NEUROSCIENCE

A Generation Gap in Brain Activity

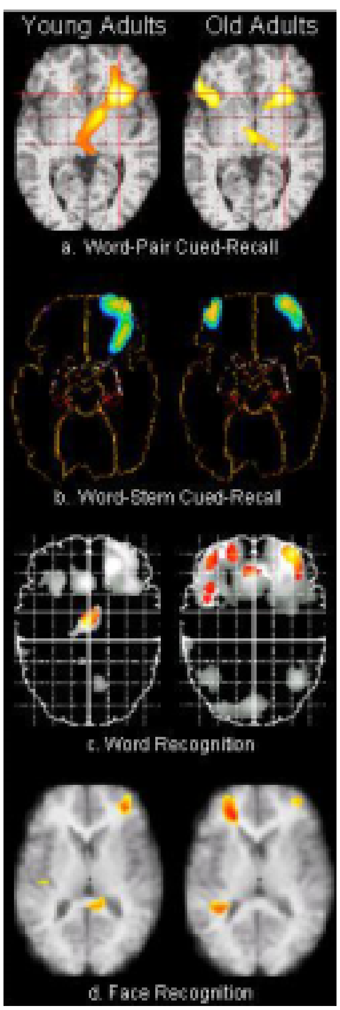
As the field of cognitive neuroscience matures, researchers are starting to see how the brain's behavior changes with advancing years

As people get older, some things just don't work the way they used to. Some of these changes seem straightforward: A once cast-iron stomach begins to balk at greasy food, or knees complain after too many trips down the ski slopes. But what happens to the aging brain has been more mysterious.

By some measures brain function appears to decline as we age. Behavioral studies have shown, for example, that older people are slower on easy tasks and less accurate on difficult ones; their memories are leaky; they're easily distracted in tests of attention. But some of these findings might simply be a function of what researchers are able to study in the lab. "Older adults don't show impairments in everyday life," says Denise Park of the University of Michigan (UM), Ann Arbor, indicating what she calls a "disconnect" with the lab results.

Hoping to see how the brain changes as it ages, researchers have increasingly been using imaging techniques for the past 5 years or so. Although they have uncovered some striking patterns—as shown by presentations at the inaugural meeting of a conference* dedicated to the cognitive neuroscience of aging—they also have added to the mystery. Some researchers have observed that certain brain areas physically shrink over time, whereas others have found that the patterns of neural activity in 60- or 70-year-olds often bear little resemblance to those in the 20-something subjects who populate most brain functional imaging studies. "We see one set of activations in young people, but older subjects are quite strikingly different," says Park.

Exactly how these changes relate to cognitive failings in old age remains unclear, however. Indeed, a major debate at the meeting centered on whether the shifts in brain activity are good news or bad. Older people might exercise extra brain areas to compensate for a decline in normal function, some suggest, whereas others view the change as a symptom or even a cause of age-related mental lapses. As John Gabrieli of Stanford University points out, "so many things are going on at once" as the brain ages that the challenge is to figure out "which changes in the brain correspond to which changes in the mind."



Mulling it over. Young people use one hemisphere for many tasks; their elders use both.

CREDITS: (PANEL A) R. CABEZA/DUKE UNIVERSITY; (PANEL B) BLACKMAN *ET AL.*, *THE JOURNAL OF COGNITIVE NEUROSCIENCE* 9, 378 (1997); (PANEL C) MADDEN *ET AL.*, *HUMAN BRAIN MAPPING* 7, 115 (1999); (PANEL D) C. GRADY/UNIVERSITY OF TORONTO

Answers to such questions might help researchers with another crucial goal, says UM's Patricia Reuter-Lorenz: figuring out which mental skills are hard-wired into specific brain regions and which can be accomplished by more than one set of regions. The latter might be more amenable to yet-undiscovered cognitive or pharmacological interventions that allow people to compensate for sputtering brain circuits.

The march of time

Death comes for some brain neurons before others. Naftali Raz of Wayne State University in Detroit has depicted the "neuroanatomy of aging" by imaging specific brain regions in healthy people of various ages. These cross-sectional studies indicate that some areas are stable over time, others undergo a seemingly inexorable decline, and some reach a turning point and only then start to dwindle.

