

CHARTING OUR PROGRESS

2016 ANNUAL REVIEW CENTER FOR **WITAL LONGEVITY**

THE SCIENCE OF THE AGING MIND

MESSAGE FROM THE CENTER DIRECTOR

Onward and Upward

im pleased to introduce the Center for Vital Longevity's annual review for 2016. As you will see, the



Center's research laboratories have continued to make excellent progress in a wide range of research topics relevant to the aging brain. These include ways of identifying who is most at risk of aging unsuccessfully, development of interventions to slow cognitive aging, and studies of how the brain's structure and function differ in healthy people at different stages of the lifespan. Our progress on these and other fronts is documented in the twenty-plus peer-reviewed publications that appeared during the year, and in the numerous scientific talks and presentations that were given nationally and internationally by Center researchers. Additionally, faculty in the Center won new competitive funding from a range of federal and non-federal organizations. This will both support existing research programs, and allow new programs to get underway.

Recognizing the potential of neuroscience research to enhance quality of life, UT Chancellor William McRaven has identified it as a research priority for the coming years, emphasizing the importance of collaborations between basic and clinical scientists. Examples of these collaborations are plentiful at the CVL, where all of our faculty enjoy productive interactions with colleagues at UT Southwestern Medical Center, our sister UT institution in Dallas. One of these collaborative projects, which recently received support from the National Institutes of Health, is briefly described in the Research Spotlight within.

While 2016 has been a successful year on many fronts, it has also been one of sadness. Bill Booziotis was the founder of our Director's Research Circle and an indefatigable supporter. With his late wife, Jean, he was responsible for the endowment that supports our annual public lecture. Sadly, Bill passed away in May. An appreciation can be found on the back page. He was an inspirational figure who exemplified the values of public service; we miss him very much.

ACHIEVEMENTS

Work, Now Funded by the Alzheimer's Association, Probes Brain Iron Accumulation

Dr. **Karen Rodrigue** and members of her **Cognitive Neuroscience of Aging Laboratory** found further evidence that excessive accumulation of iron in the brain may serve as a predictive factor of risk for cognitive decline. Earlier in the year, Dr. Rodrigue was awarded \$100,000 by the Alzheimer's Association to investigate iron accumulation as a possible indicator of neuropathological aging in the brain. Excessive iron has already been associated with oxidative stress and damaged neurons in animal model studies. If brain iron accumulation in humans is indeed a significant risk factor for cognitive decline, her research could eventually give clinicians a chance to intervene long before symptoms of dementia may appear. With the help of the Association's funding, Dr. Rodrigue has begun a study that is examining iron accumulation in cognitively healthy adults and individuals diagnosed with

mild cognitive impairment, with a particular focus on individuals with a genetic risk to develop Alzheimer's. Separately, her National Institutes of Health-supported research has shed further light on the impact of vascular health on brain and cognitive vitality in aging populations, a fundamentally important area given vascular risk factors in aging populations and the potential to prevent or control high blood pressure through lifestyle changes. Dr. Rodrigue published four collaborative scientific articles this past year as well as a book chapter reviewing the effects of hypertension



A member of Dr. Karen Rodrigue's lab highlighting a brain scan.

in cognitive and brain aging. Members of her lab presented research findings on how health factors such as hypertension, in combination with genetic risk, can influence cognitive aging, at national and international conferences in New York, San Diego and Dubrovnik, Croatia.

Further Identifying the Neural Signatures of Healthy Brain Aging

Younger people efficiently engage brain processes necessary to perform a task, while at the same time "shutting down" processes irrelevant to the task. This ability to modulate or control brain activity is compromised in older people, new research by Dr. **Kristen Kennedy** confirms. The flexibility for healthy brains to ramp up in support of a goal, while suppressing activity in areas of the brain that generally do not serve a given task, may separate those whose brain function is aging well from those who may be prone to cognitive loss later in life, she found. Young adults who engaged in increasingly difficult tasks tended to display increased activity in fronto-parietal regions of the brain, with a corresponding decrease in the default mode regions of the brain. This latest finding from



