

Educating the Brain

Lessons from Brain Imaging

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WE OFTEN THINK OF MEMORY in a nostalgic or trivial way—such as knowing the capital of the United States or being able to find our car keys—and as something relating simply to the past. Yet the reason our brains have remarkably powerful capacities for memories is that memory is actually for the future. It's the way we learn about the world so that we're more competent, more skilled, and more effective the next time we encounter a task. And so, while memory is of the past, it is a tool for the future.

How does the brain represent our experiences in a physical, real way that allows us to somehow store our experiences such that when the next moment or event arises we can use that information? In short, how is it that our brains allow us to gain and use knowledge?

The cognitive neuroscience of human memory aims to understand how we record, retain, and retrieve experience in terms of memory systems—specific neural networks that support specific mnemonic processes. Advances in the study of

the cognitive neuroscience of human memory reveal the functional neural architecture of normal human memory and illuminate why accidental or degenerative injuries to specific memory systems lead to characteristic patterns of mnemonic failure.

Much has been learned from patients with brain injuries, which can be incredibly specific in their effects. One patient, for example, damaged his orbital frontal cortex and lost his capacity for moral reasoning. We think of moral reasoning as one of the highest forms of human endeavor and believe that humans are specially endowed to make moral judgments. At the same time, this one injury to a specific part of the brain changed this patient's moral capacity. He had been a responsible, respected, and successful individual before his brain injury, but then became irresponsible, unemployable, unrealistic, and antisocial in his behavior. Other patients with injuries to a different part of the brain can no longer recognize fearful facial expressions. People with anterior temporal lesions are unable to produce proper nouns. So, each human ability has a specific and necessary instantiation in the human brain.

Within the domain of memory, patient studies have revealed that the human brain is comprised of multiple memory systems, with each system biologically engineered to be specialized for acquiring or storing a specific form of knowledge or skill. Large injuries to the medial temporal lobe, including the hippocampus, result in global amnesia—the inability to gain new memories for events that are experienced or for the information encountered in those events. Such patients have pre-

served memory of the remote past—they know who they are, and they retain intelligence, language, social norms of behavior, and memory of experiences prior to their brain injury. These patients cannot, however, form a new memory for any experience subsequent to their brain injury. No matter how often information is repeated, how emotionally powerful that information is (such as the death of a loved one), or how recent the experience (a few seconds earlier), amnesic patients cannot consciously remember any experience after the onset of their amnesia. Thus, we know that the hippocampus and related medial temporal lobe structures are essential for the creation of declarative memories—consciously accessible memories of events or facts.

Furthermore, we know that the amygdala, another limbic structure just anterior to the hippocampus, plays a specific role in emotional learning and memory. Healthy people remember emotional events better than neutral events, because emotions serve as markers for important events in our lives. Patients with lesions restricted to the amygdala fail to exhibit this amplification of memory by emotion. Their memory for neutral events is normal, but they fail to show an enhancement of memory for emotionally salient experiences.

The above examples of memory disorders relate to declarative memories of facts and events, but people can also exhibit procedural memories when they learn a skill through practice. For example, people can gain a broad range of motor (physical), perceptual, and cognitive skills through practice. Quite strikingly, amnesic patients can learn and retain many of these

skills perfectly normally. The amnesic patients cannot remember that they have gained a skill, or the episodes in which they gained their skill, but their improvement in performance, even after a year's delay, is perfectly normal. This dissociation between impaired declarative memory and intact procedural memory indicates that other brain areas, which are not injured in amnesia, must support skill learning. Indeed, patient studies have revealed that a number of brain areas in the neocortex, basal ganglia, and cerebellum are essential for skill learning. The specific brain areas essential for a particular skill depend upon the nature of the skill.

Most important things that people can learn involve a network of brain structures that interact during learning. For example, it is generally thought that learning new information involves an interaction between the hippocampus and neocortical areas specialized for storing specific kinds of information. Further, the interactions can change over time. Thus, amnesic patients remember the remote past normally because that information may be fully stored in the neocortex and no longer involves the hippocampus. But learning new information requires interaction of the hippocampus and neocortex.

We have learned a great deal about the functional neural architecture of the human brain from studying how specific brain injuries impair specific learning abilities. But this method is limited in several important ways. First, the injuries tend to occur in some brain regions and not others, so we are unsure of what many areas of the human brain contribute to learning. Further, naturally occurring injuries usually involve

multiple adjacent brain structures, each of which may have separate functions. Second, we cannot observe dynamical changes in how brain structures interact over time. Third, we can learn universal principles of how the brain works when injuries to a specific brain area result in the identical loss of learning ability, but we cannot study individual variation in the neural architectures of memory. Last, we want to understand directly how memory operates in the healthy brain. Advances in functional neuroimaging have allowed us to now go beyond patient studies in these ways.

