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fMRI Reveals Dynamics of Working Memory

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For the first time, advanced imaging techniques have revealed the moment-by-moment brain activity involved in seeing a face or a series of letters, holding it briefly in working memory, and then recalling it. Two research teams supported by the National Institute of Mental Health (NIMH) report on the studies using functional magnetic resonance imaging (fMRI) in the April 10 *Nature*. The new studies are the first in humans to demonstrate sustained activity in the prefrontal cortex while information is held in mind.

Contrary to prevailing theory, one of the studies shows that brain circuits for seeing and remembering are not separate. Rather, they span processing centers arranged along a **"continuum,"** each with its own mix of somewhat overlapping functions -- from "mostly perceptual" areas in the back of the brain, to "mostly memory related" regions in the front, report Susan Courtney, Ph.D., and colleagues of the NIMH, who examined visual memory for faces.

A research team led by NIMH grantee Jonathan Cohen, M.D., Ph.D., at Carnegie Mellon University and the University of Pittsburgh, scanned subjects during a task in which they had to hold in their minds increasingly longer series of letters. **Brain areas involved in memory** distinguished themselves by working harder as the load got heavier.

Brain circuits that process short-term information differ from those that store long-term memory, much as a computer's RAM (random access memory) differs from hard disk memory. Working memory is used for such tasks as holding a phone number in mind just long enough to write it down, as well as in higher cognitive "executive" functions -- planning, organizing, rehearsing. Recent evidence points to an impairment of working memory systems in schizophrenia* and other brain disorders.

The new studies are the first to examine the time-course of working memory using fMRI, which tracks telltale signals emitted by oxygenated blood in a magnetic field to reveal what parts of the brain are active at any given moment. Whereas earlier brain imaging studies employing radioactive tracers could only see averaged activity sustained over minutes, fMRI captures events that last just seconds.

This higher speed resolution reveals both the location and timing of brain events, permitting researchers to pinpoint and quantify the amount of activity related to perception and memory tasks for each brain area involved.

The NIMH researchers scanned the brains of 8 individuals while they performed a visual task. Subjects viewed a face on a computer monitor for 3 seconds, held the face in memory (with no visual stimuli) for an 8 second pause, and then viewed a second face for 3 seconds. They pressed a button to indicate whether or not the faces matched. Subjects were also shown scrambled faces under the same conditions, to control for mere visual stimulation.

Areas at the back of the brain activated only briefly (when the face was shown), confirming their primary role in perceptual processing, while **front areas** stayed active during the pause, signaling a predominant role in working memory. Yet, some rear areas activated somewhat during the pause, while some front areas responded modestly just to visual stimuli. Strikingly, through **six key areas** along the continuum from back to front, response to visual stimulation dropped steadily, while response during the pause steadily increased.

"We knew that the brain performs complex tasks by dividing them up and assigning jobs to specialized structures. But thanks to fMRI, we can now see that the division of labor isn't as clear-cut as we used to think," said Leslie Ungerleider, Ph.D., chief of the NIMH Laboratory of Brain and Cognition, who, along with Drs. James Haxby and Katrina Keil, collaborated with Courtney on the study.

A similar theme emerged from Cohen's study, which used somewhat different methodology. Ten subjects were scanned while they held in working memory increasingly longer sequences of consonants and were asked to match letters with ones they had seen previously.

Activity remained unchanged in rearmost visual processing areas, but as the memory load got heavier, activity increased in the front areas, which are more involved in working memory.

Two different patterns of activity emerged, depending upon the type of working memory function being performed. **A key part of the prefrontal cortex and certain other brain areas** stayed active, signaling that they were involved in the active maintenance of information in working memory. Other areas activated only momentarily, but more robustly, as the memory demands increased. This indicated that they were involved in briefer working memory functions, such as decision processes or updating the contents of memory.

Both the Courtney and Cohen findings run counter to a long-held assumption among neuropsychologists that the prefrontal cortex is the seat of "executive" control and not involved in the active maintenance of information in working memory. Cohen and colleagues suggest that the prefrontal cortex's role has more to do with "the type of information that is actively maintained or the conditions under which maintenance is required."

For example, animal physiology and human lesion studies suggest that some of the more posterior areas involved in working memory can't hold on to information in the presence of distractions, while the prefrontal cortex can.

"A football player can get hit by another player and fumble the ball, or just stumble and lose control of it. One job of the prefrontal cortex is to try to hold on to that ball -- not lose information in the face of interference or distraction," explained Cohen. The prefrontal cortex likely also specializes in handling information needed to guide action -- set goals, plans, etc -- and understand the context of words, he said.

Collaborating with Cohen in the study were: Dr. Todd Braver, Carnegie Mellon University; Drs. William Pearlstein, Leigh Nystrom, and Douglas Noll, University of Pittsburgh; Drs. John Jonides and Edward Smith, University of Michigan.

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*Schooler, Carmi., et al. "A time course analysis of Stroop interference and facilitation: Comparing Normal Individuals and Individuals with Schizophrenia," Journal of Experimental Psychology: General, Vol.126, No. 1, March, 1997, 19-36

*Cohen, Jonathan, et al. "Issues Concerning Relative Speed of Processing Hypotheses, Schizophrenic Performance Deficits, and Prefrontal Function: Comment on Schooler et al," Journal of Experimental Psychology: General, Vol.126, No. 1, March, 1997, 37-41.

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