Dr. Kennedy's **Neuroscience of Aging and Cognition Lab** was published in *NeuroImage*. A separate federally funded research project of Dr. Kennedy's continues to investigate brain structure changes over the lifespan and the reorganization of brain functions as we age, using tools such as structural and functional imaging. Dr. Kennedy found that prefrontal cortex modulation to increasingly difficult working memory tasks declines across the lifespan, and is associated with poorer accuracy on memory tests

while participants were being scanned with functional magnetic resonance imaging, as well on tests done outside a scanner. These data were collected in part with the help of a National Institute on Aging R00 grant, which is supporting the lab's large lifespan study of brain structure, function and cognition. Dr. Kennedy presented new results from the study in Croatia at the annual meeting of the International Society for Behavioral Neuroscience, of which she is now a Vice President. Dr. Kennedy was appointed as a Handling Editor at the journal *NeuroImage* earlier this year.

AND ACTIVITIES

Research into the Neural Correlates of Memory Reveals New Insights

The Functional Neuroimaging of Memory (FNIM) Laboratory led by CVL director Dr. Michael Rugg continued its focus on understanding neural circuits critical to the encoding and retrieval of memories, and how these circuits vary in their function across the adult lifespan. In three papers published in 2016, Dr. Rugg and members of his research group described their findings from a large study that used functional magnetic resonance imaging (fMRI) to examine patterns of brain activity in young, middle-aged and older individuals as they successfully learned and remembered novel links between word pairs. They chose this approach because much previous work has shown that memory for new associations is especially vulnerable to advancing age. Among other findings, the researchers established that this vulnerability results from age-related differences in brain function at the time of learning; remarkably, patterns of brain activity during the retrieval of recently learned associations were stable across the lifespan. The group identified a specific part of the brain's frontal cortex-the inferior frontal gyrus-as one of the regions where agerelated changes likely resulted in impaired associative learning.

In other work, Drs. Rugg and Josh Koen, a postdoctoral scientist in the FNIM lab, used fMRI to investigate why some memories persist in the face of the "interference" caused when new, related information is subsequently encountered. In a paper published in the *Journal of Neuroscience*, they reported

that "reactivating" or bringing to mind a recently learned memory during new learning makes the older memory less likely to be forgotten. The laboratory's work on age-related differences in memory function received additional support from the award of two new research grants. One, from the National Institute on Aging (NIA), will



support work examining whether the ability to "monitor" memory retrieval is more easily compromised in older than in young individuals. The second grant, from the National Science Foundation, will allow the laboratory to continue research into how age affects the ability to control which aspects of a memory are represented in the brain when it is retrieved. Among several international talks, Dr. Rugg delivered the Barbara Dicker Oration at Swinburne University, Australia, and the Jeeves Lecture at the University of St. Andrews, Scotland. Members of the laboratory gave several presentations at major scientific conferences over the course of the year.

Peer-Reviewed Scientific Publications in 2016

- Band G.P., Basak C., Slagter H.A., Voss M.W. (2016). Editorial: Effects of Game and Game-Like Training on Neurocognitive Plasticity. *Frontiers in Human Neuroscience*, 30, 4-5.
 Basak C., O'Connell M.A. (2016). To Switch or Not to Switch: Role of Cognitive Control in
- Working Memory Training in Older Adults. Frontiers in Psychology, 7, 1-18.
- Bischof, G.N., Rodrigue, K.M., Kennedy, K.M., Devous, M.D., Park, D.C. (2016). Amyloid deposition in younger adults is linked to episodic memory performance. *Neurology*. 87, 2562-2566
- de Chastelaine, M., Mattson, J.T., Wang, T.H., Donley, B.E., & Rugg, M.D. (2016). The neural correlates of recollection and retrieval monitoring: Relationships with age and recollection performance. *NeuroImage*, 138, 164-175.
- de Chastelaine, M., Mattson, J.T., Wang, T.H., Donley, B.E., & Rugg, M.D. (2016). The relationships between age, associative memory performance, and the neural correlates of successful associative memory encoding. *Neurobiology of Aging*, 42, 163-176.
- Festini, S.B., McDonough, I.M., Park, D.C. (2016). The busier the better: Greater busyness is associated with better cognition. *Frontiers in Aging Neuroscience*, 8, 1-10.
- Festini S.B., Preston S.D., Reuter-Lorenz P.A., Seidler R.D. (2016). Emotion and reward are dissociable from error during motor learning. *Experimental Brain Research*, 234, 1385-1394.
- Kennedy, K. M., Rieck, J. R., Boylan, M. A., Rodrigue, K. M. (2016). Functional magnetic resonance imaging data of incremental increases in visuo-spatial difficulty in a large adult lifespan sample. *Data in Brief*, in press.
- Koen J.D., & Rugg M.D. (2016). Memory reactivation predicts resistance to retroactive interference: evidence from multivariate classification and pattern similarity analyses. *Journal of Neuroscience*, 36, 4389-4399.
- Liu P., Li Y., Pinho M., Park D.C., Welch B.G., Lu H. (2016) Cerebrovascular reactivity mapping without gas challenges. *NeuroImage*, 146, 320-326.
- McDonough, I.M., Bischof, G.N., Kennedy, K. M., Rodrigue, K. M., Farrell, M. E., Park, D.C. (2016). Discrepancies between Fluid and Crystallized Ability in Healthy Adults: A Behavioral Marker of Preclinical Alzheimer's Disease. *Neurobiology of Aging*, 46, 68-75.
- Na, J. Chan. M., Lodi-Smith, J., and Park, D.C. (2016). Social-class differences in selfconcept clarity and the implications for well-being. *Journal of Health Psychology*. Online ahead of print.
- Na, J., McDonough, I., Chan, M., and Park, D.C. (2016). Social-class differences in consumer choices: Working-class individuals are more sensitive to choices of others

