Seeing the Mind

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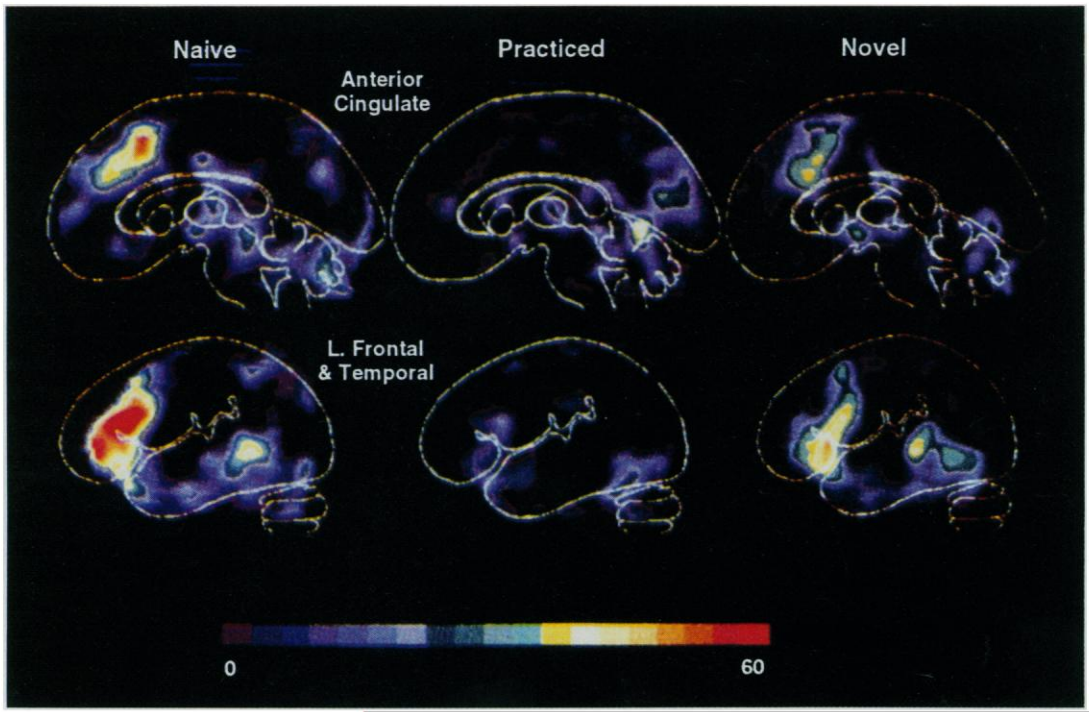
The microscope and telescope opened vast domains of unexpected scientific discovery. Now that new imaging methods can visualize the brain systems used for normal and pathological thought (*1*), a similar opportunity may be available for human cognition. Some of the data generated with these imaging techniques fits with current ideas, but much of the new information will require new theories. Here, I review three areas of cognitive psychology in which our ideas are changing as a consequence of these new results: the localization of mental operations (*2*), the identification of separate brain control systems (attentional networks) (*3*), and the convergence of sensory input and mental imagery in the same brain areas (*4*). New theories based on these findings are likely to change our interpretation of the meaning of what has already been seen and to suggest new experiments.

The major new anatomical tools all image aspects of blood vessel function that reflect nearby neuronal activity. The two most successful so far are positron emission tomography (PET) (*1*) and magnetic resonance imaging (MRI) (*5*). Although the fundamental links between blood flow and neuronal activity remain obscure, it is clear that the measurement of cerebral blood flow can tell us where neurons are more or less active in comparison to a control condition. Of course, an increase in neuronal activity may signal either inhibitory or excitatory synaptic events, so these measures must also be related to the efficiency of task performance (*2*). In addition, blood flow lags behind neural activity in time, requiring the use of other methods with time resolution in the millisecond range if changes in anatomy are to be traced dynamically during mental tasks. Methods based on noninvasive electrical and magnetic measurements (*6*) will be important in studying these dynamic changes when they can be related to the emerging functional anatomy from PET and MRI studies.

It is a popularly held belief in psychology that the cognitive functions of the brain are widely distributed among different brain areas. Even though the organization of the nervous system suggests that sensory and motor functions are localized to specific brain regions, the failure of phrenology and difficulties in locating memory traces for higher functions have led to a strong reaction against the notion of localization of cognitive processes (*7*). Nevertheless, imaging studies reveal a startling degree of region-specific activity. The PET studies show clearly that such visual functions as processing color, motion, or even the visual form of words occur in particular prestriate areas (*4*). This localization extends beyond sensory systems. When thought is analyzed in terms of component mental operations (*2*), a beautiful localization emerges. In word-reading studies, words activate specific posterior visual areas that are not affected by consonant strings, and specific frontal and temporo-parietal areas are active when subjects are required to indicate the use of a noun (for example, hammer-pound) or its classification into a category (hammer-tool) (*5*). The brain activation accompanying this form of semantic processing is illustrated in the figure, in which the subjects were asked to determine the use of visually presented nouns (*8*).

