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The proactive brain: using analogies and associations to generate predictions

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Rather than passively 'waiting' to be activated by sensations, it is proposed that the human brain is continuously busy generating predictions that approximate the relevant future. Building on previous work, this proposal posits that rudimentary information is extracted rapidly from the input to derive analogies linking that input with representations in memory. The linked stored representations then activate the associations that are relevant in the specific context, which provides focused predictions. These predictions facilitate perception and cognition by pre-sensitizing relevant representations. Predictions regarding complex information, such as those required in social interactions, integrate multiple analogies. This cognitive neuroscience framework can help explain a variety of phenomena, ranging from recognition to first impressions, and from the brain's 'default mode' to a host of mental disorders.

General framework

When we are immersed in the world of neuroscience findings, the brain might seem like a collection of many little modules, each expert in a specific task. Is it possible that, instead, one can account for much of the brain's operation using a small set of unifying principles? One such principle could be that the brain is proactive in that it regularly anticipates the future, a proposal that has been promoted in the past in different forms and contexts. Specifically, I propose that the cognitive brain relies on memory-based predictions, and these predictions are generated continually either based on gist information gleaned from the senses or driven by thought. The emphasis in this proposal is on the analogical link to memory and the role of associations in predictions, as well as on the idea that we use rudimentary information to generate these predictions efficiently. Furthermore, by developing this framework using a cognitive neuroscience approach and a minimalistic terminology, key concepts can directly be tested and used in empirical and theoretical future research.

The proposed account integrates three primary components. The first is associations, which are formed by a lifetime of extracting repeating patterns and statistical regularities from our environment, and storing them in memory. The second is the concept of analogies, whereby we seek correspondence between a novel input and existing representations in memory (e.g. 'what does this look like?'). Finally, these analogies activate associated representations that translate into predictions (Figure 1).

Each of these key components – associations, analogies and predictions – has been the focus of rich and active research for a long time. By connecting these concepts in one unifying principle of memory-based predictions, the framework proposed here builds on this valuable background to emphasize the functional coherence between the three processes.

To make the underlying mechanism more explicit, I will elaborate on each of the elements that mediate the generation of predictions. I will start with the proposal that the foundation of predictions is provided by the associative nature of memory organization.

Associations as the building blocks of predictions

How does our experience translate into focused, testable predictions? The answer proposed is that memory is used to generate predictions via associative activation. In memory, our experiences are represented in structures that cluster together related information. For example, objects that tend to appear together are linked on some level, and these representations include properties that are inherent to and typical of that same experience. Such structures have been termed 'context frames' [1,2], which are reminiscent of earlier concepts such as schemata [3], scripts [4] and frames [5], which all imply a unified, global representation of perceptual and semantic associated attributes. The structure of these context frames enables co-activations that prime our subsequent perception, cognition and action by remaining 'online' and making available predictions of what to expect in the immediate environment. For example, placing a picture of a certain recognizable object next to an ambiguous object can make that object recognizable if it looks like something familiar that is contextually congruent with the clear object (i.e. an analogy) [1]. This principle operates similarly in other domains. For example, contextual framing has a direct influence on our judgments of the emotions of others [6].

Taken together, the associative nature of memory makes it possible to take advantage of frequent trends in the environment to help interpret and anticipate immediate and future events. One basis for this proposal is provided by the literature on priming, with its various types (e.g. perceptual, semantic and contextual). These studies support

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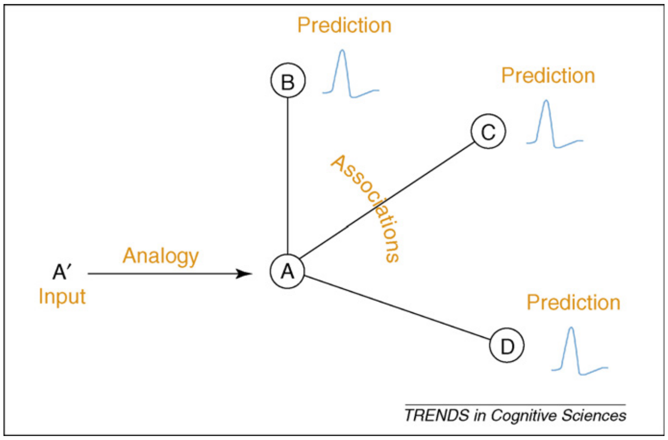

Figure 1. A minimalistic depiction of the proposed principle. An input (A′) is connected with an analogous representation in memory (A). This link results in the co-activation of related representations (B, C, D), associations that remain 'online' to provide testable predictions. The input can be either an external, sensory input, or internally generated during thought processes. Furthermore, the input can be of varying degrees of complexity, which would result in predictions that are correspondingly of different levels of elaboration, encompassing the range from perceptual to executive predictions.

Box 1. The brain's 'default' mode and associative processing

A collection of cortical regions is consistently active when human subjects are not engaged in a goal-directed behavior. This network has been termed the 'default network' [9], and is currently drawing a large amount of attention.

