Matters of the Brain: Neurodegeneration

THE PARTNERSHIP FOR BAYLOR COLLEGE OF MEDICINE

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DR. STEPHEN SIGWORTH

Dr. Stephen Sigworth is Associate Professor of Medicine at Baylor College of Medicine and Vice President and Chief Medical Officer. He is board certified in internal medicine by the American Board of Internal Medicine. His clinical interests include pre-operative evaluations, preventive health and general medicine.

Dr. Sigworth earned his medical degree from the Medical College of Virginia at Virginia Commonwealth University, where he also completed residency training and fellowship.

He sees patients at the Baylor Clinic, Suite 1225. For appointments, call 713-798-2500.

DR. MELISSA YU

Dr. Melissa Yu is Assistant Professor of Neurology at Baylor College of Medicine. She is board-certified in neurology by the American Board of Psychiatry and Neurology. Her primary clinical interest is general neurology, with special interest in management of patients with dementia.

Dr. Yu received her medical degree from the Mt. Sinai School of Medicine and conducted an internship and residency at St. Luke's-Roosevelt Hospital Center and Baylor, respectively.

She sees patients at the Baylor College of Medicine Medical Center, 7200 Cambridge St. For appointments, call 713-798-2273.

DR. HUDA ZOGHBI

Dr. Huda Zoghbi is Professor of Pediatrics, Molecular and Human Genetics, Neurology, and Neuroscience at Baylor College of Medicine and Director of the Jan and Dan Duncan Neurological Research Institute at Texas Children's Hospital.

A member of the National Academy of Sciences and a Howard Hughes Medical Institute Investigator, she has pioneered research on Rett syndrome and other rare brain disorders, and has advanced research of more common conditions including autism and adult neurodegenerative diseases.

Dr. Zoghbi is a native of Lebanon, where she graduated from the American University of Beirut, going on to earn her medical degree from Meharry Medical College in Nashville, Tenn.

PROTECTING YOUR COGNITIVE HEALTH

Three steps patients can take to help protect their cognitive health:

1. Be physically active
2. Reduce cardiovascular risk factors (including hypertension, diabetes and smoking).
3. Manage medications and health conditions that could affect cognition.

Other actions that may promote cognitive health:

- Be socially and intellectually active, and continually seek opportunities to learn
- Get adequate sleep and seek professional treatment for sleep disorders, if needed.

Source: Institute of Medicine

STRUCTURED ACTIVITY IS IMPORTANT TO LIVING WITH ALZHEIMER'S DISEASE

A structured environment is the key to easing some of the sleep-related problems facing people with Alzheimer's disease.

The most common sleep issue for those with Alzheimer's disease is a fragmented or erratic sleep pattern that usually occurs in the later stages of the illness.

"It is normal to have sleep changes as we age, such as waking up earlier in the morning, going to bed earlier, frequent awakening and a decrease in deep sleep time," said Dr. Susan Rountree, Assistant Professor of Neurology at BCM. "Patients with dementia can have other problems like obstructive sleep apnea or restless leg syndrome that disrupt sleep."

Waking up during the night or not being able to sleep at an appropriate bedtime becomes a problem when the person suffering from Alzheimer's disease is roaming the house, unfamiliar with his or her surroundings.

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10 WARNING SIGNS FOR DEMENTIA

1. **Memory loss that disrupts daily life**
2. **Challenges in planning or solving problems**
3. **Difficulty completing tasks at home, at work or at leisure**
4. **Confusion with time or place**
5. **Trouble understanding visual images and spatial relationships**
6. **New problems with words in speaking or writing**
7. **Misplacing things and losing the ability to retrace steps**
8. **Decreased or poor judgment**
9. **Withdrawal from work or social activities**
10. **Changes in mood or personality**

Source: Alzheimer's Association

WHAT TO DO IF YOU NOTICE THESE SIGNS?

If you notice any of the 10 Warning Signs above in yourself or someone you know, don't ignore them. Schedule an appointment with your doctor.

With early detection, you can:

- **Get the maximum benefit from available treatments.** You can explore treatments that may provide some relief of symptoms and help you maintain a level of independence longer. You may also increase your chances of participating in clinical drug trials that help advance research.
- **Learn more about treatments.**
- **Learn more about clinical studies.**
- **Have more time to plan for the future.** A diagnosis of Alzheimer's allows you to take part in decisions about care, transportation, living options, financial and legal matters. You can also participate in building the right care team and social support network.

