

Catalyst

R e s e a r c h

The Aging Brain

**Brandeis scientists
tackle Alzheimer's
and Parkinson's at
warp speed**

**Mental exercises to
sustain the brain**

**Poor hearing may
cause poor memory**

Dear Reader



Think about the fact that in the next 50 years, 25 percent of the world's population will be at least 65 years old. The impact of the aging process across the globe will be felt in many aspects of our lives—from the creation and movement of goods and services to the politics and public policies that will deal with age-related issues worldwide. Just imagine the pressure that these numbers will place on the economics of the health-care delivery system as America's aging population surges.

The aging process is, after all, a universal one. Aging affects each of us to some degree uniquely, yet it does not favor gender, race, ethnicity, or status, uniting us instead through its own trademark characteristics. At the core of the aging process is, of course, the brain. This issue of *Catalyst* explores the inexorable process of aging by focusing on the complex changes that take place in the brain over time.

Will the brain let us down in our dotage? Neuroscientist Art Wingfield suggests not—describing ways that the aging brain compensates—while psychologist Margie Lachman says we have more control over the process than we think. Research on healthy aging characterizes much of the work of Brandeis scientists. You will also want to learn more about how two visionary scientists here are accelerating the discovery of drug treatments for crippling neurodegenerative diseases like Parkinson's and Alzheimer's.

Take a few minutes to learn more about some of the groundbreaking aging research that will affect us all. I hope you enjoy this issue and welcome your comments. Please write to me at catalyst@brandeis.edu and visit the website at brandeis.edu/catalyst, where you will find news of other age-related research initiatives at Brandeis.

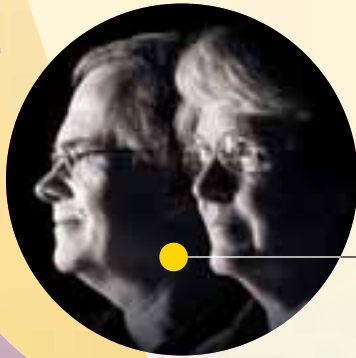
I look forward to hearing from you.

A handwritten signature in black ink that reads "Maria Pellegrini". The script is elegant and cursive.

Maria C. Pellegrini, PhD
Vice President for Research

Catalyst

Volume 1 Number 2



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About Face

Research demonstrates that first impressions are far more than skin-deep, generating conclusions about others' psychological traits based on their facial appearance. Moreover, there is widespread agreement on what particular facial characteristics suggest, says psychologist Leslie Zebrowitz, the Manuel Yellen Professor of Social Relations. A "baby face," for example, with such features as a round face, large eyes, and a small nose and chin, suggests naiveté and weakness, while competency is associated with facial maturity. A pioneering researcher in the field of facial impressions, Zebrowitz recently won funding from the National Institutes of Health to research the role of facial qualities in forming age stereotypes using functional brain imaging, or fMRI. With collaborators at Massachusetts General Hospital and Boston University, Zebrowitz is studying where neurons are activated in the brain in subjects when they are shown different faces. The research seeks to answer how and why physical qualities such as facial attributes contribute to prejudicial stereotypes about older people as well as how stereotypical reactions can be modified.

Social Support Eases Chronic Illness

With support from the National Institute on Aging, psychology professor Aurora Sherman is studying the connection between social relations and how older adults cope with osteoarthritis (OA), a degenerative



joint disease afflicting more than twenty million people in the United States. Sherman has found that older adults with OA who report having supportive relationships have fewer depressive symptoms than those with less support and more negative relationships. Depressed adults are less likely to take their pain medication on time or exercise to maintain muscle tone and control weight, Sherman says. "If we're going to educate people how to cope with osteoarthritis, we have to consider much more than just the disease," she says. "We may need to intervene not just at the individual level but the family level as well."

Older Adults Wear Rose-Colored Glasses

Despite the unwelcome signs of aging, older adults gravitate toward positive feelings and associations, according to a new Brandeis study published in the journal *Psychology and Aging*. The research suggests that old age itself



motivates adults to limit their exposure to negative information and focus their attention on the positive. Using sophisticated eye-tracking technology, scientists in Brandeis's Emotion Lab recorded the eye movements of test subjects looking at a series of faces portraying different emotions. While older participants (ages 57 to 84) preferred happy faces and avoided

angry ones, younger subjects (ages 18 to 21) showed a preference only for fearful faces. “By focusing more on positive things and avoiding negative ones, older adults are able to maintain emotional resilience, which becomes acutely important in the face of dwindling time,” says psychology professor and lead author Derek M. Isaacowitz.