The primary method of considering neuroimaging data is to subtract the signal elicited by one condition from the signal elicited by another condition. To look at the main effect of a single condition – how did this condition affect activity in the brain – one typically uses a 'baseline' condition in which a fixation cross is presented. The implicit assumption in the many studies that have used this method was that the brain uses these fixation intervals for resting. However, increasingly more imaging studies are reporting negative activations ('deactivations') when one condition is compared with the fixation 'baseline'. Regions that demonstrate such deactivation are taken to have been more active during the fixation baseline then during the compared experimental condition, although what are the cognitive processes that are carried out by this network during rest is still unclear. This default network is remarkably similar, in its medial view, to the network activated by contextual associations (Figure I) [8], supporting the proposal put forward here that the brain is continually engaged in the generation of associations-based predictions.

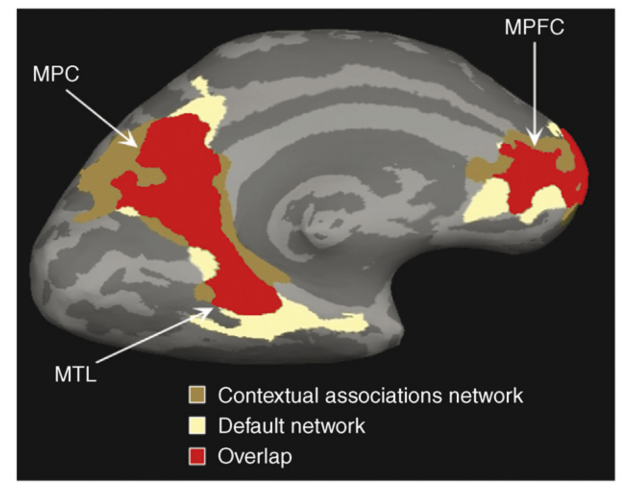

Figure I. Medial view of the typical default network and the typical contextual associations network. The default network regions are those that tend to show deactivation during the experimental task. In other words, these regions are more active during fixation rest than during task performance. The context network activations were obtained from the contrast between strongly contextually associative objects (e.g. a tennis racket) and weakly contextual objects (e.g. cherries). Importantly, the superimposed labels demonstrate the striking overlap between associative processes and resting, task-independent processes [8].

the idea that the perception of a certain stimulus co-activates the representations of related items [7], although these items have not been experienced as part of the present physical environment. Indeed, recent neuroimaging studies demonstrate the involvement of associative predictions in cognitive facilitation [2].

The proposal promoted here is that the brain is continually engaged in generating predictions, and that these predictions rely on associative activation. Taken together, it is important to demonstrate that the brain is frequently busy with associative processing, an idea dating back to Plato, Aristotle, Hobbes and the Empiricists. Support for this idea comes from a recent link we have made [8] between the neural underpinnings of associative processing and reports regarding the cortical activation that is considered to reflect the brain's 'default' mode [9]. Specifically, we showed that significant parts of the default network, which refers to the collection of brain regions that are consistently activated when subjects are not engaged in a task-specific cognitive effort, overlap with the regions activated by tasks that recruit associative processing [8] (Box 1). This remarkable overlap between the default network and activity attributable to contextual associative processing demonstrates that what people do when their mental capacity is not completely consumed by a specific task is to generate associations. In other words, associative activation is an integral process of the brain's mental 'default' mode. Given the proposal that predictions are derived from associations, this overlap is in agreement with the idea of a continuous generation of predictions.

Associations, therefore, provide the representational tool used for predictions. In the next section I will consider the mechanism that activates these associations, and how it does so most effectively such that only the associations and predictions that are most relevant and most helpful for a given situation are activated.

Analogies as the trigger of predictions

I propose that our brains are equipped with the ability to extract gist, minimally analyzed information, from a situation and to use it to derive an analogy, mapping the novel input to similar representations in memory. Figure 2 depicts a simple example, where a new exemplar of a certain object class is analogically mapped to the corresponding prototype, and in Box 2 I describe a model of how such an analogy can be accomplished rapidly using coarse information.

Traditionally this process has been considered as recognition, classification, or even a type of memory retrieval, but in the present context I treat this process as analogy-making instead. In the process of recognition or retrieval, the task is to answer the 'what is it?' question, whereas, in analogy, the emphasis is on 'what is it like?' In other words, although it might seem like an issue of terminology, in

Box 2. Top-down facilitation based on rudimentary information

In the framework outlined here, the activation of a memory representation based on a sensory or internally generated input is a process of analogical mapping. A central question is how gist information, how ever defined, can be sufficient for mapping the input onto an analogous memory. One model (Figure I), from object recognition, postulates that rudimentary information in the image (i.e. low spatial frequencies), which is extracted rapidly, is sufficiently powerful to activate expectations about what the observed object might be [14,75]. A similar mechanism is proposed to be operating on multiple levels, although the representation of gist information on higher levels of analysis is yet to be defined (see Concluding remarks section). Note that the gist-based initial guess could elicit more than a single alternative. This ambiguity is resolved gradually as high-spatial frequencies arrive with the bottom-up streams. But it can also be resolved more quickly by incorporating other rapidly extracted sources of information, such as context [2], which would fine-tune this analogical mapping to have fewer alternatives and, thus, less ambiguity.