- than middle-class individuals. *Personality and Social Psychology Bulletin*, 42, 430-443. Park, D.C. and Festini, S.B. (2016). Theories of memory and aging: A look at the past and a glimpse of the future. *Journal of Gerontology: Psychological Sciences*. Online ahead of print.
- Qin S., Ray N.R., Ramakrishnan N., Nashiro K., O'Connell M.A., Basak C. (2016). Ilusory conjunctions in visual short-term memory: Individual differences in corpus callosum connectivity and splitting attention between the two hemifields. *Psychophysiology*. 53, 1639-1650.
- Rieck, J.R., Rodrigue, K.M., Boylan, M.A., Kennedy, K.M. (2016). Age-related Reduction of BOLD Modulation to Cognitive Difficulty Predicts Poorer Task Accuracy and Poorer Fluid Reasoning Ability. *NeuroImage*, 147, 262-271.
- Savalia, N.K., Agres, P.F., Chan, M.Y., Feczko, E.J., Kennedy, K.M., Wig, G.S. (2017). Motion-related artifacts in structural brain images revealed with independent estimates of in-scanner head motion. *Human Brain Mapping*, 38, 472-492.
- Song, Z., McDonough, I., Liu, P., Lu, H., Park, D.C. (2016) Cortical Amyloid Burden and Age Moderate Hippocampal Activity in Cognitively-Normal Adults. *NeuroImage:Clinical*, 12, 78-84.
- Sweeney-Reed C.M., Zaehle T., Voges J., Schmitt F.C., Buentjen L., Kopitzki K., Richardson-Klavehn A., Hinrichs H., Heinze H.J., Knight R.T., & Rugg, M.D. (2016). Pre-stimulus thalamic theta power predicts human memory formation. *NeuroImage*, 138, 100-108.

Sweeney-Reed C.M., Zaehle T., Voges J., Schmitt F.C., Buentjen L., Kopitzki K.,

Richardson-Klavehn A., Hinrichs H., Heinze H.J., Knight R.T. & Rugg M.D. (2016) Clinical, neuropsychological, and pre-stimulus dorsomedial thalamic nucleus electrophysiological data in deep brain stimulation patients. *Data in Brief*, 8, 557-561

Thakral P.P., Wang T.H., Rugg M.D. (2016) Decoding the content of recollection within the core recollection network and beyond. *Cortex*. Online ahead of Print.

Wang, T.H., Johnson, J.D., de Chastelaine, M., Donley, B.E., & Rugg, M.D. (2016). The effects of age on the neural correlates of recollection success, recollection-related cortical reinstatement, and post-retrieval monitoring. *Cerebral Cortex*, 26, 1698-1714.

Wisse, L. E. M., Kennedy, K. M., Rodrigue, K. M., and 21 others for the Hippocampal Subfields Group (2016). A harmonized segmentation protocol for hippocampal and parahippocampal subregions: Why do we need one and what are the key goals? *Hippocampus*, 27, 3-11.

