Since the early days of neuroscience, pessimists have wondered whether the brain is actually smart enough to ever understand its own workings. A long-lost lapel pin of mine read, “If the brain was simple enough for us to understand, we would be too stupid to understand it.”

Along with many other brain scientists, however, my colleagues and I at the CVL do not share this pessimism. For one thing, as discussed previously in this column (“Collaboration in Science,” Winter 2013), scientists do not work alone. Indeed, the rationale for centers such as CVL is to facilitate interaction among scientists. Problems are puzzled over not by brains in isolation, but by brains working together, yielding insights beyond what could be achieved by a single individual. Of course, this doesn’t mean that the talent and ability of the individual scientist is not important, but the adage that “the whole is greater than the sum of its parts” has never been truer.

Another reason for optimism is that extraordinary progress continues to be made in developing methods that allow us to study the living brain in health and disease. As we have previously described (“Are we making progress on Alzheimer’s disease?”, Fall 2012), only a few years ago it first became possible to image the protein fragment beta-amyloid, one of the hallmarks of Alzheimer’s disease, in the brain. This has led to an explosion of new information about Alzheimer’s, including the ability to identify and study people at risk years before symptoms emerge – a major focus of the research of Dr. Denise Park and her group here at the CVL (see p. 2).

A related and very recent development – the ability to image tau proteins, which are the other constituent of the plaques and tangles characteristic of Alzheimer’s, offers the promise of more progress in the study of the genesis and progression of the disease.

With a stellar and growing (see New Faces, p. 6) team of scientists, and access to advanced imaging technology shared with our sister campus at UT Southwestern, we are superbly well-placed to capitalize on this and other future advances in imaging the brain’s structure and function. As we pursue our efforts to understand how to protect and enhance the mind as we grow older, research findings increasingly...
Making Progress in Alzheimer’s Detection and Treatment

Seeing a Potential Culprit

Thus far, clinical trials testing the benefits of clearing out a protein that accumulates in the brains of patients with Alzheimer’s disease shared similar outcomes: failure. The trials were successful in reducing or eliminating this protein — beta amyloid — from the brain, but not in reducing the symptoms of dementia associated with Alzheimer’s. “The studies have focused on treating patients who had been diagnosed with Alzheimer’s disease, and it appears that they are being treated too late in the disease,” says CVL’s Co-director Dr. Denise Park. “We think that amyloid protein may deposit many years before symptoms of dementia appear and that effective treatments will need to occur much earlier.”

That insight, combined with imaging advances that allow scientists to measure levels of amyloid in the brain, have changed how researchers conduct clinical trials for Alzheimer’s disease. The research focus has shifted — from testing on those who already suffer from dementia, now recognized as a late stage of the disease — to participants who have detectable amyloid but no apparent symptoms of Alzheimer’s.

One of the biggest advances came when researchers at the University of Pittsburgh developed an amyloid imaging agent called “Pittsburgh Compound B” (PiB) for use in positron emission tomography (PET) scans. Previously, amyloid deposits on the brain could only be studied at autopsy. Recently, the Food and Drug Administration approved the first commercially available amyloid imaging agent, Florbetapir. Similar to PiB, Florbetapir is a radiopharmaceutical that binds to amyloid plaque and “lights up” on a PET scan, allowing radiologists to identify the presence of the harmful protein. It’s currently being used both clinically and in research projects.

This imaging agent is used in The Dallas Lifespan Brain Study (DLBS) — a major study of brain aging, that is led by Dr. Park at the CVL and funded jointly by the National Institute on Aging and Avid Radiopharmaceuticals, a Division of Eli Lilly. Dr. Park pioneered the research on amyloid deposits in healthy adults in collaboration with Center scientists Drs. Karen Rodrigue and Kristen Kennedy, and Dr. Michael Devous, formerly a professor of radiology at UT Southwestern, who recently joined the science team at Avid.

They have now used the FDA-approved drug in studies of more than 250 healthy adults who participate in the DLBS. The inclusion of amyloid imaging on the DLBS research project has made the Center a national leader in the study of understanding the meaning of amyloid deposition in the brains of healthy adults.

Nearly all studies of amyloid are focused on disease, and the Center research is unique in its focus on investigating the resilience of the aging brain when confronted with neural pathology.