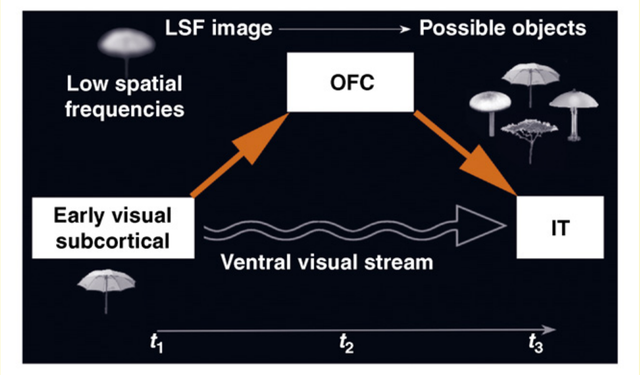

Figure I. A top-down facilitation model. A partially processed, low spatial frequency (LSF) image of the visual input is rapidly projected to OFC from the early visual cortex and/or from subcortical structures such as the amygdala, while detailed, slower analysis of the visual input is being performed along the ventral visual stream. This 'gist' image activates predictions about candidate objects that are similar to the image in their LSF appearance, which are fed back to the ventral object recognition regions to facilitate bottom-up processing. Reproduced with permission from Ref. [14].

recognition *per se* we recognize by linking to memory to interpret the input, whereas in analogy the input is linked to memory not only for the sake of interpretation, but also for the purpose of projecting attributes and generating predictions. Therefore, by using the term analogy, the emphasis is placed on the associations-based predictions that analogies elicit beyond mere recognition, and it is this extra step that is the focus of the proposed framework.

Nevertheless, analogical mapping still serves to interpret the input: inferring what physical input caused a certain percept, an issue that has received a lot of attention [10–12]. Therefore, the analogy itself also provides an important top-down prediction regarding the identity of the input using initial bottom-up information [13,14] (Box 2). However, the focus here is on the considerably less explored type of predictions: forecasting that pertains to what is about to happen, what is likely to appear in the same context, and what is the most beneficial action that needs to be taken given the specific input. In other words, the analogy in Figure 2 mediates interpretation, by linking input to memory, whereas forecasting predictions stem from the subsequent activation of information associated with that analogy (e.g. Figure 3).

Box 3. Questions for future research

- What are the computational operations and the underlying cortical mechanisms mediating the transformation of a past memory into a future thought?
- How does the brain handle completely novel situations where no reliable predictions can be generated?
- To what extent are we aware of our predictions and their origin? In some cases, such as in stereotypical thinking, being aware of these predictions can eliminate unwanted influences.
- What does it mean for predictions to provide a perception of stable environment? In most typical situations, we know what to expect and what not to expect. How is finding something alarmingly incongruent with our expectations (e.g. an elephant in the living-room) different from finding something unexpected yet insignificant (e.g. a shoe in the living-room)?
- How do we become aware of a mismatch between predictions and perception? And how do we incorporate lessons from prediction errors into future behavior?

This principle is not limited to the realm of visual recognition, but rather encompasses a wide variety of domains where input can be linked to memory to generate predictions. For example, imagine meeting a new person. Our first impressions are rapid [15,16] and are based on rapidly extracted coarse information [15]. According to the present proposal, this process is mediated by linking the features of the new person to the most similar representation in memory; someone we know and that looks to some extent like this new person. We automatically project information such as personality attributes to the new person based simply on this analogy. Although this analogy is an approximated set of traits, it might be beneficial, at least under some circumstances, to not start interactions without any assumptions on that new person.

Analogies can be based on similarity on various levels, including perceptual similarity (e.g. in shape or smell), abstract conceptual dimensions, and goals [12]. Analogy-based mappings of properties manifest themselves in processes ranging from perception and memory [17] to stereotypic judgments and prejudice [18].

It is important to note that the input is rarely mapped with a single analogy directly to memory. Instead, the function of analogies can be based on the integration of multiple analogies that accumulate to complex mapping. For example, if you are trying to understand a conversation that is taking place on a screen when watching a new movie, you will have to map novel sounds to similar and familiar sounds in memory (which will then be connected with their associated linguistic meaning), to map the novel face appearances to similar and familiar face expressions (which will then be connected with the intentions associated with them), the context in which the conversation is taking place will be mapped to other similar contexts in memory and, when combined, these analogies can help map the complete, new situation to a collection of fragments in memory that together can allow you to understand the scene, and to forecast what is likely to be next.

While our existing memories are used to derive analogies and activate predictions, they are constantly being updated. The analogical process, in addition to affording the interpretation of our environment, subsequently augments previous representations in a way that fosters increasingly flexible future analogies.

