may reflect reduced pattern separation and recollection (hippocampal functions) when items are encoded within schema-congruent contexts.

Using a similar task during fMRI, participants encoded item–context associations by rating their congruency (e.g., umbrella–racecourse) [60]. Congruency effects for items and their associations were reported as well as parametric mPFC increases and hippocampal decreases with

increasing encoding congruency [60]. Similarly, subsequent memory effects for verbal PAs revealed hippocampal–mPFC connectivity for subsequent non-schema- but not schema-related item memory [61], with similar patterns of hippocampal connectivity with the superior temporal sulcus (STS) and inferior frontal gyrus (IFG) also reported. Such evidence is consistent with the SLIMM model by demonstrating a tradeoff between schema-driven memory enhancements mediated by mPFC–cortical interactions and detail-accuracy memory mediated by hippocampal–cortical and possibly hippocampal–mPFC coupling.

Other studies, however, suggest that – rather than a functional tradeoff – the mPFC and hippocampus both serve (complementary) roles during schema-mediated memory formation [9,41,62]. For example, in the associative inference paradigm described above [19,20], increased vmPFC–hippocampus coactivation presumably reflects replay of the premise information during encoding of new related associations, and the extent of coupling predicts successful expression of inferred associations [9]. Thus, rather than inhibition, during formation of overlapping associations the vmPFC exerts control that allows conflict resolution between competing associations in the hippocampus and the creation of an integrated schematic representation. Several studies have observed increased coupling between the vmPFC and hippocampus during schema-related encoding [16,47].

Not all studies report mPFC activation or interactions with other structures during schema-related encoding of new information. In a continuous recognition paradigm, to-be-recognized objects were presented with either a congruent or an incongruent background [63]. Neither encoding nor repetition at these very short lags revealed mPFC activation, but instead schema-related retrieval was associated with hippocampal and posterior temporal and visual regions [63]. Similarly, there was no reliable mPFC activation or connectivity when medical students encoded face-diagnosis PAs before and after they acquired medical expertise [14]. It was suggested that only when congruence with prior knowledge is perceived subjectively is the mPFC recruited, which is not the case for face-diagnosis PAs [14]; While task demands are probably important, it is worth noting that faces and houses are also not inherently congruent or incongruent, yet strong mPFC effects were reported [47].

One important question is to what extent the neural effects observed during schema-related encoding of new information (Figure 2B) are independent of schema instantiation. Some neuroimaging analyses suggest independent contributions of prior knowledge effects and subsequent memory effects within the same neural network [47]. Electrophysiological studies also suggest that schema-related subsequent memory effects have spatiotemporal signatures that differ from those of schema instantiation (see the above section on schema reinstatement and instantiation). ERP effects of online integration during schema-related encoding were observed later (~400 ms) [64] than those associated with schema instantiation (~170–270 ms) [30,50–52]. Subsequent correct recognition was associated with greater amplitude for schema-congruent items over frontocentral electrodes around 400 ms, which is likely to be related to initial semantic access, and was clearly distinguishable from the later subsequent memory effect at ~650 ms that was insensitive to congruence effects [64].

New Learning: Consolidation and Retrieval

Prior knowledge also exerts its influence on the integration of new information through delayed offline processes of consolidation, transformation, and reorganization. One of the dramatic findings arising from landmark animal studies [4,6] (Box 2) is that novel schema-congruent information rapidly becomes hippocampal-independent through processes of increased neocortical plasticity. Historically it was believed posterior neocortical structures are incapable of rapid consolidation because in distributed neural networks new associative connections override old connections leading to catastrophic interference [65]. However, modified models

demonstrate that even distributed networks can integrate new information through rapid changes in their representational layers (as opposed to hidden layers) with little evidence for interference [66] if that information is congruent with prior knowledge. Empirical neurobiological research supports this notion and demonstrates that neocortical catastrophic interference can be avoided only when the new associations are related but nonoverlapping [67]. Representational layers in neural networks are likely to correspond to posterior neocortical regions, and rapid integration appears to involve lateral and inferior temporal cortices and the TPJ [24,68,69]. Importantly, it appears that rapid neocortical consolidation is greatly enhanced when prior knowledge is simultaneously activated with incoming information [8,70,71], leading to synchronized activity between relevant representational nodes [30,72]. Thus, for rapid neocortical integration of new associations to occur, other, amodal cortical hubs such as the vmPFC or ATL may need to potentiate neocortical synchronous activity. This prior-knowledge-dependent rapid neocortical consolidation process [66] certainly can occur with even minimal hippocampal involvement; whether it can be hippocampal independent is not yet known.