Measuring the Impact of Fearful Faces on Cognition

An unregulated amygdala can be a frightening thing

As the brain’s primary structure for the formation of memories associated with emotional events — particularly frightening ones — the amygdala is also involved in the genesis of many fear responses, defensive behavior (so-called “fight or flight” reflexes), and other signals that directly influence the nervous system. Changes in blood pressure, heart rate and the release of stress hormones can all be triggered by the amygdala’s reaction to external stimuli.

In a healthy individual with normal levels of anxiety, the amygdala operates in sync with the prefrontal cortex, which acts as a governor on impulses that have been part of the human psyche since time immemorial, i.e., how we react to danger cues in our immediate environment and how we interpret certain threats or perceived threats.

Dr. Paul J. Whalen, a professor of psychology and brain sciences at Dartmouth College, spoke in February on the role of the amygdala in recognizing fearful facial expressions, as part of the CVL’s Brown Bag Science Luncheon Series. Dr. Whalen delivered his talk, “Neural responses to facial expressions predict attention, bias and personality,” to an audience of post-doctoral researchers, Center faculty and students, as well as guests from the UT Dallas campus, and UT Southwestern Medical Center.

Since beginning his studies at the University of Vermont, Dr. Whalen’s research has centered on the role of the amygdala, with his latest research using psychophysiological and imaging studies showing that fearful facial expressions spur reactions in those seeing them, often triggering increased attention and new learning.

The amygdala typically operates concurrently with processes in the prefrontal cortex, Dr. Whalen said, which helps mediate the amygdala’s conversation with the nervous system to allow increased anxiety responses when called for, and guard against unnecessarily elevated levels of anxiety when maladaptive. Through this dialogue between the amygdala and the cortex, the human brain can put into context what is being seen, in the case of Dr. Whalen’s research, the images of fearful faces used in his studies.

“Fear can be broadly characterized as uncertain negativity,” Dr. Whalen said. “The amygdala notifies the cortex that this is an important instance to become more vigilant and learn, and the cortex in turn, decides on the proper course of action and updates the amygdala on its decision through a longer cognitive process.”

In this way, the amygdala plays an important role in vigilance and priming the rest of the brain for learning, he said. The calculation of actual danger is not always accurate, however, especially in anxious individuals who may be experiencing what could be called a “hyper-vigilant” state that instantly creates a toxic change in the brain’s “readiness” to respond.

In many cases, with proper modulation and taking into account other factors (e.g., previous experience), the person observing a fearful face can empathize with the person showing fear, and seek to help someone who is facing what is ultimately a threat to that individual alone — a more appropriate reaction in certain circumstances.

The typical effect of looking at a fearful face, and the vigilance these faces induce, is to generally diffuse attention, where the subject looks for other information about a threat that cannot be gleaned from just the face alone. By contrast, when presented with an angry face, the subject focuses attention on the individual alone, and whether he or she represents a real threat.

Therefore “anger tends to be certain negativity” that focuses attention in the onlooker, he said, and primes the body for action that may be key for survival in the moment.
EXAMINING THE IMPACT OF EXERCISE ON COGNITIVE AGING

The hippocampus is a structure within the brain that plays an important role in long-term memory, and in spatial navigation. Humans and other mammals have two hippocampi, one in each side of the brain. Hippocampal volumes are generally larger in physically fit adults, but the extent to which aerobic exercise training can modify hippocampal volume in late adulthood was largely unknown.

In a randomized controlled trial with more than 100 older adults, Dr. Basak and the team showed that aerobic exercise training increases the size of the anterior hippocampus, and improves memory. Exercise training, they found, increased hippocampal volume by 2 percent, effectively reversing age-related loss in volume by one to two years. Dr. Basak will be discussing these and other important findings that indicate aerobic exercise training may play an important role in improving memory function in late adulthood.

As part of a conference track that includes identifying predictors of a healthy aging brain, and certain lifestyle interventions that can modify or stave off disease processes, Dr. Basak hopes to show this week that exercise can have an immediate impact on improving cognitive health in older adults, she said. Other researchers in the track, from SUNY Upstate Medical University, UT Southwestern Medical Center, Baylor, and the University of Washington will be giving a series of presentations on Alzheimer’s, and links to diabetes, mild cognitive impairment, and depression.

Park Lab Tip
START THE SEASON OFF RIGHT

Spring into action and learn a new activity

New research from the Center for Vital Longevity has revealed that staying mentally engaged appears to be an important key to promoting brain health in older adults. Socializing with friends, reading, and listening to music will certainly not hurt and can add a level of enjoyment to your life. Interestingly, however, research from the Synapse Project shows that the most beneficial way to boost your brain is to engage in activities that are mentally demanding and expand your existing knowledge.