A review of Center activities over the past year, including those within the 6 laboratories that are the Center's core.

Expanding Theories of Aging and Cognition, while Sharing Research Abroad

The **Aging Mind Laboratory** led by Dr. **Denise Park**, CVL Director of Research, was focused on the Dallas Lifespan Brain Study (DLBS), funded by the National Institute on Aging, Avid Radiopharmaceuticals, AWARE and the Aging Mind Foundation for a total of over \$8 million since the project was initiated in 2008. The study includes over 500 healthy participants (age 20 to 89) and 350 of them received a PET scan that reveals amyloid plaques on the brain—a characteristic of Alzheimer's Disease. Many have had two amyloid scans four years apart, allowing lab scientists to track changes in both amyloid and cognition. Recently, imaging of the toxic tau "tangles" that infiltrate the brain with Alzheimer's Disease was added. The DLBS provided a continuing picture of both brain and cognition changes that occur over time. A study published in *Neurology*, led by Dr. Gerard Bischof, showed that middle-aged adults with relatively high amyloid deposits evidenced subtle deficits in memory compared to others their age. Another study, led by Dr. Zhuang Song, revealed that healthy adults aged 60 to 79 with high amyloid showed depressed activity in the hippocampus, an important brain region for memory. Focusing on cognitive vitality, Dr. Sara Festini, the Aging Mind Foundation Postdoctoral Fellow,



reported that DLBS participants who reported being very busy had better cognitive function than those who were less engaged. She received national media attention that included *National Public Radio* and *Time* magazine. Spreading the word, Dr. Park delivered a keynote address at the national Alzheimer's Association Research Roundtable in Washington, D.C. She was also appointed to the National Institute on Aging Behavioral and Social Science Review Committee to evaluate grant applications. Lab members secured excellent positions upon completion of training—Dr. Festini as an assistant professor of psychology at the University of Tampa, and Michelle Farrell accepted a postdoctoral fellowship with Drs. Reisa Sperling and Keith Johnson at Massachusetts General Hospital/Harvard.

Study of Neural Networks Recognized by the James S. McDonnell Foundation

Dr. Gagan Wig and his Cognitive Neuroimaging Laboratory continued their study of agerelated cognitive decline from a complex networks perspective with the help of funding awarded by the James S. McDonnell Foundation. Dr. Wig was one of eight recipients of the 2016 Understanding Human Cognition Scholar Award, which consists of \$600,000 spread over six years. The award is geared toward



researchers who are studying how neural systems support cognitive functions and how cognitive systems are related to observable behavior. An important strand of Dr. Wig's research in 2016 involved collaboration with researchers in UTD Dallas' Arts and Technology program (ATEC) to develop a "data stethoscope." This new tool will allow neuroscientists to gain additional understanding of the intricate patterns of connections between brain regions by the use of sound. In addition, Dr. Wig's lab manager, Neil Savalia, was the first-author on a paper in Human Brain Mapping that explored the influences of head motion on measurements of brain anatomy, which are present while participants are being scanned using MRI. Savalia and Dr. Wig, the senior author on the paper, have developed criteria that can be used to "flag" individuals whose scans are not of sufficient quality. The methodological innovations gleaned from this work will be useful in characterizing how brain anatomy changes over the lifespan.

Determining the Cognitive Benefit of Video Game Training and Exercise on Memory

The Lifespan Neuroscience and Cognition (LiNC) Laboratory, led by Dr. Chandramallika Basak, continued its focus on the cognitive and neural mechanisms of complex skill learning, and the effects of cognitive training, including video games and memory exercises, in younger and older adults. In the lab, Dr. Basak and her colleagues studied real-time strategy video games and the demands that interacting with different visual content can place on a person's ability to problem solve when presented with new information. The question is whether there are any types of video-game training that have a positive impact on cognitive abilities, including attention, memory and the ability to switch tasks efficiently. In other work, LiNC lab member Shuo Qin was awarded funding from Canada's Natural Sciences and Engineering Research Council, Canada's equivalent to the U.S. National Science Foundation, to evaluate how physical fitness may influence memory performance and brain in older adults.