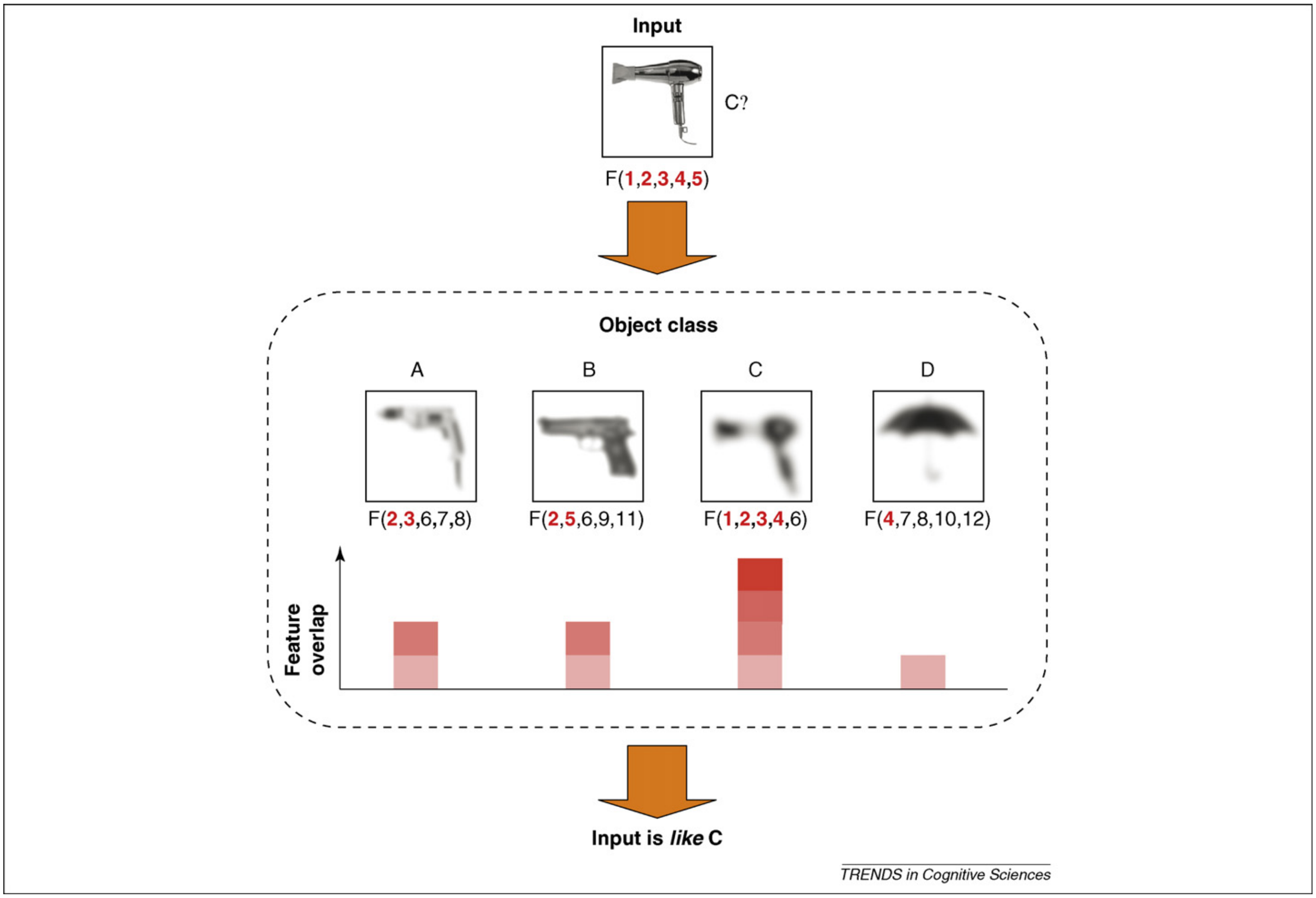

Figure 2. A simplified mechanism for analogy whereby the analogous representation is selected based on the maximal amount of feature (F) overlap with the input. This is a basic model, which has been used often in the past, and is introduced here to demonstrate the primary element of analogical mapping between input and memory. Such analogies can rely on similarity on various levels (e.g. physical, conceptual and function). I treat this process here as analogy, rather than classification, to emphasize that the main purpose of this process goes beyond mere interpretation of the input, to connect the input with known and predicted attributes that are manifested as predictions.

Finally, the activation of associations for prediction will not be as useful if it simply activates automatically all the information associated with the linked representation(s) in memory. Instead, it needs to take into account the context in which this input is encountered, and selectively activate the most relevant associations [2]. For example, an object such as a hairdryer can be naturally encountered in several possible contexts: hair-salon, appliance store, bathroom, as well as associated with abstract contexts (Figure 3). If the hairdryer is encountered in the hair-salon context, there is no need to activate objects that are typically found in bathrooms and appliance stores, which would not only be wasteful but also generate incorrect predictions. By taking context cues into account, this switchboard-like mechanism will only activate the most relevant associations, which will result in the generation of the most accurate predictions.

To summarize, analogies map novel inputs to representations in memory that most resemble this input. Subsequently, information associated with these representations is activated to provide predictions about what else might be expected in the same situation. By taking context into account in this associative activation, only the most relevant predictions are generated. In the next section I will describe possible neural underpinnings for associations, analogies and predictions.

Possible neural underpinnings

Neural substrates

Many cortical projections that connect separate regions are known to be reciprocal [19–22], which suggests bi-directional cortical communication. According to some estimates, the number of feedback (top-down) projections might even exceed the number of feedforward (bottom-up) connections [23]. Although this aspect of the anatomy is known, and the implication of omnipresent bi-directional flow consequently seems highly reasonable, this finding has not yet been sufficiently incorporated into contemporary thinking regarding cognitive processing. However, this 'provocative' anatomy implies something profound about how the brain works. Specifically, the reciprocal connections might provide the infrastructure that supports the continuous top-down involvement of internal representations with the interpretation of the world around us.