National Aging Study Takes the Pulse of Midlife

Psychology faculty members Margie Lachman and Patricia Tun are making major contributions to a nationwide study examining the health and well-being of middle-aged adults. The Midlife in the United States (MIDUS)



survey assesses a range of age-sensitive mental abilities, including verbal memory, working memory, executive function, reasoning, and speed of processing. The Brandeis researchers developed the survey so that the battery of cognitive tests can be given over the phone, making it possible to include a greater cross section of the nation.

“Overall, in the different cognitive areas we tested, we saw smaller differences between younger and middle-aged groups, and larger differences with the older group,” said Tun. Another finding: in general, higher educational levels are associated with better performance. “We will also link the cognitive data

with a wealth of other key variables from the MIDUS survey such as health, personality, and life experiences involving work and social relationships,” said Tun.

Poor Hearing May Impair Memory

Older adults with mild to moderate hearing loss might spend so much effort on hearing accurately, their ability to remember spoken language suffers as a result, according to researchers in the Memory and Cognition Lab at the Volen National Center for Complex Systems. In one study, even when older adults could hear words well enough to repeat them, their ability to memorize and remember the words was poorer when compared with that of other individuals of the same age who had good hearing. “There are subtle effects of hearing loss on memory and cognitive function in older adults,” said Arthur Wingfield, the Nancy Lurie Marks Professor of Neuroscience and director of Volen. “This study is a wake-up call to anyone who works with older people, including healthcare professionals, to be especially sensitive to how hearing loss can affect cognitive function.” Individuals who interact with older people with some hearing loss should speak clearly, pausing after clauses or chunks of meaning, not necessarily slowing down speech dramatically.

Budding Breakthroughs

What can budding yeast reveal about the aging process? By studying how broken chromosomes are repaired in *Saccharomyces* yeast, biologist James Haber and his lab have made

fundamental advances in understanding the molecular mechanisms underlying certain cancers and even rare diseases, such as Werner syndrome, in which a genetic defect causes extreme premature aging. His lab has described two alternative mechanisms of maintaining the length of chromosome ends—telomeres—whose progressive shortening correlates with cell aging.

One of the most-studied model organisms in science, yeasts are relatively similar in structure to human cells and many of the rearrangements in chromosomes and the sources of genome instability that can result in yeast are analogous to events that



occur in human tumor cells. Haber is interested in the specific biochemical roles that proteins play in DNA recombination, repair, and replication.

His lab has demonstrated the importance of this “in vivo” biochemistry approach by identifying several independent and competing pathways of both homologous recombination and DNA end-joining—clues for identifying normal as well as abnormal cellular processes. “DNA repair is critical to the maintenance of life; my goal is to define the steps of the repair process,” says Haber.

Walter Leutz, PhD'81

Closing the Gap in Chronic Care



Catalyst: You assert that people with chronic illnesses or disabilities are best served through a combination of medical-care services, provided by doctors and hospitals, and community-care services, provided by homemakers, personal care attendants, and the like. Yet you say these two sectors often operate in “parallel universes.” Can you give an example of that?

Leutz: The one that people run into most often—and where people are most vulnerable—is after-hospital care. For example, a person on a prescribed set of medications goes into the hospital, where there exists a different formulary for medication. The hospital changes the patient from this heart drug to that heart drug, from this blood-pressure pill to that blood-pressure pill. After he’s sent home, the linkage between the hospital and the home-care system falls apart. The families and the home-care providers are left not knowing what they should be doing.

Catalyst: How do we better integrate medical-care and community-care services?

Leutz: For the typical elder person with a disability or a chronic illness, I’ve argued for a system I call coordination, in which a single point of contact who has standing in both the medical system and the home-care system—usually a nurse—can monitor the patient and call a doctor when there is an issue. You don’t have to set up special payment systems, you don’t have to assemble teams, and it’s feasible for a very broad segment of the population.

Catalyst: What are the main impediments to the two systems’ better working together?

Leutz: The lack of home-care benefits, except for the poor through Medicaid, is the biggest problem. But that’s not all. Medical providers—doctors, nurses—are interested in diagnosis, in

treatment, in cures. On the home-care side, you have social workers, early-childhood education professionals, and therapists who are interested in functionality and social relationships. It’s a challenge to have people from different orientations collaborating.

Catalyst: You’re a strong proponent of Social HMOs. How do they work?