In other words, how you “use it” will help determine how much you “lose it.” The research suggests that not all forms of activities are created equal and participating in new leisure activities that challenge your existing boundaries appears to be the most likely candidate for preserving brain function. If you would like to become more comfortable with technology or would like to learn a new language, take a class on a regular basis. If you have always wanted to learn chess or how to quilt, get started!

For every person, the new activity could be different – the important point is that the activity is challenging to you and stays challenging through continuous advancement of skills. Remember that it is never too late to learn something new and embrace life. Plant the seed, and it will grow.

DIRECTOR’S MESSAGE
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suggested it is important to develop mind-protective strategies, including regular physical activity, early in one’s life – well before damage to the brain has begun (see Park Lab Tip above). For example, aerobic training may increase the size of the anterior hippocampus, leading to improvements in spatial memory, whereas, as research conducted here at the CVL shows, participating in new leisure activities that challenge one’s existing boundaries appears to be helpful in improving memory more generally.

In short, we are in better shape than ever to apply the best possible science to the urgent problem of maintaining cognitive vitality throughout the whole of our lives.

Please enjoy this Spring issue of Neurocognitive, where you’ll learn more about the latest Center activities, while appreciating the enhanced look of this publication. You can also learn about our stronger online presence (p. 7), including a new video featuring CVL faculty and some of you – supporters and members of our extended CVL family.

As always, we thank you for your support.

Dr. Michael Rugg

Dr. Basak’s talk comes after a visit from Dr. Arthur Kramer, the director of the Beckman Institute for Advanced Science & Technology and the chair of psychology and neuroscience at the University of Illinois-Urbana-Champaign, in January. Dr. Kramer, a colleague of Dr. Basak’s while she was a postdoctoral fellow at Illinois, spoke at the Center for Vital Longevity Director’s Research dinner, which the night before preceded a half day symposium at the CVL.

Dr. Kramer illustrated the complexity of such a seemingly simple question in a keynote talk that highlighted studies that demonstrate improvements in memory as a result of aerobic exercise – versus toning and stretching, which did not yield the same results.

The theme for this year’s symposium on Jan. 29 was “Harnessing Brain Plasticity to Maintain and Improve Cognitive Vitality,” which explored several questions related to exercise and cognition. For instance, do walking and other physical activities lead to the enhancement of cognitive and brain health across the lifespan? The answer may seem to be an unequivocal “yes,” but it’s not that simple.

Dr. Basak, now an assistant professor in the Center, followed his talk with a presentation on “Action vs. Strategy: Cognitive and Neural Correlates of Complex Skill Acquisition and Transfer,” in which she probed the changes in cognitive and behavioral plasticity induced by decidedly non-aerobic (yet still beneficial) cognitive training, such as working memory training or video-game playing.
Neurodegenerative Diseases Center Opens in Germany with CVL Present

Dr. Michael Rugg delivered a talk at the opening symposium of a newly created federal research center for neurodegenerative diseases in Germany in February.

The center is one of nine that are being set up across Germany under a major initiative to stimulate research into age-related disorders.

The opening symposium for the Deutsches Zentrum fur Neurogenerative Erkrankungen research center (DZNE or the German Center for Neurodegenerative Diseases) took place over two days at the end of February in Magdeburg, Germany. The DZNE site in Magdeburg houses 80 scientists from ten nations involved in studying neurodegenerative diseases. A new building at the Magdeburg University Hospital has been dedicated to work similar to what is being done by the CVL. DZNE Magdeburg has provided space for MRI-PET imaging for training studies, as well as biomedical laboratories.

At DZNE Magdeburg, researchers are analyzing how physical activity and certain cognitive tasks improve memory function in the elderly, and perhaps delay the onset of Alzheimer’s. Furthermore, DZNE scientists study how these processes can be stimulated and supported by medication.

Have you visited the CVL website recently? You may have noticed these new and improved features

- **Video** — Expertly produced HD video on the role of the Center, in Texas and beyond, featuring community partners in Dallas, study participants, and faculty members speaking about ongoing research in cognition across the lifespan.
- **Research News Bytes** — An informative and accessible lay summary of science and talks emerging from the Center.
- **Media Placements** — Links to recent media coverage, including last month’s Dallas Morning News exclusive coverage of Dr. Park’s Synapse Project, interviews with the Boston Globe, National Geographic and more.
- **Twitter** — Borne out of necessity (getting the word out to friends and family of the Center during the treacherous ice storm that buffeted Atlanta, and the rest of the South). Twitter—@CVLNeuro. Science made easier for non-scientists.