Functional Neuroimaging

Functional neuroimaging studies typically use positron emission tomography (PET) or functional magnetic resonance imaging (fMRI) that permits the visualization of mental processes in the healthy brain and allows for the design of psychological experiments targeted at specific memory processes. These tools are limited, however, by several factors. PET and fMRI derive their signals not from neural activity, but rather from changes in blood flow or metabolism correlated with neural activity. In the case of a PET scan, the local vascular changes affect the distribution of a radioactive substance injected for the scan. The fMRI measures changes in magnetic properties that are blood-oxygen-level dependent: when the mind is engaged in doing something, it activates certain parts of the brain, and the neurons there start firing. Oxygen is needed to support

those neurons, so, very briefly, there's a dip in the oxygenation in the vasculature surrounding those neurons. We can't measure that dip—it's too brief and weak to be measured reliably. Instead, what we measure is a secondary, compensating mechanism that shunts a huge amount of extra oxygenation to active tissue. It's as if the brain is designed to not fail at its given task, so it overcompensates by sending far more oxygenation to support the tissue than is needed. That change in the oxygenation level alters the magnetic property of the tissue, which is what the fMRI actually measures.

PET was developed before fMRI and has enabled spectacular work, allowing us to visualize mental operations occurring in the human brain. The primary difference between PET and fMRI is that PET requires the injection of a radioactive substance, which is not only expensive but makes many researchers hesitant to use it for pure research, particularly with children. fMRI is a natural procedure that involves no drugs or electrical stimulation and thus is noninvasive, less expensive, and, for most studies of the brain, more precise in brain location. Today it is available for research in far more university settings than PET.

Making Memories

In many ways, what we know is who we are—we know our names, our loved ones, the values we hold, the abilities and disabilities we have, the facts of the world we inhabit. We

knew none of this at birth—we came to know all of this through the making of memories. But we make memories in a highly selective fashion. We experience many things, but remember only a small fraction of those experiences. That selection, therefore, is essential in establishing which memories make us who we are.

To demonstrate that we are selective in which experiences we remember, consider something that you have seen at least 10,000 times by the time you're 40 years old: a penny. Does Lincoln's profile on the penny face left or right? What, if anything, is above, below, to the right, or to the left of Lincoln's profile? You probably have to guess to answer that, despite 10,000 exposures to that information. The important question this raises is, what brain mechanisms determine what we will remember and what we will forget?

The making of a memory involves three stages: (1) encoding (what happens in your brain as you record an ongoing experience); (2) storage (maintaining knowledge of that experience); and (3) retrieval (finding and using that knowledge at a later time). Injury to the medial temporal lobe prevents amnesic patients from remembering a new experience, but we cannot tell if the medial temporal lobe is essential for encoding, or storage, or retrieval, because damage to any one or more of these memory stages would ultimately result in failed remembrance. Further, the medial temporal lobe region is comprised of a number of small, adjacent structures including the hippocampus, subiculum, entorhinal cortex, perirhinal cortex, and parahippocampal cortex. Amnesic patients typically have injury to

many of these structures, so we cannot learn about the different roles these specific structures play in human learning and memory.

Unlike studies of patients with brain injuries, fMRI experiments can distinguish between the encoding and retrieval of memories by measuring brain activation at each stage of memory. In one experiment related to visual memories, six normal subjects each underwent four fMRI scans, each consisting of 24 color pictures of indoor and outdoor scenes selected to be similar in complexity and quality. During scanning, subjects judged whether each picture depicted an indoor or outdoor scene. Thirty minutes after scanning, the subjects were given an unexpected memory test. They were shown the 96 previously seen pictures and 32 new pictures, presented individually on a computer monitor, and were asked to judge whether or not they had seen each picture during scanning.

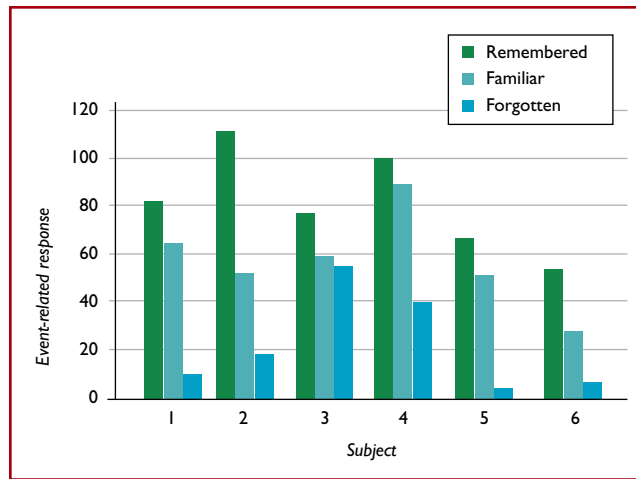
For pictures judged as previously seen, the subjects reported whether their judgment was based on a distinct recollection of having seen the picture (“remembered”) or on a less certain feeling (“familiarity”). Thus, each studied picture had one of three memory outcomes—well remembered, familiar but not well remembered, or forgotten (pictures that subjects had seen but denied having seen).