Leutz: They’re programs that add a long-term-care benefit to Medicare. Members join like they join an HMO. The program delivers all their medical services, and if they have a disability, they are assigned a care coordinator who helps them choose long-term-care supports. There’s a saying that goes, “Medicare stops at the bathroom door.” Medicare will pay for a wheelchair, which will get you to the bathroom, but it won’t pay for bath bars, it won’t pay for raised toilet seats.

Catalyst: You spent a year studying the new national long-term-care insurance programs in Germany and Japan. What did you learn?

Leutz: That they accept that we’re all in it together. They set up systems for long-term care that pay for everybody, and they finance it through broad-based tax mechanisms.

Catalyst: If you could wave a magic wand and change one thing about the way America cares for its elderly, what would it be?

Leutz: I would create an entitlement for home- and community-based long-term care and a care coordinator as part of Medicare. It creates a stable friend as a resource for families. That person who knows the system and is an advocate for people is really important.

Walter Leutz is an associate professor at The Heller School for Social Policy and Management.

Margie Lachman

Remembrance of Things Past

By Laura Gardner

At the beginning of the twenty-first century, the average lifespan is thirty years longer than it was at the dawn of the last. That's the good news. The bad news is that human evolution did not anticipate such longevity, and as a result, millions are faced with figuring out how to make the twilight years twinkle instead of slip away into a fog of forgetfulness or worse.

Margie Lachman has spent more than two decades researching healthy adult development and aging through the prism of memory and cognitive function. She says there are a number of strategies and beliefs older adults can adopt to leverage both memory and cognitive function as they age. Simply put, how we age, to some extent, is up to us.

Indeed, the notion that we can control outcomes in our lives is deeply embedded in American culture. In fact, one recent poll suggests that Americans believe more than citizens of any other country that they can influence how things turn out in their lives.

"So it's no surprise that age-related losses or lapses in memory can challenge our deeply embedded sense of control," says Lachman. "Thus, we find an increase with age in beliefs that memory declines are an inevitable, irreversible, and uncontrollable part of the aging process."

Yet Lachman's research demonstrates that middle-aged and older adults can often improve memory performance by improving their self-confidence and employing techniques like visualization, rehearsal, note taking, or other mnemonic strategies to help encode the information and aid in retrieval.

In a new study published in the *Journals of Gerontology: Psychological Sciences*, Lachman demonstrates a link between actual declines in



cognitive functioning and a low sense of control. The study found that middle-aged and older adults who perceived greater control over cognitive functioning had better recall performance.

"One's sense of control is both a precursor and a consequence of age-related losses in memory," says Lachman. "The theory says the more you believe there are things you can do to remember information, the more likely you will be to use effort and adaptive strategies and to allocate resources effectively, and the less you will worry about forgetting."

In a related study, Lachman examines the relationship between anxiety and recall performance in young, middle-aged and older adults. Before the test, all age groups reported roughly the same levels of anxiety, but stress hindered the performance only of middle-aged and older adults on the memory test.

Lachman has also investigated the effect of resistance training on working memory span among sedentary older adults with at least one disability. In a study published in the *Journal of Aging and Physical Activity*, she found that strength training increased the participants' working memory span. In fact, the higher the level of resistance, the more memory improved, suggesting that strength training benefits not only the muscles but also the mind.

"Our research shows that mental and physical exercise, combined with a sense of control and self-confidence, can provide measurable benefits as we age," says Lachman. "The future of aging has never looked better."

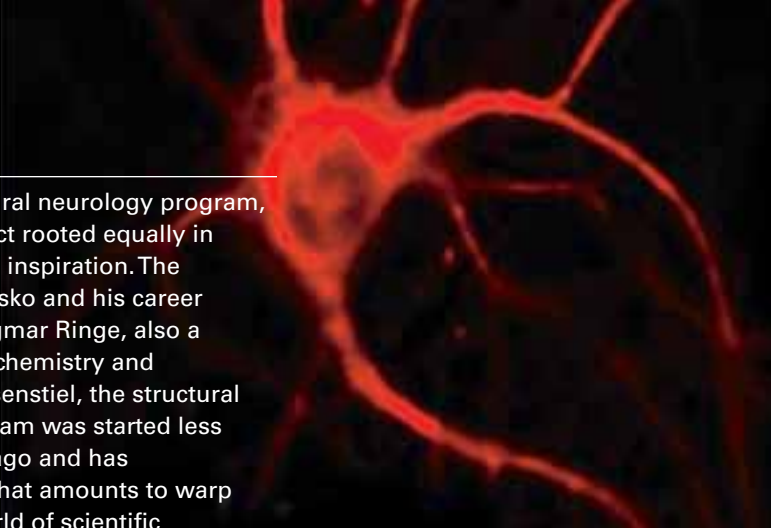
Professor Margie Lachman is chair of the psychology department and director of the Lifespan Lab.