Much of the evidence for rapid neocortical consolidation processes in humans comes from schema memory and sleep studies that demonstrate unique patterns of sleep-related memory reactivation and transformation (Box 3). Several studies have investigated post-encoding offline processes associated with schema-related information during wakefulness. In a pioneering study, participants viewed the first half of a movie either intact or temporally scrambled and the other half on the next day during scanning [7]. Having intact prior narrative induced greater intersubject synchronization in the vmPFC during encoding of the second part and weaker mPFC–MTL functional connectivity during encoding and post-encoding rest. Greater vmPFC–hippocampal crosstalk in this case may be necessary to compensate for the poorly organized prior knowledge to support consolidation or schema-mediated gist extraction (Figure 1B).

Box 3. Sleep and Schemas

Reactivation during sleep plays a central role in episodic memory transformation (i.e., semantization or gist extraction) [92,93]. It appears that slow wave sleep (SWS) is critical for both initial schema formation and the integration of distinct memories into an existing schema [92,93]. According to one model [93], during SWS slow oscillations (0.5–4 Hz) arise in the neocortex generating widespread synchronization. During the synchronized depolarization, faster oscillations called spindles (11–15 Hz) originate from the thalamus and spread to the neocortex, creating optimal conditions for neural plasticity, while high-frequency ripples (100–300 Hz) occur in the hippocampus that are associated with neuronal reactivation (“replay”) and facilitate the transfer of information from the hippocampus to the neocortex [92]. Also during SWS, synapses of recently potentiated neurons are thought to be downscaled to a proportion of their strength with only the strongly potentiated interconnections surviving [94], increasing signal-to-noise ratios in relevant brain circuits. Wake-dependent replay may also occur, tagging relevant memories for reactivation during subsequent sleep [95], and this preselection process is likely to be influenced by currently activated schemas. This results in the reactivation of shared elements of several memories leading to greater strengthening of their commonalities, which will then be preserved during downscaling, than of episodic idiosyncrasies, which will be lost.

Schema and sleep studies have provided support for aspects of this model. Associating new memories with prior knowledge was found to be essential for successful memory reactivation and schema integration via increased spindle activity [96]. Slow oscillations and spindles are also critical for the integration of new lexical [97] and semantic [98] information into preexisting neocortical representations, while sleep spindle density predicts accelerated hippocampal disengagement in schema-dependent consolidation [11].

By contrast, during associative and creative thinking preexisting schemas must be disbanded to create new schemas. This schema disintegration is thought to preferentially occur during rapid eye movement (REM) sleep, which fosters creativity [99]. This may explain why REM sleep has been associated with a consolidation memory benefit for the memorization of tonal melodies and is thus consistent with a Westerners schema of music but not for atonal, schema-inconsistent melodies [100]. Thus, while the reactivation of overlapping memories may act synergistically with neural downscaling during SWS to initially form and update various abstract networks of neural nodes into a single refined relational representation (i.e., schema), disintegration and flexible representation of schemas could rely on REM sleep.

Others, however, found greater vmPFC–hippocampal interactions during rest when new information was related to prior knowledge compared with unrelated associations [21]. As described above, these discrepancies could be related to the fact that in the first study some prior knowledge (albeit poorly connected) was present in the ‘no schema’ condition while in the latter unrelated associations were arbitrary. Interestingly, in other domains vmPFC signals show nonlinear relationships with psychological and behavioral measures [102–104]. The same might be true of schema functions where vmPFC–hippocampal connectivity is weak for new information that is completely arbitrary or for new information that is very strongly related to prior knowledge. The interaction between the vmPFC and hippocampus may be strongest for mid-range relatedness and reflect the reinstatement of relevant overlapping associations to support memory integration.

Finally, very few studies have investigated the neural basis of retrieval of information encoded in the context of prior knowledge [12,16,63,73,74]. Some of these appear to indicate the reestablishment of thematic context to support retrieval. For example, subsequent true- and false-memory effects for objects that were either congruent or incongruent with previously encoded thematic scenes (bathroom, farm) demonstrated that strong schematic contexts lead to an increase in both correct and incorrect memories. Lateral temporal cortices and the mPFC were associated with schema-related retrieval regardless of accuracy, whereas recollection of true memories was associated with greater activity in the hippocampus and posterior visual cortex [74]. Others, however, argue that congruence-related differences are less pronounced during retrieval, when all memories may begin to depend more on schematic information, irrespective of an event’s original congruence with prior knowledge. Using a human analog of the rodent spatial schema task [4], it was found that retrieval of schema-defining PAs was associated with mPFC activity while schema-related new associations were associated with greater reaction times and greater activity in frontoparietal networks, including the AG, possibly reflecting greater top-down attention to memory [12].