Earlier in the year, Qin and Dr. Basak published a paper in *Psychophysiology*, which explored how people with less connectivity between the two hemispheres of the brain through its major connecting structure called—the corpus callosum—

might actually be less susceptible to blending the characteristics of objects they have seen into a false or hybrid memory. Two additional papers were published from Dr. Basak's lab in 2016: an editorial on the effects of video-game training on neurocognitive plasticity, and a paper on the role of cognitive control in working memory training in older adults. Dr. Basak wrote the editorial on the effects of video game training on neurocognitive plasticity with colleagues from Holland, in the journal *Frontiers in Human Neuroscience.*



Researchers in Dr. Chandramallika Basak's lab ready a computer-based cognitive test.

CENTER TALKS & EVENTS



The 2016 Jean & Bill Booziotis Lecture Features MIT Neuroscientist

The Center for Vital Longevity held its third annual Jean and Bill Booziotis Distinguished Lecture at the Communities Foundation of Texas in April, welcoming Dr. **John Gabrieli**, the Director of the Athinoula A. Martinos Imaging Center at the McGovern Institute for Brain Research at the Massachusetts Institute of Technology, for a talk on "neuroindividuality." The lecture highlighted what principles of brain organization are consistent across individuals, and how brains vary across people due to age, personality and

other dimensions of individuality. Nearly 300 guests attended the free public talk, thanks to the generosity of the late Mrs. and Mr. Bill Booziotis. Touching on personality types, gender and culture, and the way these differences influence how our brains interact with the world, Dr. Gabrieli described how such hard-to-quantify factors might be better understood through imaging.

Biennial Science Symposium Features Expert on Brain Aging and Structural Changes

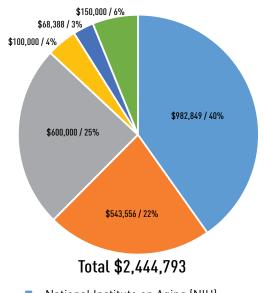
Dr. **Naftali Raz**, the Director of Lifespan Cognitive Neuroscience at Wayne State University, explained some of the latest findings in brain aging, and how the structure of the brain changes over time, at the 2016 CVL Science Symposium held in February. As the symposium's keynote speaker, Dr. Raz offered a detailed review of his research on the changes in brain structure that occur with age, while noting the different rates at which these changes occur in different individuals. He also spoke about genetic modifiers of aging, and how inflammation, normally a helpful biological reaction, can have an adverse effect on the brain. Other speakers outside the Center included UT Southwestern's Dr. Elena Ivleva, an assistant professor in the Department of Psychiatry, who spoke about an effort to develop a new classification system for psychosis. From the Center, Dr. Denise Park highlighted research that examines the impact of accumulation of beta-amyloid in the brain on cognitive function, while Dr. Michael Rugg delivered a talk on how communication between different brain regions differs for successful and unsuccessful learning and memory.



Wayne State's Dr. Naftali Raz was the featured speaker

at the 2016 CVL Science Symposium.

CVL Research Funding New in 2016



- National Institute on Aging (NIH)
- National Science Foundation
- James S. McDonnell Foundation
- Alzheimer's Foundation
- Private Gifts and Individual Donations
- AVID Radiopharmaceuticals

WEALT OUTSIDE TALKS & PRESENTATIONS

In 2016, Center scientists gave *more than 50* presentations & invited talks at such meetings as:

- Human Amyloid Imaging Conference, Miami, Fla
- Alzheimer's Association Research Roundtable, Washington, D.C.
- International Society of Behavioral Neuroscience, Dubrovnik, Croatia
- Memory Disorders Research Society annual meeting, Princeton, N.J.
- The International Imaging Genetics Conference, Irvine, Calif.
- Society for Neuroscience annual meeting, San Diego, Calif.
- Cognitive Aging Conference, Atlanta, Ga.
- Cognitive Neuroscience Society annual meeting, New York, N.Y.
- Neuroscience@Work Seminar—Ericsson North America, Plano, Texas
- International Meeting of the Psychonomic Society, Grenada, Spain
- International Conference on Memory Budapest, Hungary
- Defense Advanced Research Projects Agency Rhythms of the Brain Meeting, New York, N.Y.
- Alzheimer's Association International Conference, Toronto, Canada
- International Conference on the Functional Architecture of Memory, Magdeburg, Germany ♥

RESEARCH SPOTLIGHT

Building on the Collaboration with UT Southwestern: Monitoring of Neurosurgery Patients Presents an Opportunity for Researchers to Better Understand Memory





Dr. **Brad Lega.** Dr. Lega uses a method of localizing seizures in epilepsy patients called stereoelectroencephalography (SEEG), which involves the surgical implantation of electrodes in the brain to identify areas involved in a seizure. Patients with epilepsy who are under consideration for surgical treatment sometimes undergo such brain monitoring beforehand. This

collaborating with UT Southwestern neurosurgeon

Researchers in the CVL's Functional Neuro-

imaging of Memory Laboratory (FNIM) are

period of pre-surgical monitoring presents an opportunity to better understand the structures and networks involved in memory, while potentially improving clinical outcomes and research methods.