A “perfect storm” of neurodegenerative disease is brewing across the globe, with hot spots in the United States, Western Europe, and Japan. Its threat is gradually rising, fueled by aging societies, a glacial and hugely expensive drug-development process, and no real remedies in sight.

A new prescription for drug discovery

By Laura Gardner



The forecast goes like this: in less than fifty years, more than a quarter of the world is going to be at least 65 years old—a staggering first in human history. Since age is the biggest risk factor for Alzheimer's and Parkinson's, people will become increasingly vulnerable to these diseases over time. Today, about 4.5 million people in the United States have Alzheimer's; in two decades, that number is expected to triple. About 60,000 people are diagnosed with Parkinson's each year; currently, 1.5 million Americans have it.

Meanwhile, discovering and commercializing one new drug can take up to thirteen years and about \$900 million in research and development. Moreover, of every five thousand new compounds identified, only about five will eventually be deemed safe enough for testing in humans. There is no cure for either disease, and treatment is symptomatic only.

The hope, of course, is that the global scientific engine fueling research into neurodegenerative diseases will radically alter this bleak forecast. But time is of the essence in an era in which centenarians are the fastest-growing age group, says Greg Petsko, the Gyula and Katica Tauber Professor of Biochemistry and Chemistry and director of the Rosenstiel Basic Medical Sciences Research Center at Brandeis.

"If the population is aging so rapidly that we are going to be inundated with people with neurodegenerative diseases in the next twenty-five or thirty years, then taking thirteen years to develop a drug just doesn't cut it," says Petsko. "We have to find ways of accelerating that process."

Enter the structural neurology program, a research project rooted equally in pragmatism and inspiration. The brainchild of Petsko and his career collaborator Dagmar Ringe, also a professor of biochemistry and chemistry at Rosenstiel, the structural neurology program was started less than two years ago and has progressed at what amounts to warp speed in the world of scientific research.

That's because of their approach to drug discovery. Using x-ray crystallography to determine the three-dimensional structure of proteins involved in neurologic disorders such as Alzheimer's and Parkinson's, Petsko and Ringe are able to bring insights about the structure and function of these molecules to bear on the drug-discovery process.

This approach has already paid off handsomely: in fewer than eighteen months, the Petsko/Ringe lab has produced crystal structures of three important targets for Parkinson's and has discovered several new genes associated with Alzheimer's.

But the duo—collaborators for twenty-five years—didn't stop there with their novel approach. They joined forces with the Center for Neurologic Diseases at Harvard Medical School in a singular collaboration that has dispensed entirely with the barriers that typically keep basic research scientists from working with clinicians, and senior scientists confined within their own small area of research.

In less than fifty years, more than a quarter of the world is going to be at least 65 years old—a staggering first in human history.

“These two have turned up the intellectual intensity here because they come from a different perspective with fresh ideas.”

“The Center for Neurologic Diseases is one of the few places in the world where people look at these diseases from the level of proteins and molecules; of all the labs focused on diseases, we’re the most primed to take on Dagmar and Greg,” explains Peter Lansbury, professor of neurology at Harvard Medical School. “These two have turned up the intellectual intensity here because they come from a different perspective with fresh ideas.”

Dr. Michael Schlossmacher, another key Harvard collaborator, put it this way: “We’re marrying two very different sets of skills in this project, without rank, title, or stature inhibiting the free-flowing exchange of ideas.”

The teams regularly swap insights in both the lab and the classroom into clinical disease, molecular details, genetic mutations, and gene-expression patterns in autopsy tissues, collectively piecing together the complex puzzle of neurodegeneration. In broad terms, Brandeis is supplying the structural biology expertise—the knowledge about the structure and function of potential drug targets—while Harvard brings clinical expertise in neurology and the ability to conduct cellular experiments that provide the basis for screening drug compounds.

Brandeis chemist Jeffrey Agar, who is researching Lou Gehrig’s disease in collaboration with Petsko and Ringe, says, “Greg and Dagmar’s recent groundbreaking research has proved beyond a shadow of a doubt that this is the right approach. They are redefining how quickly research can go in the area of neurodegenerative disease.”

“With this kind of arrangement, we’re better, they’re better, the whole field advances both at the level of research and at the level of education,” says Petsko. “It’s worked out better than we could have ever imagined.”