Box 4. Schema Functions and Decision-Making

Both animal and human research point to the vmPFC as a central structure mediating schema representation and its influence on new learning. The vmPFC, however, also plays a central role in value-based decision-making [101], leading some to suggest common mechanisms across domains [103–105]. Evidence for such a link within decision-making research comes from the observation that personal prior experience with particular rewards and punishments is considered key to the vmPFC’s role in decision-making [106,107].

Schematic memory is a particularly strong candidate for supporting value-based decision-making and some have even proposed that a central role of schema extraction is to optimize reinforcement-driven behaviors in dynamic environments [44]. Value-based decision-making depends on one’s prior experiences with the available options and on the specific context in which the decision is made. Schemas are powerful cognitive structures that organize prior knowledge and therefore could bias the process of decision-making, either consciously or preconsciously, and promote its efficiency. In more strategic decision-making, they can provide frames of reference through which decision-makers can represent complex strategic problems, draw analogies across similar schemas from other domains, or directly apply previously acquired schema to a current problem. Thus, the posterior vmPFC may serve a domain-general role in biasing relevant long-term representations in the posterior neocortex. These serve to assess the subjective relevance and value of new information to the current context, a function that occurs rapidly and automatically. Automatic biases often drive behavior, as reflected by phenomena such as intention superiority effects in action-based prospective memory that involve the implicit maintenance of bias [108,109] probably mediated by the vmPFC. Similar ideas of vmPFC biasing representations in a context-sensitive manner have been proposed with respect to its role in the extinction of conditioned fear responses [110]. In this view, fear extinction constitutes a new learning of a conditioned stimulus (CS)–no unconditioned stimulus (US) association and is highly context specific. The posterior vmPFC appears to bias the expression of one set of associations over another in a context-sensitive manner based on prior subjective experiences.

Concluding Remarks

Schemas exert dramatic effects on the way events are processed and integrated into memory. Some of the basic neural systems and neurobiological processes that are associated with these influences have been elucidated in recent years. Particularly intriguing are discoveries on the modulation of early perceptual processing, distortion of information processing at encoding, acceleration of neocortical integration, and changes to offline processing during sleep and wakeful rest. Many studies, however, use relatively low-level, informationally specific knowledge structures that may harness some of the subprocesses recruited by general-purpose schemas. It remains unclear whether the activation of general-form higher-order reference templates simply recruits a broader compilation of these processes or is qualitatively different. Particularly lacking are insights into how schemas themselves are constructed and accommodated, as most research focuses on assimilation of new information.

Perhaps the greatest progress was made in identifying the neural systems that support schema-related functions, with particular emphasis on vmPFC–hippocampal–posterior cortical interactions. Here, too, many questions are left unanswered (see Outstanding Questions). For example, the vmPFC is also identified as key to many other, seemingly unrelated, cognitive functions (e.g., decision-making, fear extinction; Box 4). It could be that the vmPFC serves a general-purpose function of biasing information processing in a context-sensitive manner. It is a ‘schema structure’ only in the sense that context-appropriate representations and actions are determined by the accumulation of subjective experiences. Its participation in multiple memory-related domains may arise because of its role in the detection and establishment of meta-mnemonic structures that support specific-event gist extraction, inference of non-presented relationship, superordinate organization of **concepts** and action plans, and so forth.

Acknowledgments

The authors thank Adina Levi for her assistance in the literature review and preparation of coordinates for the ALE analysis. A.G. is supported by the Natural Sciences and Engineering Research Council of Canada (grant 405649) and the Canadian Foundation for Innovation/Ontario Innovation Trust and the Heart and Stroke Foundation Centre for Stroke Recovery.

Supplemental Information

Supplemental information associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.tics.2017.04.013>.

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Outstanding Questions

Are the neurocognitive systems and neurophysiological processes that support schemas qualitatively different from those that support the multitude of other, related types of prior knowledge?

Can statistical learning on its own account for the development of rich, structured, symbolic schematic knowledge, as suggested by some models, or does prior knowledge need to be assumed, constraining schema acquisition?

A related question is what is the role of abstract hierarchical knowledge in accelerating the information learned through statistical learning?

How do the temporal dynamics of activity and cross-communication between neuroanatomical regions determine schema instantiation and schema-mediated mnemonic processes?

What are the roles of synchronous and desynchronous neural oscillation in preparing the relevant neural networks for processing of schema-relevant information?

Under what schema-related conditions is there an inhibitory relationship between the vmPFC and hippocampus and when is there interactive facilitation?

Is the relationship between extent of prior knowledge and vmPFC–hippocampal interaction linear or nonlinear?

Can schemas support rapid neocortical consolidation independently of the hippocampus or is some initial hippocampal support always needed?

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