We examined what brain regions were involved in selecting which ongoing experiences would be powerfully encoded and therefore later remembered, versus weakly encoded and therefore later forgotten. Although many regions of the brain were activated upon presentation of the pictures to the subjects,

only those areas of the brain associated with declarative memory showed reliable correlations with subsequent memory.

The fMRI scans revealed seven focal regions where the magnitude of activation reliably predicted whether pictures would be remembered, familiar, or forgotten—six of which were in the bilateral parahippocampal cortex. The responsiveness of these brain regions seemed to determine the mnemonic destiny of ongoing experience—whether that experience was fated to be remembered or doomed to be forgotten.

Figure 1 illustrates the mean response in the parahippocampal areas, showing significant correlation with subsequent



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Figure 1. Relations Between Brain Activation and Memory in Individuals

memory: brain activations were greater for remembered than for familiar pictures and for familiar than for forgotten pictures.

The contribution of other brain regions to the making of memories is also being clarified via brain imaging. For example, we know from behavioral studies that people remember information better when they think hard about that information (elaboration) and when they think about the conceptual nature of information rather than its surface or sensory qualities. Activation in the frontal lobe has been associated with conceptual elaboration that enhances memory. We also know that some memories retain perception-like features, when we feel like we can remember the actual sound we heard or sight we saw. Activation has been observed in auditory regions of the brain when people remember an experience that was auditory and in visual regions when the original experience was visual. The perceptual modality of an experience may be part of the memory we store in our brains; when we remember that experience, the relevant perceptual record of that experience is accessed. Within visual regions, there are differences in brain activation as people remember pictures (a drawing of a cat) or words (having seen the word “cat”). Thus, various neocortical regions appear to store specific features of an experience.

The most vivid memories we have are those that are the most emotionally salient—for example, memories about people we love or things we fear. Patient evidence that the amygdala is essential for enhancing memory on the basis of emotion is corroborated by imaging studies. In one study, people viewed a va-

riety of neutral and emotionally provocative scenes and rated the intensity of their emotional response to each scene. More intensive subjective emotional experience was associated with greater amygdala activation. This is an example in which fMRI can illuminate the brain basis of how we feel, of subjective personal experience. When memory for the scenes was tested three weeks later, amygdala activation was relevant only for scenes rated as most intense. For those most intense scenes, greater amygdala activation during encoding three weeks ago predicted a greater likelihood for remembering the scenes. Thus, the amygdala appears to play an essential and selective role in enhancing memory for emotional experiences as well.

The engagement of the amygdala in response to emotionally charged displays shows considerable variation among individuals. For example, fMRI studies have shown that subjects' personalities affect amygdala activation in response to positive and negative pictures. Highly reliable personality tests can identify whether subjects are introverted or extroverted; amygdala activation in introverted subjects is significantly greater in response to negative than to positive images, whereas the reverse is true for extroverts. That is, amygdala activation in extroverts is significantly greater in response to positive images, such as happy faces, and exceeds the response of introverts to the same objective experience (viewing happy faces). These results demonstrate that personality traits influence some brain responses to emotionally salient perceptions. It seems that the amygdala acts as a sort of memory filter based on one's personality predisposition. Extroverts seem to have greater responses

to positive stimuli, and these greater responses may lead to a view of the world as more full of positive experiences.

Quite striking differences in amygdala responses have also been reported between men and women in several papers. Aging also alters emotional memory formation and amygdala function. In the course of normal aging, there is a disproportionate loss of negative as opposed to positive memories. We think this reflects a change in priorities at different stages in life: at a certain age we may achieve a sort of emotional wisdom that focuses on a day-to-day positive outlook that can be measured both psychologically and physically in the brain. Indeed, imaging has shown that healthy older adults have a disproportionate decline in amygdala activation in response to negative relative to positive scenes. This may be part of the change in brain functions that supports a positive bias in normal aging. Thus, imaging is beginning to reveal how human individuality in many dimensions (whether we are extroverted or introverted, a man or a woman, younger or older) may be instantiated in the brain.

Suppressing Memories

We seldom want to forget experiences we have had or information we have learned, but there are situations in which the voluntary suppression of memory is desirable. For example, individuals who have had traumatic experiences can be haunted by memories of those experiences. Environmental cues can evoke

memories that promote craving in people trying to escape addiction. Even in everyday life, some unpleasant or embarrassing experiences might be better forgotten. Under such circumstances, the selective and voluntary suppression of a memory may be a source of resilience.