Perhaps the fundamental energy sustaining this project is the knowledge that this isn’t just basic research but research whose goal is to treat disease. “I want people who are working on these diseases to keep their eyes on the prize,” says Petsko.

In the Petsko/Ringe lab, the road to treatment begins with figuring out the three-dimensional shapes of target molecules in the cell to which drugs will bind and interact.

“It’s a bit like trying to find the shape of a lock,” explains Petsko. “If I ask you to build a key that can open the door, but I don’t give you the shape of the lock,



The structure of UCH-L1, a protein associated with Parkinson’s as well as cancer, was solved in the Petsko/Ringe lab in collaboration with Peter Lansbury’s group at Harvard Medical School.

all you can do is try keys at random until you find one that might fit. The trouble is that key might be a skeleton key that would open up many doors. We call that ‘side effects’ in the drug-discovery business. But if I give you the shape of the lock, then you have a much better chance of building a key that opens that door and no other door. It fits that lock and no other lock.”

Once the three-dimensional shape of the drug target is known, chemical compounds can be screened for their ability to fit into that target molecule as precisely as the right key fits into the right lock. One way to do this is to take a thousand compounds and experimentally measure how they bind to the target, looking for a good fit.

But this approach is both tedious and expensive. With the structure of a drug target in hand, much of the experimental slog can be skipped in favor of a computerized approach that can rank a half million compounds or so—many of which are known drugs—according to how well they fit into the target. At that point, actual experiments can be done on the top hundred chemical compounds with a greater likelihood of success because they have been preselected.

The greatest advantage of the structural neurology program over conventional drug research is its ability to cut by half the six- to seven-year research period leading up to clinical trials. And since time is money, this method could also reduce the cost of research and development by a factor of two or three.

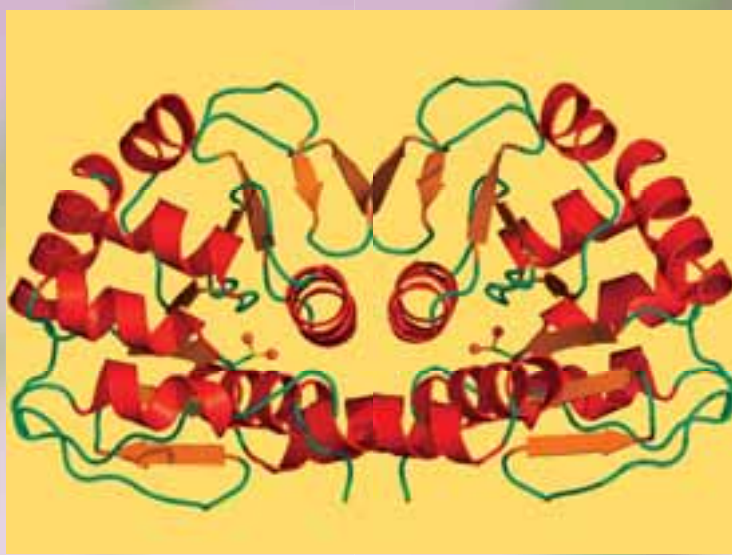
The collaboration’s pragmatism goes even a step further. Since Alzheimer’s and Parkinson’s are age-related diseases, buying time—delaying the onset of symptoms—can be as good as a cure. “If I can delay the age of onset by ten years and delay the rate of progression by a factor of two, these diseases are no longer a significant health problem,” explains Petsko.

Lansbury echoes that goal: “Identifying those at risk, then treating the disease early—long before symptoms develop—will change the course of neurodegenerative disease and have a huge effect on its prevalence and severity.”

