

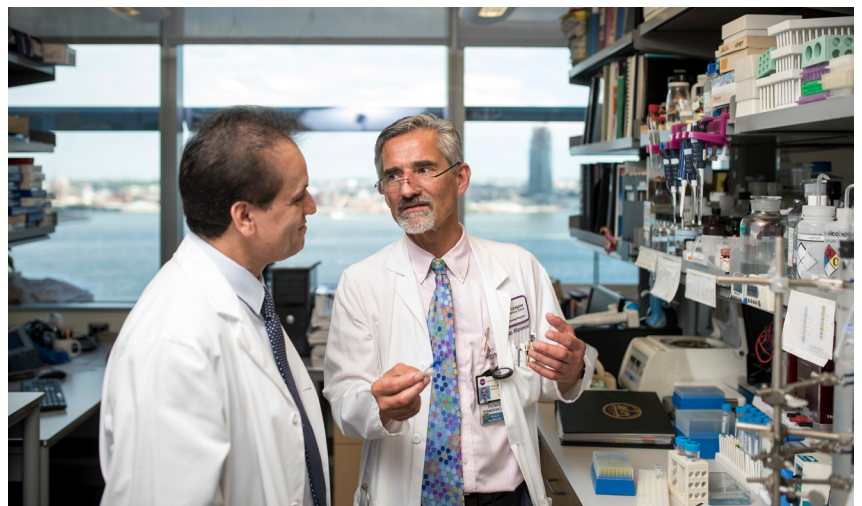
Mind Matters

Alzheimer's Disease Research Center Center for Cognitive Neurology

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Section 1: COVID-19 Biomarkers and Clinical Outcomes in Older Adults *By: Ashley Clayton, MA*



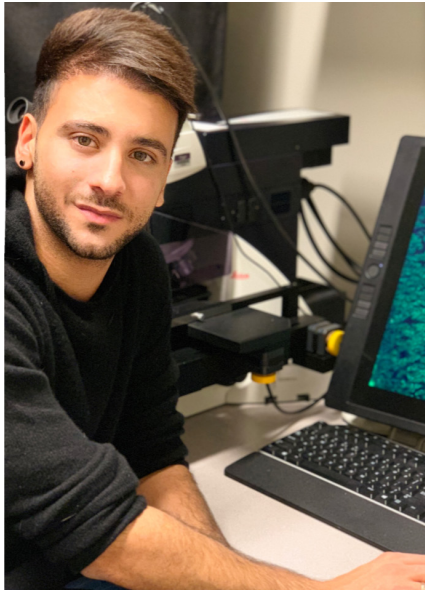
While the Alzheimer's Disease Research Center (ADRC) continues to carry on with study visits, either in-person or remotely, some very exciting, additional research is happening just a few blocks away over at the basic science labs! Our Alzheimer's Disease Research Center Director, Dr. Thomas Wisniewski, has recently been awarded a prestigious National Institutes of Health (NIH) grant as a supplement to our larger ADRC award. Dr. Wisniewski along with some other NYU Langone Health (NYULH) collaborators, including Dr. Jennifer Frontera from the Department of Neurology at NYULH Brooklyn and Dr. Laura Balcer, NYULH Department of Neurology Vice Chair, have teamed up to evaluate if cognitively impaired individuals are at a greater risk of developing more severe neurological complications following a COVID-19 diagnosis.

Blood samples of patients collected during COVID-19 hospitalizations will be analyzed to test the hypothesis that the presence of plasma biomarkers associated with Alzheimer's disease (AD) and/or blood-brain barrier dysfunction in older patients with or without a prior diagnosis of Mild Cognitive Impairment (MCI) or AD predisposes them to more severe pulmonary and systemic disease.

This NIH grant has also allowed our center to purchase a state-of-the-art Quanterix SIMOA system that is fully automated and will be used for running the blood sample immunoassays and comprehensive cytokine profiling. The SIMOA technology is novel due to its ultra-sensitive detection of biomarkers such as Tau, a protein in plasma that may be a marker of neuronal damage often found in those with Alzheimer's disease. Stay tuned for our next ADRC newsletter, where we will hopefully have some fascinating results following this unprecedented research!