One of the better preserved parts of an older brain is the occipital cortex, the region at the back that largely handles visual information. The frontal lobes are less fortunate. Raz found that one section, the so-called dorsolateral prefrontal cortex, shrinks by about 5% per decade between the ages of 20 and 80. The hippocampus, a part of the brain crucial for memory, holds its own until middle age. But after age 45 or so, it loses about 7% of its volume per decade.

Comparisons between different people of different ages, no matter how well matched they are on measures of health or education, leave open the possibility that factors other than age might account for some of the apparent changes. But Raz says they don't appear to. At the meeting, he presented new data from a longitudinal study that tracked the same subjects' brains for 5 years, confirming the pattern seen in the cross-sectional studies.

Gabrieli points out that it's tricky to "relate specific biological changes to specific cognitive changes," but he says the patterns seen by Raz and others might reflect what he identifies as two major changes that shape the aging brain. The first is a gradual, lifelong decline in circuits that include the frontal lobes. Thanks to this effect of age, over time people are slower to process complicated visual scenes, get tripped up on complex reasoning tasks, and have a lower capacity for so-called working memory, or keeping thoughts in mind for later use. As behavioral tests on older subjects have shown, this slowdown hits pretty much everyone and is part of normal aging.

The second effect, related more directly to memory, hits some people harder than others. It centers on the hippocampus and surrounding tissue called the entorhinal cortex. Gabrieli and colleagues have followed a group of healthy old people since the early 1990s. Some have very good memories; others are more forgetful, although none have been diagnosed with Alzheimer's disease. Those with good memories have entorhinal cortices that look pretty hearty, whereas in those with the worst memories, the region is relatively small—a possible early sign of Alzheimer's, Gabrieli says.

A whole-brainer

Neuroimaging studies have uncovered another major shift that occurs as people age—one some researchers see as hopeful. Neurobiologists have long known that the left and right sides of the brain have specialized functions. When young people exercise their so-called verbal working memory—say, by keeping a list of words in mind for a few minutes—the left frontal lobe lights up.

* Symposium on Neuroscience, Aging, and Cognition, San Francisco, 12–13 April.

In contrast, when they juggle spatial information, such as recalling where a dot appeared on a computer screen, the right frontal lobe is in charge.

But older people, it appears, are more broad-minded: They use both frontal lobes when performing either type of working memory task. "We saw this in 1997 but didn't put too much importance in it," says Roberto Cabeza of Duke University in Durham, North Carolina. But as study after study began uncovering the same double activity, "it started looking like a phenomenon." The "long-standing view" in neuroscience, Reuter-Lorenz says, is that certain parts of the brain perform certain functions, but studies showing widespread activation in older people make it clear that this "may have to be revised."

People are still trying to figure out what the phenomenon means. One question is whether the difference is "neurogenic"—due to age-related changes in neural connections—or "psychogenic"—a side effect of older people using different mental strategies to solve the same problem. For instance, an older person wary of relying on spatial skills to remember a location might come up with a verbal description of the spot, thus calling the left hemisphere into play.

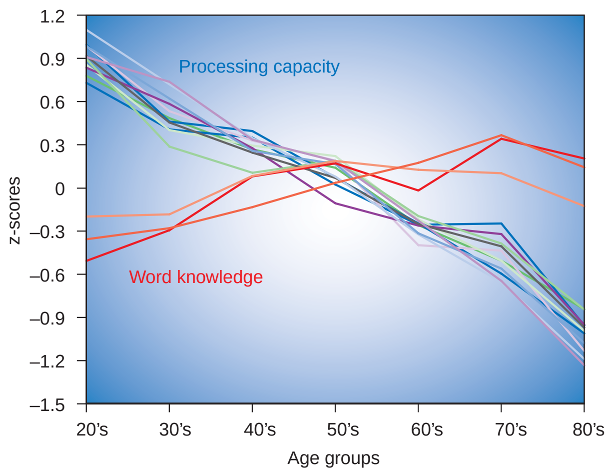
Cabeza says that the evidence points to a neurogenic source in most cases: The furious firing in the front of older brains shows up whether people are remembering pairs of words, recognizing faces, or preparing to match up locations in space. It's unlikely that the strategy would work well in such different tests, he maintains.