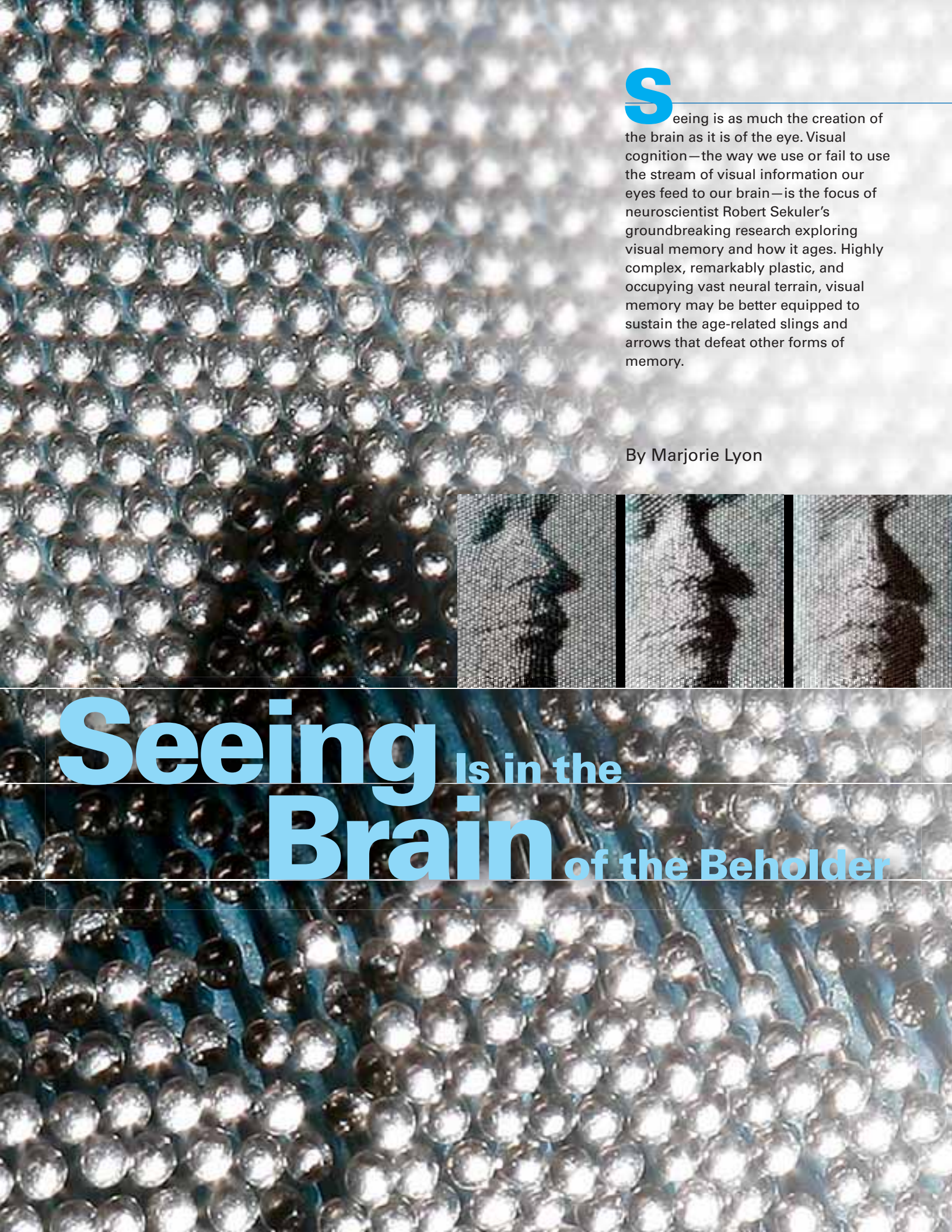
Of course, forecasting in the drug-discovery business is highly speculative. But if past performance is the best predictor of future results, this unique collaboration may be well on its way to changing the tragic face of neurodegenerative disease.

Says Petsko: “These are diseases where all the clinician can do is make you as comfortable as possible and help you and your family deal with what’s coming next. Our goal is to change the shape of that world completely. Our goal is to find a treatment.” ■

...this isn't just basic research but research whose goal is to treat disease.

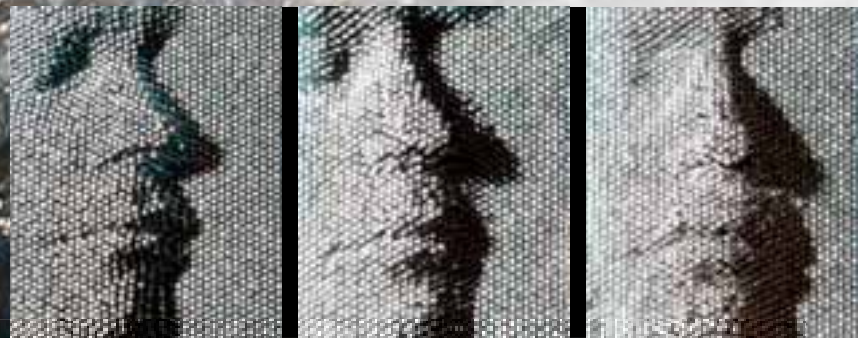


A 3-D structure of DJ-1, a protein of unknown function associated with Parkinson's, crystallized in the Petsko/Ringe lab.