The work is considered particularly relevant for regions of Germany that are seeing an exodus of young people to metropolitan areas, leaving behind an older population that is vulnerable to cognitive decline, Dr. Rugg says.

SEEDS OF GROWTH

As we have reduced the death rate of other life-threatening diseases, the challenge of dementia and Alzheimer’s still remains,” says Warder, who recently became CEO of the O’Donnell Foundation. “This is like the cancer of the ’60s and ’70s — it’s a disease everyone faces if they live long enough. If we can minimize the risk of dementia, it would be wonderful for society, a victory for public health and incredibly cost-saving.”

In the spirit of spreading knowledge, it may be time to ask yourself, have you ever made a gift? How can you make it further? Many companies have a matching gift program.

In the spirit of spreading knowledge, CVL is on Twitter and tweeting every day about news, events and items of interest to the Center. Follow us @CVLNeuro. Neurons Activities is published by the Center for Vital Longevity at UT Dallas.

Alex Lyda, Editor
Susan McReynolds, Designer

For the ten years, Vivian worked at the University of Maryland College Park in the Department of Dining Services where she assisted the Sr. Associate Director of Retail Operations and HR for a department of 1,300 employees during the semester. She assisted in the employee enrichment program, teaching food safety and alcohol service and organizing employee training days as well as hiring and employee relations. Vivian often did behind-the-scenes expediting and organizing of special events, including a gigantic strawberry shortcake and a display of 50,000 cupcakes for the University’s Maryland Day. Last April she moved to Dallas with her husband. So far her favorite place in Dallas is the Arboretum. Vivian likes the punk-rock band The Ramones, knitting and gardening.

Vivian Brockwell
Administrative Assistant

At the opening symposium of the newly created federal research center for neurodegenerative diseases in Germany, Dr. Song enjoyed a dialogue between two generations. “I’m a 72-year-old skilled in handling cars, and I’ve overcome my fears,” says Dr. Song. “I can still rise to the challenge of driving a car.”

Dr. Song arrived at the Center in February, by way of California, most recently at UCSD, where he studied functional changes that correlate with early Alzheimer’s disease, as an associate research scientist.

Prior to the Bay Area, Dr. Song was in San Diego conducting postdoctoral studies in the cognitive neuroscience of memory with Dr. Larry Squire at UCSD. Dr. Song first became interested in neuroscience while he was studying physics in China, which led him to the University of California, where he received his doctorate in 2008.

Now he is working together with some of his colleagues back in China. “While working at UCSD, I have had the chance to develop a lot of new ideas and explore new areas of research,” he says. “I’m excited to start a new chapter in my career here working together with my colleagues and Primary Investigators at the Center.”

For his efforts in cataloging the history of the Center and its impact on the Dallas community, Richard was awarded the DZNE’s opening symposium award. “I am honored to be one of the first residents at the DZNE,” Richard says. “I look forward to the opportunity to contribute to the Center’s mission in ways that will benefit both the elderly and the rest of us.”

Richard Innis
Research Administration Manager

Richard joined the Center in February, from North Carolina, specifically North Carolina State, where he was a grants administrator. Richard holds a bachelor degree in business and marketing from North Carolina Central University. In his spare time, Richard enjoys playing billiards and darts. He hopes to join a pool and dart league in Dallas soon, and is an avid fan of both Kansas State and North Carolina State sports.

Richard made the road trip from North Carolina during an ice storm that buffeted Atlanta, and the rest of the South. Richard hopes to bring other areas of federal funding to the Center, and possibly get some of the Primary Investigators here working together with some of his colleagues back home on research projects.

Zhuang Song, Ph.D.
Research Scientist, Park Lab

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Prior to the Bay Area, Dr. Song was in San Diego conducting postdoctoral studies in the cognitive neuroscience of memory with Dr. Larry Squire at UCSD. Dr. Song first became interested in neuroscience while he was studying physics in China, which led him to the University of California, where he received his doctorate in 2008. When the opportunity arose to study the healthy aging brain at the Center, it was important for him to come here, he said. In his spare time, Dr. Song enjoys classical music and getting lost in nature.

The work is considered particularly relevant for regions of Germany that are seeing an exodus of young people to metropolitan areas, leaving behind an older population that is vulnerable to cognitive decline, Dr. Rugg says.
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