However it arises, loss of specialized activity in the brains of older subjects could be an unfortunate development. Having specialized brain regions is generally thought to be a good thing—a division of labor that, for example, lets the left hemisphere build sophisticated language abilities while the right concentrates on navigation.

When a younger person is working a verbal puzzle, Randy Buckner of Washington University in St. Louis and others have shown, there's some activity in the right hemisphere at first, but it's quickly squelched. This efficient silencing is lost in older people, Buckner suggests, through a breakdown in communication between the hemispheres. The two sides of the brain are "just not recruited well," he says—a sign of underlying pathology that creeps in with age.

Others look on the bright side. Reuter-Lorenz, for one, sees extra frontal activation as a "correlate of graceful aging." The elderly subjects in her experiments are just as accurate in working memory tests as young college students. And in some cases, the fastest old subjects are the ones with the greatest activity in the "extra" hemisphere. Older people might be "recruiting additional brain areas in a compensatory way," she says, and brain imaging studies are capturing what is simply a healthy response to what she calls the "decline in efficiency of circuitry typically used in younger brains."

Cabeza tested this notion directly. He classified his older subjects as either high-functioning or low-functioning according to a battery of standardized tests. Then he observed their brains under positron emission tomography (PET) scans as they recalled pairs of words. In young subjects, the left side of the brain lit up, as expected, during this verbal task. Old subjects with poor memories likewise relied upon the left hemisphere. But old subjects who performed as well on memory tests as young people used both the right and left hemispheres, he reported at the meeting—suggesting that extra activation is indeed beneficial.



Measurable skills. With age, people perform worse in spatial, memory, and problem-solving tests—but their vocabularies grow.

Potentially compensatory changes aren't limited to the frontal cortex, as shown by Cheryl Grady of the Rotman Research Institute at the University of Toronto. When young people try to recognize pictures of faces, a constellation of brain regions lights up. But Grady and her colleagues found that in older people matching faces, accuracy was correlated with activity in the amygdala—a region that normally processes emotions. Older subjects might pay more attention to facial expressions to aid their memories, Grady says, possibly in a case of psychogenic compensation.

But even Cabeza, Reuter-Lorenz, and others who suggest that extra activity helps an older brain cope admit that what they see as compensation might come at a cost. The frontal lobes do most of the brain's glamorous work—the problem solving, working memory, and other tasks that fall under what psychologists call "executive control." If what's easy for a 20-year-old requires a lot of effort when one is 70, Reuter-Lorenz asks, "what happens when the going gets rough?" Other studies have shown that even young subjects sometimes use both hemispheres if they're really concentrating; perhaps older subjects tax the frontal lobes' processing power even during simple tasks, she suggests, and aren't able to access it in more trying times.

It's also not clear when the differences in brain activation kick in—whether 40-year-olds' frontal lobes act more like those of their children or their parents. "We know nothing about middle-aged adults," says Park of the dearth of functional imaging studies that include people from a range of ages.

Wisdom

Pinning down where and when certain abilities falter with age might suggest ways to counteract the changes. Finding out what happens when extra areas of the frontal lobe are recruited in older people is "something that's on a lot of people's minds," says Reuter-Lorenz. Some abilities might be hard-wired, performed by strictly defined circuits whose signals can't be rerouted. But others might be amenable to compensation from more spry parts of the brain.

Despite some grim findings of cognitive loss described at the meeting, Park points out that people have plenty of areas of expertise that are preserved or even grow over time. For example, vocabulary tests are one of the few lab measures that show a reliable advantage for older subjects—which should come as some comfort to those who have been trounced by a great-aunt in a game of Scrabble. But researchers don't have standardized tests for other advanced skills—knowledge of banking, say, or how to navigate a city's streets. "People develop a large mental scaffolding for expertise," says Park, "and it's relatively easy to hang new information on a scaffold created over time."

Researchers have even less of a handle on how to measure intangible qualities, such as wisdom. "We all hypothesize that as you get older, you get wiser," says Park. But it's awfully tough to find a quantitative measure, much less one that can be assessed while the aged but wise recline in a PET scanner.

–LAURA HELMUTH