Seeing is as much the creation of the brain as it is of the eye. Visual cognition—the way we use or fail to use the stream of visual information our eyes feed to our brain—is the focus of neuroscientist Robert Sekuler's groundbreaking research exploring visual memory and how it ages. Highly complex, remarkably plastic, and occupying vast neural terrain, visual memory may be better equipped to sustain the age-related slings and arrows that defeat other forms of memory.

By Marjorie Lyon



Seeing Is in the Brain of the Beholder

Although much is known about the way the human eye works, Sekuler, the Louis and Frances Salvage Professor of Psychology and Volen National Center for Complex Systems, wants to understand how the brain uses visual information to remember what we have seen, to navigate complex environments, and to observe and then imitate the actions of other people. Think of two separate categories: good vision (the eye) does not guarantee successful use of visual information (the brain). "For example, children with good vision can do poorly when it comes to imitating their sports coach's actions, or adults with perfectly good vision may encounter difficulty remembering where they have been and finding their way around a museum," explains Sekuler.

Funded by the National Institutes of Health and the National Science Foundation, Sekuler's Visual Cognition Laboratory has already revealed a simple way to improve the method a coach or parent uses to instruct a child how to accomplish such complex tasks as tying a shoelace or performing a martial arts move.

Using electrophysiological techniques to study visual cognition, Sekuler attaches 120 electrodes to the scalps of subjects who are performing various tasks at a computer. Researchers observe very dramatic differences in brain circuits that people use to perform exactly the same task at exactly the same level. "We are able to identify where in the brain the information is being processed that involves not just vision but memory, and we've also begun to look at how well people can intentionally keep things out of memory," explains

Sekuler. "Memory doesn't fail as you get older; what fails is the ability to be selective in what you do remember or don't remember." In the lab, Sekuler studies how people can choose to keep extraneous things out of memory so that memory can be more focused and effective.

Surprisingly, Sekuler's studies of subjects in their 70s and 80s has found that although aging does impair many forms of memory, recent visual memory is strikingly robust, virtually unaffected by age. "Some functional brain-imaging work gives us tantalizing clues about how the human brain reorganizes itself to preserve visual memory," Sekuler says. It appears that the aging brain reorganizes itself, recruiting into the service of visual memory some regions that would otherwise (in young people) be given over to other functions.

Using a computer game to test how people learn to navigate their environment, Sekuler asks subjects to drive a taxicab through a virtual town. Given a task to pick up a passenger and take him to a specific place, a subject must try to navigate unfamiliar streets, building up memory of the town's layout. Some landmarks stick in memory, but others don't. And some subjects get lost, while others seem to be able to find the target with uncanny ease.

"If we can identify what helps people to become expert imitators or expert navigators, then we could transfer this knowledge to help teach skills more effectively," Sekuler says. "Our hope is to be able to develop diagnostic tests for the learning style that people have for particular tasks, and develop ways to teach people to exploit those techniques." This could be applicable to people who have suffered strokes and need to relearn specific daily tasks. The virtual cab-driving work is being done in collaboration with Michael Kahana, formerly at Brandeis and now at the University of Pennsylvania, and Brandeis student Jeremy Manning '06 (see page 12).

Sekuler says that even the briefest experience with this game reveals the large range of individual abilities. "We expect that this particular line of research will produce methods by which people's way-finding styles (what information they attend to, what information they ignore) can be assessed and improved by specially designed training." ■

Try it yourself at <http://people.brandeis.edu/~sekuler/>



Jeremy Manning '06

Think Maps

By Marjorie Lyon

Picture yourself driving a taxicab down city streets arranged in a grid. You pick up a passenger, and he asks you to take him to a particular store in the city. So far, so good. But there's a problem: you have never been here before. How do you navigate the shortest route to your destination? Indeed, how do you find it at all?

Welcome to the virtual taxicab video game created at Brandeis and used by Jeremy Manning '06, a double-major in computer science and neuroscience who does research in Robert Sekuler's Visual Cognition Laboratory (see page 10). Articulate, thoughtful, and deliberate, Manning listens intently and chooses his words carefully. To better understand human spatial navigation—how people get from place to place—Manning has designed a computer model that mimics the way-finding strategies of virtual taxicab drivers. The computer model visually represents what is going on inside the subject's head.

Some who play the game do extremely well while others are completely stymied; Manning wants to know how and why. "As the subjects play the game, their deliveries become more and more efficient. The computer model should explain the subject's improvement over time," Manning says, adding that he is working with younger participants now and will test older subjects next.