There are three main components in this proposal: associations, analogies and predictions, and they interact with each other regularly. Associations have largely been found in the medial temporal lobe (MTL), in the hippocampus [24,25], and in the parahippocampal cortex (PHC) [26]. As reviewed above with regard to the overlap seen between associative processing and the default network, other medial regions, such as the medial prefrontal cortex (MPFC) and medial parietal cortex (MPC) are involved as

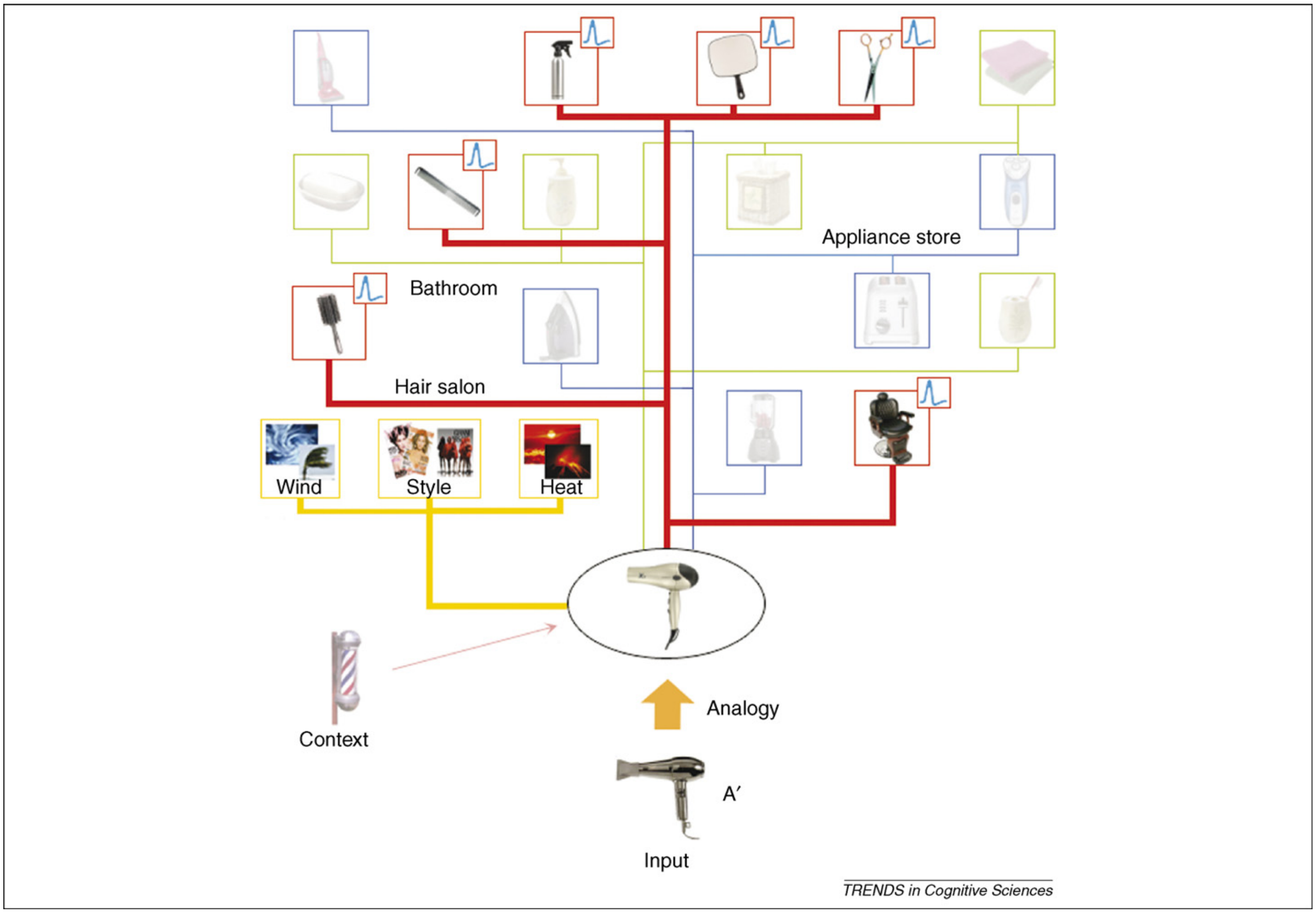

Figure 3. Translating analogies to predictive associative frames. The linked stored representation (i.e. an analogy mapped as depicted in Figure 2) activates only the associations that are relevant in the specific context, which provides focused predictions. In the example depicted here, although a hairdryer is associated with many objects, and multiple contexts (e.g. bath, hair-salon and appliance store), only the appropriate subset of predictions will be activated based on the associations relevant in the specific context (e.g. hair-salon). These connections result in predictions that are then tested against the input (sensory, or internally generated).

well. Given the diverse types of possible associations, it is indeed expected that they will be mediated by a large collection of regions, depending on complexity, modality and purpose. For example, other types of associations, such as visuomotor associations, seem to be represented in other regions, such the basal ganglia.

The brain regions that mediate analogical thinking are much less explored. Nevertheless, some types of analogical thinking have been found to activate the lateral and medial PFC [27,28].

Regarding the neural regions that mediate predictions, there are multiple sub-processes that need to be considered: the generation of predictions, their verification, and their updating. Expectations-based preparatory activation has been observed in numerous domains. For example, anticipating a somatosensory stimulus activates the somatosensory cortex [29]; pictures of food activate gustatory cortices [30]; visual imagery, even if not in a directly predictive task, activates the visual cortex, and has even been shown to activate early visual cortex in a retinotopically organized manner [31].