Freud introduced ideas about repression and suppression of memories that have become both widely known and highly controversial. Often repression refers to involuntary blocking of a memory, whereas suppression refers to voluntary blocking of a memory.

The controversy arises from the difficulty in scientifically demonstrating that a memory is truly repressed or suppressed. Claims of repressed or suppressed memories are often made in situations involving many complex emotions and motivations, such as psychotherapy or court cases. Remarkably, the first scientifically controlled and validated demonstration of suppressed memories occurred only a few years ago. We subsequently used the same paradigm to discover what neural mechanisms in the human brain allow for the voluntary suppression of unwanted memories.

In this study, healthy young volunteers learned three sets of moderately related pairs of words (a well-controlled laboratory paradigm, but far from the circumstances of real-life trauma), such as ORDEAL-ROACH, STEAM-TRAIN, and JAW-GUM. They learned that when presented with the first word of a pair (for example, ORDEAL), they should recall the second word from memory (ROACH). After learning all the pairs, subjects participated in an imaging session. One set of word pairs was

not used in the imaging session and served as a baseline measure (BASELINE). During scanning, a second set of word pairs was used in a REMEMBER condition. When subjects saw “STEAM- ?” in green letters, they were to think of the word learned with that word (TRAIN). The third set of word pairs was used for the SUPPRESSION condition. When subjects saw “JAW- ?” in red letters, they were asked to *not* think of the associated memory (GUM). After scanning, subjects were tested for their memory of all the word pairs. Their memory was best for the word pairs in the REMEMBER set that had been studied repeatedly before and during scanning. Their memory was second best for the BASELINE set, which had been studied before but not during scanning. Memory was worst for the SUPPRESSION set, showing that voluntary suppression of those learned words pairs during scanning had blocked memory for the word pairs even when people later really tried to remember those word pairs. This was evidence of memory suppression.

There were two main findings associated with the voluntary suppression of memories in the brain. First, there was greater activation in the hippocampus for remembering than for suppressing memories. This is consistent with the important role of the hippocampus in memory formation discussed above. Second, there were many areas more active for suppression than remembering, especially in the frontal lobe. The frontal cortex is known to be essential for the voluntary control of thought. Thus, suppression of a memory may involve the recruitment of frontal cortical areas that keep a memory out of

mind and prevent the hippocampus from making that memory available to conscious report.

Skill Learning and Brain Plasticity

As reviewed above, many forms of skill learning involve procedural memory systems that do not include the medial temporal lobe. Brain imaging has allowed us both to discover the neural systems that mediate various forms of skill learning and to see how those systems alter during the course of skill learning. For example, when people are asked to read mirror-reversed words, they read them slowly and make more errors than when reading normal words. With practice, people become faster and more accurate in reading the mirror-reversed words. Amnesic patients cannot remember what words they have read, but they gain the ability to read mirror-reversed words normally.

A brain imaging study took before and after snapshots of brain activation in healthy people gaining this skill. In the first “before” session, imaging occurred while subjects read mirror-reversed words slowly. Then, subjects practiced reading mirror-reversed words on several occasions during a week. The practice led to a proficiency in their speed and accuracy of reading the mirror-reversed words. Finally, in the second “after” session, imaging was performed while subjects read mirror-reversed words quickly. So, a comparison could be made within the same brain between initial, unskilled performance versus final, skilled performance. During initial, unskilled

performance, there was a great activation in the right parietal cortex, an area of the brain known to be important for spatial cognition. Presumably, subjects were initially treating the mirror-reversed letters as unusual spatial displays that required the mental rotation of each letter. This activation disappeared during final, skilled performance. On the other hand, a new activation appeared in the second session in the left temporal cortex, an area of the brain important for language and reading. Perhaps subjects had learned to map the mirror-reversed text to neural systems typically involved in reading. Thus, what was initially a spatial problem became a verbal task through practice.

Functional neuroimaging can reveal alteration in brain networks used by people as they acquire a new skill. This alteration presumably reflects learning-related physical changes in brain connectivity, known as brain plasticity. The same principles of brain plasticity probably underlie many forms of skill learning, from learning to read to learning mathematics to gaining skill in university administration. Functional neuroimaging now allows us to visualize how the brain changes as a skill is gained.

Conclusion

Rapid advances in the field of cognitive neuroscience have been made possible over the last decade or so by technological developments, particularly the emergence of functional mag-

netic resonance imaging. The ability to create images of brain activity in healthy people holds tremendous potential for deepening our understanding of the effects of our experiences and personal traits. The implications of this knowledge for teaching and learning are vast—and developing quickly. Indeed, we are close to uncovering what will arguably be valid alternatives to testing for measuring the efficacy of various teaching methods and learning. And while it is sensible to be cautious as we enter this new realm of possibilities, it is also advisable to prepare for what the future holds by thoughtfully encouraging and considering research that can potentially make an important contribution to the quality of people’s education and lives.

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