A likely possibility is that the participants are building up a "cognitive map" of the environment as they explore the virtual city. For example, Manning has found that "drivers" who pick up "passengers" in unfamiliar



locations can nonetheless navigate their way to familiar destinations. How subjects construct the map is still a mystery.

Some subjects readily find new locations in a strange city, even though each environment is randomly generated. "We think that subjects in environments that the model finds easy will do better than in environments that the model finds difficult," Manning explains.

Manning wants to answer some fundamental questions that intrigue him: Why are we here? How do our minds work? Ultimately, he would like to apply computational neuroscience techniques and algorithms to artificial intelligence (AI). "In achieving AI, perhaps we will unlock the key to our own minds," he says.

Lest you think he spends all of his time working on a computer, consider this: Manning is a PADI-certified, open-water scuba diver and an experienced lifeguard who also enjoys sailing, snorkeling, jet-skiing, and water-skiing. When not outdoors, he can be found playing jazz trumpet, working on three-dimensional modular origamis, hunched over a chess game or a Rubik's Cube, practicing Okinawan Uechi-Ryu karate, or—yes, you guessed it—playing video games.

Manning will continue to explore the human mind next fall as a graduate student at the University of Pennsylvania, working with former Brandeis professor Michael Kahana to develop a system which will allow subjects to control the taxicab in the video game using thought.

Arthur Wingfield

Stability in the Changing Brain

What makes the study of human aging special at Brandeis is the openness of faculty laboratories and groups to sharing their ideas and research with colleagues in other disciplines. Let me give one example from a surprising source.

A question that has long intrigued me about mental performance and aging, especially in language comprehension, something that is so central to our everyday lives, is what can be called stability in the face of change. As we age the brain changes, in volume as well as in the effectiveness of neurons to form the large-scale networks that support mental activity. Working memory, processing speed, and often hearing acuity are all dramatically affected, yet the comprehension of spoken language remains extraordinarily resistant to the effects of aging. This clearly presents a paradox: How can language comprehension remain stable in the face of the manifest neural changes that take place in normal aging?

I never thought I would be gleaning insights into human aging from developing lobsters, crabs, mice, and rats, none of whom, I hasten to report, deal in their daily lives with human language. Two of my neuroscience colleagues in the Volen Center, Eve Marder and Gina Turrigiano, are also intrigued by this question of stability in the face of change.

Turrigiano, using a rodent model, has been exploring one aspect of this scientific puzzle: How do changes in synaptic strength that accompany learning avoid destroying the functioning of the already in-place circuits? Marder's question arose from studies of the anatomy and physiology of the nervous system



of baby lobsters. By the time a baby lobster is just an inch long, it looks exactly like an adult lobster; it moves the same way, it breathes the same way, it grinds its food in the same way.

As baby lobsters grow, their nerve cells also grow in size, and yet the patterns of neural activity remain the same, showing how the same output of the nervous system can be generated in a number of different ways. This phenomenon could be described as a changing brain finding new ways to solve old problems, and solving them with considerable success.

What my colleagues were showing, at the neural systems level, was how a nervous system can produce stable behavior in the presence of neural change. This observation swept through my lab, where we are studying language and memory in human adult aging. It presents an intriguing way to view the process of compensation underlying preserved language performance and the age-related changes in patterns of neural activation we observe in brain-imaging studies.

This vignette does not end the story: in fact, it describes a beginning in the way we are coming to think about how the aging brain and sensory systems produce stability in speech comprehension.

Arthur Wingfield is the Nancy Lurie Marks Professor of Neuroscience and Director, Volen National Center for Complex Systems.

memory makers

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Easy Listening

Ask rapid-fire speakers to slow down.

Keep It Simple

To remember a conversation, turn off the radio or television and try to find a quiet place to listen.

One Thing at a Time

Focusing on one activity at a time is a simple way to improve your memory. Talking on a cell phone, even a hands-free one, diminishes driving performance.

Pay Attention

If you don't pay attention to something while it is happening, you won't remember it well later.

Associate

When you meet a new person, form as many mental associations as you can.

Make a Note of It

Use external cues such as lists whenever possible.

Eat Your Veggies

Vegetables and fruits such as blueberries have been shown to be good for your memory as well as your body.

Take a Hike

Even moderate exercise such as walking can significantly improve performance on mental activities.

Reach Out

Social activity, as well as physical activity, is associated with better mental functioning in older age.

Use It or Lose It

Engage in active, mentally challenging activities. These include reading, crossword puzzles, games such as bridge or chess, learning a new language or taking classes.