We have previously proposed a neural mechanism in the domain of context-based predictions and visual recognition [2,14,36]. Briefly, the associations relevant to the present discussion seem to be represented by the MTL in general, and the PHC in particular. The retrosplenial complex (RSC in the MPC), which is consistently found to be recruited in associative tasks (Figure I in Box 1), has been suggested to represent prototypical, rather than episodic, information about associations [26]. In other words, the PHC represents stimulus-specific context and associations, which are sensitive to specific appearance (e.g. *my* kitchen), whereas the RSC/MPC represents knowledge about associations related to the prototypical context (e.g. *a* kitchen). Their combined contribution presumably elicits prediction-related representations in the PFC (orbitofrontal cortex, OFC, in particular), as well as in a domain-specific cortex such as the fusiform gyrus in the case of object recognition.

Neural mechanisms

The neural mechanism that generates predictions is largely unknown, but it is thought to be mediated, or at least balanced, by neural oscillations and synchrony [32], and some evidence for such a mechanism in the PFC exists [33]. However, in addition to synchrony, there are other promising proposals [10,34,35] that are appealing and could benefit from further physiological and cognitive testing.

Predictions are proposed to be activated rapidly, using information that is available relatively early (i.e. low spatial frequencies; LSF). Such LSF-based predictions can be triggered in the PFC for the purpose of object recognition while interacting with the visual occipito-temporal cortex [14], and for context-related predictions while interacting with MTL and MPC [2]. The generation of object-related predictions in the PFC by rudimentary information is elaborated in Ref. [14], and how LSF rudimentary information might activate context-related predictions is elaborated in Refs [2,37,38].

Bayesian analysis is a natural computational formulation that can be used for capturing the idea that experiences accumulated in our memory guide our predictions and behavior. Every moment of our lives involves some level of uncertainty, and associative memories can help cope with this uncertainty. The statistical history of events and stimuli in our surroundings guides the activation of what is the most appropriate information to expect. Such statistical regularities can be extracted from our environment [39,40]. We frequently use the Bayesian principle that past experiences shape the priors for predicting aspects of the environment in everyday life, and there are sound reasons to suggest that the brain operates according to these principles [10,41,42].

Detecting errors in predictions

Humans can detect and learn from regularities in the environment, even without awareness [40]. When the predictions derived from these learned associations are violated, people can nevertheless detect them [43]. The neuronal and computational mechanisms that subserve the detection of prediction violation have been considered in the past [44,45]. The fMRI signal that corresponds to a detection of a violation of expectations seems to concentrate on the lateral ventral prefrontal cortex [46]. This suggests that the mechanisms that detect and potentially correct mismatches are mediated by at least partially different regions than those that participate in the medial network that is proposed here to generate predictions. Various other cortical regions have been implicated in processes related to prediction errors. For example, activity in the anterior cingulate cortex (ACC) has been reported to correlate with the likelihood of prediction error [47]. Prediction errors are detected for the purpose of adjusting the specific prediction for the immediate context, as well as for learning and updating internal generalizations that will help improve predictions in the future. Such errors can be detected internally, via mismatches between predictions and perceptions, and they can be detected using external cues, such as reward and punishment. Our brains seem wired to detect change efficiently, at various levels. It is possible that the comparison between predictions and perception is processed outside of awareness and we become aware of it only when a meaningful mismatch is encountered.

In learning and developing the ever-evolving knowledge-base from which predictions are later generated, we frequently face a choice between relying on what we know (i.e. exploitation) or attending novel aspects that can augment our existing knowledge (i.e. exploration). This is particularly pronounced in conditions of uncertainty [48,49], which in the present framework might reflect reduced ability to rely on analogies when such analogies cannot be mapped with high confidence. Interestingly, the same prefrontal regions that are proposed to be involved in predictions, OFC and the ACC in MPFC (e.g. Ref. [8]), have been theorized to monitor exploration and exploitation behavior (via the locus coeruleus) [50]. The MPFC, in particular, has been proposed to be crucial for cognitive control and specifically for evaluation of potential outcomes (see Ref. [51] for review). How is this related to the present attribution of a predictive function to regions of the MPFC? Processes such as evaluation of performance and outcomes, coping with response errors, response conflicts, and decision uncertainty all have in common an extensive reliance on predictions. This can further help explain why the same MPFC area is also activated by a diverse range of additional processes, including error detection [51], contextual activations [2], and ‘reading’ somebody else’s mind (i.e. theory-of-mind) [52].

Additional factors related to the neural substrates that subserve the proposed framework will be interspersed in upcoming sections, but in general, given the amount of available reports, it is hard to say substantially more on this theme without being overly speculative. Among the relevant issues that deserve extensive future research (Box 3), of particular interest are the spatiotemporal interactions among the various components of this network.

Applied predictions

Predictions, as described here, span a wide spectrum of complexity and function. At one extreme, there is the simple prediction that stems from a simple association (e.g. knowing to expect pain after bumping your toe on the leg of the sofa). At the other extreme, one can anticipate complicated experiences, plan far ahead, or mentally ‘travel’ in time to the future, based on simulations and memory. In spite of this extreme variety, there is no evidence to indicate that predictions of various levels of complexity, abstraction, timescale and purpose use mechanisms that are qualitatively different. As suggested earlier, simple perceptual predictions can be a result of direct analogical mapping followed by the automatic activation of a Hebbian-like association. By contrast, complex executive predictions result from the integration of multiple smaller analogies and ‘atomic’ associations.

Our accumulated experience creates an ever-evolving platform for predictions, and the influence of these predictions can be observed on many levels. In this section I will briefly review findings from such various domains that all demonstrate the ubiquitous role of predictions in the brain and in behavior, as well as the ways in which predictions rely on associations and analogies.