Patients with seizures often suffer memory problems because the same brain networks and

structures implicated in epilepsy are important for memory processing. These structures include the hippocampus. This structure, located deep within the brain's medial temporal lobe, is particularly important for episodic memory—our ability to remember unique events and the contexts in which they occurred. Over the long term, repeated seizures can damage the hippocampus.

For roughly the one-third of epilepsy patients whose seizures cannot be controlled by medication, surgery to remove the origin of the seizure is an option—but one that can run the risk of severely impairing memory if the surgery leads to the removal of areas that are necessary for memory function. This fact helped motivate the new collaboration between CVL and Dr. Lega.

Lasting up to two weeks in some cases, SEEG monitoring is conducted in a hospital setting with significant periods of "down-time" for patients—a window that can be exploited by neuroscientists studying memory, Dr. Lega says. The unique aspect of the collaboration with Dr. Rugg's laboratory is that patients in whom brain activity is recorded during a memory task with SEEG also perform the task while undergoing fMRI. This allows the fMRI data—which is currently the only method allowing activity in regions like the hippocampus to be examined in healthy individuals—to be directly linked to precise measurements of electrical brain activity from the same regions.

"After we've recorded brain activity while patients perform a memory task, we can then go back and analyze it to map patterns of functional connectivity associated with successful remembering," says Dr. **Danielle King**, the FNIM postdoctoral researcher who is part of the collaboration. "It's a unique opportunity because it allows researchers to directly compare, within the same patients, measures of functional connectivity acquired with SEEG and fMRI."

Modern methods of imaging and recording brain activity have made great progress toward accurately mapping the connections, both structural and functional, that are key to episodic memory but we are "one or two insights away from possibly changing the way we do surgery and post-operative follow-up" to make them as precise and effective as they can possibly be, Dr. Lega says. "This is where my practice has something to offer researchers like those at CVL and vice versa; my surgical treatments can be informed by the latest evidence-based research in neuroscience."

2016 CVL ADVISORY COUNCIL

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- Ms. Lisanne Glew, First Vice President, UBS
- Ms. Roslyn Thibodeaux Goodall, Community
- Volunteer Ms. Jannah Hodges, Managing Partner,
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- Mo. Lindo Im. Community Volunt
- Mr Ken Kay Partner Armanino III
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- Ms. Lisa Shardon, President, Home Health Companion
- Dr. John Stilwell, Clinical Professor, UT Dallas

In Memoriam

Tireless CVL Supporter and Namesake of Annual Public Lecture Series Passes On

In May, the Center experienced the profound loss of Mr. Bill Booziotis, a dear friend and staunch CVL supporter who worked vigorously to connect the Center, since it was founded, to the philanthropic community in Dallas. Bill attended the first dinner associated with the Dallas Aging and Cognition Conference in 2010, and his steadfast support soon followed, with the development of the CVL Director's Research Circle (DRC).

The DRC rapidly became a key community funding vehicle for the Center. Bill served continuously on the Center's Advisory Council and played a significant role in every major step forward that the Center has taken. An architect by training, Bill was a recognized civic leader and unparalleled supporter of the Center. He founded Booziotis & Company



Architects in 1989. With clients including Texas Instruments, the University of Texas and the Dallas Museum of Art, his work can be seen in projects from museums, churches and university buildings to sleek modern single-family homes and the restoration of historic Dallas homes. He also designed and conceived the Communities Foundation of Texas building on Caruth Haven Lane, where the annual CVL public lecture bearing his late wife's and his name takes place every April. The Center has come a long way from 2010 with Bill at its side, and his lasting contributions have ensured the Center will continue to make an impact in the field and on the future of Dallas for years to come.