The PET method used in the figure required averaging among subjects within a normalized brain space and revealed the surprising fact that the anatomy of this high-level cognitive activity was similar enough among individuals to produce a focal average activation that was both statistically significant and reproducible (*2*). Functional MRI studies allow examination of brain activity in each individual in relation to their own brain structure and are likely to extend the PET findings so that individual differences in brain anatomy can be related to mental operations (*5*).



Thinking. A PET scan of the left hemisphere while the subject thinks of a use for each visually presented noun. (The neural activation for reading the nouns aloud is subtracted from the image.) The left column illustrates the initial performance of the task, the middle column is the activity after practice with the same list of words, and the right column is after switching to a new list. The top row (medial surface) shows activation of the anterior cingulate, thought to be involved in focal attention. The bottom row (lateral surface) shows language-specific activation in the frontal lobe and Wernicke's area (*8*).

Imaging has also taught us how our brain pays attention to certain stimuli. A common method in functional imaging is to compare a passive control condition with active conditions, such as generating the meaning of a word (*9*). Some brain areas are activated when subjects have to perform active tasks irrespective of their content. These areas appear related to focal attention, as described in cognitive studies. In the figure, when subjects are first gener-

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ating the meaning of nouns, there is activity in a midfrontal area called the anterior cingulate gyrus, but after practice with a list, the activity is reduced and returns when a new list is given. Areas in and around the anterior cingulate are active during tasks that involve words, spatial objects, or motor learning and do not seem to be specific to any particular domain of activity (*4, 10*). During generation of novel word meanings, in addition to the anterior cingulate, two left cortical areas known to be related specifically to word processing are also activated. In general, attentional networks appear to comprise a number of subcortical areas that may differ depending upon whether their function is to orient to sensory stiumli, maintain the alert state, or carry out a variety of executive operations (*3*). These anatomical results open up the possibility of progress in many topics: what brain structures are involved in awareness, in voluntary control of information storage, in motor responding, and in maintaining current goal states (*11*).

The new brain imaging techniques have revealed a convergence of what we see and what we think; thinking about a telephone activates some of the same brain areas as seeing a telephone. Specific brain areas are activated when people are presented with sensory stimuli. These activations are in the areas one would expect on the basis of the type of sensory stimulation involved (*4*). For example, activations have different locations within the primary visual cortex when visual events are presented at different retinal locations, as would be expected from many visual mapping studies (*12*). When the visual stimuli utilize color or motion, prestriate areas become active that correspond to what would be expected from studies of cellular recording in monkeys (*4*).

When subjects are instructed to attend to color or motion, there is an increase in activation in the same prestriate areas that process these sensory dimensions (*4*). Moreover, if subjects are asked to create a visual image based on their remembered knowledge of a visual form, areas in the visual system also show increased activation (*13*). These findings support the general idea that processes initiated internally from instructions can activate the same sensory areas where these computations are performed on actual sensory events. The finding that imagery and perception share some of the same neural machinery was anticipated by many cognitive theories, but the topic had been subject to seemingly endless dispute before this evidence from brain imaging methods was available (*14*).

Understanding of how voluntary attention affects the activity within sensory-specific cortex requires an analysis of the brain circuits by which higher level instructions influence sensory areas. Because of the relatively long delay between neural changes and the changes in blood vessels, it is useful to relate the functional anatomy method of PET and MRI to time-dependent measures involving surface or depth recording of electrical or magnetic potentials (*6*). These methods allow a precise measurement (in milliseconds) of changes between experimental and control conditions and can be used for tracing the circuitry of a particular mental activity. Methods of recording electrical and magnetic activity outside the head have improved in recent years and we now know that there are specific generators of these signals. This knowledge has already helped to spur developments relating the two types of measures (*15*).

The ability to study the human brain by physiological methods is likely to transform our understanding of what the brain does. If the neural systems used for a given task can change with 15 minutes of practice as in the figure, how can we any longer separate organic structures from their experience in the organism's history? We must be able to trace the changes in the brain that occur with experience. Individual genetic makeup and learning together shape brain structure. We now have methods to understand how this takes place and what it means for the limits of human potential.

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Molecular Genetics of Neurological Diseases

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Over the past century physicians, primarily neurologists, have meticulously collected and categorized families with Mendelian-inherited neurological syndromes. The phenotypes of these disorders, of which there are more than 1000, have provided the framework in the past decade for rapid advances in identifying genes that cause them. To date, mutations of genes have been characterized in more than 40 disorders affecting the central and peripheral nervous system, and precise chromosomal localizations have been determined in many more (*1*). Genes have been identified for Duchenne muscular dystrophy, neurofibromatosis type 1 (NF1), Huntington's disease (HD), familial amyotrophic lateral sclerosis, neurofibromatosis type 2 (NF2), and for several muscle disorders including myotonic dystrophy, hyperkalemic periodic paralysis, and malignant hyperthermia.

These discoveries have led to several new concepts that have caught the attention of human geneticists. Perhaps the most important is the recognition that mutations consisting of unstable trinucleotide repeats within exons or in nonexpressed regions near a gene correlate with the disease phenotype (*2*). To date, five neurological disorders, several of which appear first at mid-

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