The first is a phenomenon termed ‘representational momentum’ [53]. This term pertains to the finding that a sequence of static photographs that implies a certain type of motion (e.g. imagine a rectangle that in each consequent image is rotated a few degrees clockwise) significantly affects the subjects’ performance on the last, target image, as a function of its rotation difference from the previous image in the sequence. This robust demonstration suggests that subjects generate the representation of the anticipated next image before it is presented. A related fMRI study [54] showed that when human subjects view static images with implied motion (e.g. an athlete about to jump), the motion-processing areas in the middle temporal and the middle posterior superior temporal sulcus are activated although the images are static.

Demonstrations of contextual priming [55,56] provide another example of the generation of visual predictions, where seeing a certain object activates the representations of other objects that are likely to appear in the same environment. Furthermore, predictions have a clear and crucial role in language comprehension and sentence integration [57,76], and being able to predict the intentions and actions of others is beneficial, and has recently been shown to confer direct facilitation on sensory processing [58]. Finally, studies have shown that activity in task-specific regions during anticipatory preparation is predictive of subsequent performance success [59]. These findings indicate that by generating a prediction, the brain activates the specific regions that are responsible for processing the type of information that is about to be encountered.

Louis Pasteur said that ‘chance favors the prepared mind’. According to the proposal described here, the ‘preparedness’ of the mind is derived from the generation of specific predictions, which shapes the pre-sensitization of the representations of some information and not another. Therefore, what we see can be driven by our motivations, goals and desires, which all might bias attention and sometimes determine our perception [60]. Therefore, by enabling privileged processing of anticipated information, regardless of the source of this anticipation, predictions might be seen as constraining the selection of what aspects of the environment will be primed and perceived, and how they will be interpreted.

Predictions have ubiquitous clinical implications. On the debilitating end, predictions and associations can provide the basis for anxiety disorders and phobias, as well as post-traumatic stress disorders. But predictions in other clinical circumstances can result in a positive influence, such as in placebo effects. Indeed, placebo analgesia that is enhanced by expectations has been shown to activate regions in the PFC, such as the OFC [61], which are proposed here to be part of the network that generates predictions.

Beyond helping us anticipate, prepare and simulate, the continual generation of predictions has another purpose, which is to help us to perceive stability and coherence in our environment. Our senses deliver a profoundly impoverished version of the environment to us, due to factors such as the massive reduction in the amount of information reaching the visual cortex from the retina, the presence of clutter and noise, and the fact that even familiar items vary in their appearance from one occasion to another. So predictions, derived from memory, fill-in the gaps based on experience.

This reconstructive contribution of predictions can be helpful not only when dealing with impoverished sensory input, but could eliminate the need to attend every aspect of our environment exhaustively, and could also be the reason why our brain can often ignore details and encode in memory only a reduced, gist-based version of actual memories because these details can later be reconstructed with sufficient resolution.

Predictions from within: mind-wandering and mental time travel

The focus here has been on predictions triggered by and geared towards the sensory world around us. But thinking about the future is often oriented internally, as we do when we plan, imagine, reason, fantasize, and so on. There has been a recent surge of interest in the subject, which includes stimulating findings from neuroimaging and patient work [62–65]. This ability to project oneself into the future and imagine upcoming or imaginary situations can be seen as a prediction tool, which also relies on analogies and associative processing, and whose primary goal is preparatory in nature. The areas involved seem to be highly overlapping with the associative and the default networks (Box 1).

An interesting aspect common to those findings is that systems that are typically associated with memory, primarily in MTL, are consistently active when people think about the future. This does not change the function that these memory regions have been implicated with, as some have suggested, but it does underscore the fact that to consider the future we need to retrieve information from our memory of the past (i.e. analogies and associations in the terminology used here). This makes sense, given the supreme importance of our acquired memory for our future survival and interaction with the environment. In that regard, it might be overly broad to look at the involvement of memory structures in internal mental processes as linking memory and imagination [66], because the specific part of imagination that recruits memory is, according to the proposal described here, the generation of predictions. Consequently, the cardinal purpose of memory starts to seem less for leisured reminiscing, as in the famous example of Proust’s madeleine, and more as a knowledge-base that guides our lives in an increasingly more informed manner.

It is important to consider the potential functional role of mental time travel. My proposal is that its primary role is to create new ‘memories’. We simulate, plan and combine past and future in our thoughts, and the result might be ‘written’ in memory for future use. These simulated memories are different from real memories in that they have not happened in reality, but both real and simulated memories could be helpful later in the future by providing approximated scripts for thought and action. This could be why athletes often report that they find imagining a future race helpful in the race itself. Therefore, simulating the future guides us by providing a rudimentary script for the optimal course of action when the anticipated future arrives.

Concluding remarks and predictions about predictions

I propose that the knowledge that is stored in our memory exerts its contribution to behavior by way of predictions, and that our perception of the environment relies on existing knowledge as much as it does on incoming sensory information. The framework proposed here is composed of three main ingredients: associations, analogies and predictions. It can be summarized as follows: the input is linked to memory via analogies, and once an analogy has been found, it elicits the activation of the representations associated with the input. This co-activation of related items provides on-line, focused predictions on what else is highly likely to be relevant in that specific situation. Regardless of whether oriented internally and externally, the primary role of these predictions is to guide our actions, plans and thoughts.