ALZHEIMER'S DISEASE RESEARCH AT THE JAN AND DAN DUNCAN NEUROLOGICAL RESEARCH INSTITUTE

Alzheimer's disease is the most prevalent age-related neurodegenerative disease in the world. As the number of elderly individuals continues to rise, Alzheimer's has become a profound concern, exacting a staggering personal and financial toll and absorbing vast resources. Worldwide, it is estimated that more than 35 million individuals suffer from some form of dementia. One in nine people over the age of 65 and one in three people over the age of 85 have Alzheimer's disease.

Researchers and physicians are implementing a revolutionary approach to attack this devastating disease and develop a robust pipeline of potential treatments. Desperate to find a cure, too many companies have rushed drugs into clinical trials, only to have those trials fail. Instead, there must be hard, detailed and rigorous work upfront to ensure researchers pursue only the most promising targets are. At the Jan and Dan Duncan Neurological Research Institute, the research strategy holds promise for discovering new therapeutic opportunities. Researchers work simultaneously from the bottom up, at the most basic genetic level, and from the top down, taking advantage of sequencing data to identify vulnerabilities and locate the mutations, deletions, or duplications causing the disorders. The work is multidisciplinary and integrated to determine the best and most viable candidates for treatment.

This new and rigorously thorough disease discovery method radically shifts the research paradigm. The NRI is deploying its resources to increase the depth and breadth of neurodegeneration research by addressing it gene by gene across a wide spectrum, investigating 7,600 genes in the human genome that are potentially druggable, an unprecedented undertaking.

Genomic technology has evolved greatly in the last decade. Parallel sequencing technologies have transformed the landscape of cancer genomics. This technology, however, has not been applied to neurodegeneration research. Instead, researchers have historically focused on one gene or pathway, with very limited results. It is only with a complete and accurate view of the underlying molecular genetics and pathways that we can begin to understand the mechanisms that drive disease and to identify the most effective points for therapeutic intervention.

The team at the NRI has made critical discoveries in several important areas that point to unifying themes in the mechanisms underlying seemingly disparate neurodegenerative diseases such as balance disorders, Parkinson's disease and Alzheimer's disease. By discovering the common links across these diseases, scientists may detect treatments that work for all of them.

The key proteins driving disease in Alzheimer's are known. Specifically, amyloid precursor protein (APP), tau, and alpha synuclein tend to accumulate with age, and when increased due to genetic defects, cause early-onset Alzheimer's disease. The overarching goal, therefore, is to discover candidate therapeutic targets that can decrease these disease-driving proteins.

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APPOINTMENTS

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https://www.bcm.edu/healthcare/care-centers/neurology

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STRUCTURED ACTIVITY

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A primary contributor to the sleep problem is lack of day time stimulation and opportunities for socialization.

Many people with Alzheimer's disease struggle to maintain a daily schedule on their own. They may lose the ability to pursue favorite hobbies, and may avoid social settings that can confuse or agitate them. All this can contribute to day time napping which can then lead to wakeful nights.

Structure and routine needs to be set up through family and friends or a paid caregiver if possible.

Caregivers can help people with Alzheimer's disease avoid erratic sleep habits or night time wakening by establishing a strict bedtime and a definite waking time.

They can also help them increase activity during the day. They might consider supervised walks in the park or enrollment in a wellness program specifically for those suffering from dementia.

Rountree says using over-the-counter sleep aids can cause problems. In some cases, she said, they might make the dementia symptoms worse. Certain prescription medications can also worsen problems with memory or confusion and increase the risk of falls in elderly individuals. Giving special attention to sleep hygiene is very important before using medications. Finding a way to keep people with the disorder active during the day and stop napping is the first option families should try, she said. "Seek a doctor's advice when these approaches fail," said Rountree.

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Lloyd and Amy Kirchner

ALZHEIMER'S DISEASE (continued from page 2)

To this end, an innovative strategy has been devised to inhibit every gene in the genome that can be targeted pharmacologically using genetic approaches. This will allow researchers to identify as many potential candidate therapeutic targets (drug targets) in the human genome as possible. By testing all 7,600 potentially-druggable genes, compelling drug targets hitherto overlooked may be revealed.

The NRI's integrated approach of unbiased, large-scale genetic screens in multiple systems promises to identify the best targets and ultimately produce effective treatments, and this ground-breaking work may lead to important breakthroughs in the treatment of Alzheimer's and other age-related diseases.