As discussed in the introduction, several of these concepts have been studied individually in the past. However, the present proposal integrates these concepts in a single unifying framework, with a cognitive neuroscience perspective. The synthesis proposed here might nevertheless be seen as related to notions such as 'embodied cognition' [67,68]. Embodied cognition is a movement involving primarily philosophy and artificial intelligence, and it is related to situated cognition [69]. The sense of similarity between the frameworks stems from the following elements of embodied cognition: that the brain 'has an agenda' and, thus, that it is proactive, as proposed here too; that it takes context (i.e. the situation) into account; and that memory is embodied (e.g. not amodal) to promote interactions with the world. However, other claims diverge significantly from what is promoted here. For example, the idea that the function of cognitive processes is directed solely towards the body's interactions with the world, the suggestion that the mind cannot be studied in isolation, and that the outside world is part of the cognitive system and, therefore, that representations in memory have a lesser role than the one endorsed here. In other words, embodied cognition links even the most abstract processes to sensorimotor low-level processes, whereas the framework proposed here relies on mental simulations, foresight and various types of anticipation that cannot always be directly mapped to low-level actions.

Humans seem to minimize processing of incoming information when this information is predictable (e.g. habituation, repetition blindness, change blindness, inhibition of return), and in parallel encourage the allocation of mental resources to unexpected and/or novel information (e.g. orienting response toward novel and unexpected stimuli, perceptual pop-out). How does this somewhat circular mechanism work? After all, we should process the input (i.e. find an existing analogy) to understand whether there is something unexpected there or not. The bias to not invest in the predictable is proposed to be primarily a top-down, internally driven process, whereas the alertness for detecting the novel and unexpected is primarily a bottom-up, sensory-driven process [70]. One possibility is that the decision is made based on the evaluation of a match between perception and prediction using only gist information that is available early (Box 3).

An interesting direction for future research concerns the roles of the different types of memory in predictions. I have concentrated here on episodic memory, the central role of which is supported by the repeated activation of the MTL in prediction-related processing, but it is reasonable to hypothesize that semantic memory plays a role as well. Studying how these memory types interact, as might be reflected by interactions between the medial network discussed here and, for example, the dorso-lateral PFC will be crucial for such understanding.

In spite of the advantage that predictions provide for behavior, they can sometimes interfere and put us on the 'wrong path'. Examples range from a baseball illusion called the rising fastball [71], to smell judgments that vary significantly based on how that smell was labeled [72], to demonstrations of false-memory in social cognition [73]. In addition, there are other phenomena that might be explained as interference from predictions, although they have not been portrayed as such. For example, that cognitive performance can be improved when subjects are instructed to be passive and not to 'try hard' [74]; when we are unable to retrieve a memory and the same incorrect memory keeps coming up; or when a break from a persisting intellectual problem seems to be all that was needed to then find a quick solution upon returning to the problem. The common component in these cognitive phenomena might be top-down predictions that are persistent but unhelpful and we have to find ways to ignore them altogether in such cases.

The independent role of predictions, analogies and associations in our mental lives hardly requires further demonstrations, given the rich and fruitful research of these concepts. However, their integration and orchestration here under a single framework could nevertheless benefit from direct testing. One hypothesis that stems from the current proposal is that because predictions are derived from analogies, increased similarity between novel input and representations in memory should result in increasingly efficient predictions. This could be tested on multiple levels of predictions, ranging from perceptual to more executive predictions. Another interesting test will be of the notion that analogies and predictions are generated based on gist. Although this has been specified and tested in fields such as recognition (e.g. LSF-based; Box 2), it becomes more challenging when one considers higher levels of abstraction. It seems reasonable that gist will be helpful in abstract analogies as well, and characterizing how abstract gist (such as that often also used in the memory literature) is extracted, represented and used will be necessary.

Given the omnipresence of predictions, their influence pervades far more processes than can be treated here. These include predictions in emotion, their effects on awareness and their interactions with attentional allocation. These are major issues, and addressing them will be crucial for any complete theory of the human brain.

In regard to clinical implications, aging seems to compromise many of the regions that are proposed here to constitute the network of associations-based predictions: MTL, MPC and MPFC. Therefore, older adults should have a diminishing ability to predict future events. However, at the same time, the observation that older adults can use their increased experience to derive improved expectations is common. Gaining a better understanding of which predictions are affected by atrophy, and of what regions, will help chart the global network of predictions as well as characterizing any qualitative differences between different types of predictions, both of which will ultimately improve future cognitive approaches to aging-related decline. Furthermore, several clinical disorders, such as major depression, are associated with a reduced ability to take context into account during everyday judgments and decisions. This could be seen as intuitive when considering the debilitating tendency of depressed patients to ruminate on a (usually negative) thought. As elaborated here, context consists of associations, and associations provide the basis of predictions. It is possible that engaging such patients in cognitive programs that train them to activate predictions that rely on associations from a wide variety of contexts would help alleviate their symptoms. Such optimistic prospects will have to be tested explicitly in the future.

Finally, according to the proposal outlined here, the brain constantly anticipates the future, and to do this it constantly accesses information in memory. This implies that our subjective feeling of present is actually an integration that also includes past and future information: we need to know where we were (both in time and space) and what is next, in addition to our present state. Indeed, people who study meditation initially find it extremely difficult to eliminate any future and past thoughts. Understanding how the brain integrates and holds simultaneously information from multiple points in time is an important question for the future.

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