Section 2: Identifying Molecular Targets in Alzheimer's Disease

By: **Geoffrey Pires, PhD candidate in Thomas Wisniewski's laboratory**



Research supported by brain banks is increasingly critical with today's rising rate of neurodegenerative diseases. In the U.S. alone, 5.8M people currently live with Alzheimer's disease (AD), making it the nation's sixth leading cause of death. By 2050, the affected population is projected to increase to almost 14M, costing the nation more than \$1.1 trillion as compared to \$305M today. As ADRC participants, you probably often hear that one donated brain

can provide resources for hundreds of research studies—and it is true! There simply is no substitute for human brain tissue. However, you may still wonder: why is brain donation so important to AD research, and what really happens in the lab once a brain is donated? This month, we will get down into the nitty-gritty at the “research bench”, where we strive to gain critical knowledge in order to provide insight regarding improving treatments and medications, and ultimately, increasing the odds of finding a cure.

Why is brain donation so important? - Let's start with some important facts: animals do not get AD in the same way as humans, but they develop some of its markers. Most of the treatment advances made using animal and cellular models poorly translate as effective, innovative therapeutics in patients, so that 99.6% of human AD-related clinical trials end in failure. I like to look at the research process as that of writing a novel, where molecules are letters, cells are words, and animals are sentences that together form a full story. For years, researchers have tried to tell the story of AD in this way; however, it had become more apparent that this book was written in a language that we did not yet speak. Therefore, we must reverse the process and first understand the meaning of the whole book of AD, before attempting to dissect its sentences, words and letters.

What happens after a brain is donated? - Shortly after the brain autopsy is performed, brain tissue is processed, preserved and made available to scientists for research. Part of the brain is made into slides for microscopic evaluation and diagnosis. This step is extremely important as it is currently the only way to reach a definite diagnosis of AD. Here, neuropathologists look for the main pathological hallmarks of AD: amyloid plaques, neurofibrillary tangles and vascular amyloid deposits. While amyloid plaques are toxic clumps that form in the spaces between the nerve cells by a protein called beta-amyloid, neurofibrillary tangles are formed by

a protein called Tau inside the neuron itself. In cognitively normal patients, Tau is a regular protein that gives the neuron its shape and functional integrity. However, in AD, this same protein undergoes major changes and starts playing a completely different role. Just like beta-amyloid, Tau starts aggregating into intracellular clumps and prevents neurons from functioning and communicating properly. While the contribution of beta-amyloid and pathological Tau (pTau) to AD is undeniable, researchers recently started to understand that these two proteins are probably not doing their job alone. They need to physically associate with other proteins to go awry and cause disease. Identifying these partners in crime could provide insights into how these proteins mediate their toxicity in AD. However, our knowledge of these partners has been surprisingly limited until now.

In the Wisniewski laboratory, postmortem samples from the NYU ADRC have already supported major breakthroughs. A recent study, led by Dr. Eleanor Drummond and myself, identified the reference map of pTau interactions, which we refer to as the “pTau interactome”. Using a cutting-edge technology called Affinity-Purification Mass-Spectrometry (AP-MS), we were able to identify hundreds of pTau-interacting partners. Our findings suggest new potential drug targets for the treatment of AD. More extensive studies are underway to examine interacting proteins and unravel their role in AD and other dementias.

Section 3: At Home Activities for Seniors

By: **Gabriella Tedesco**

Many seniors rely on places such as senior centers, gyms, and community centers to socialize and stay active. With the ongoing closure or limited hours of many of these locations due to COVID-19, older adults may be feeling lonelier than ever. Not only is it important to stay active for your mental health, it is beneficial to be active physically for healthy brain aging as well. As older adults are at a higher risk for more severe illness, many are fearful to even step outside. But, even so, no one should feel lonely or unconnected to the outside world. There are so many at-home activities to be a part of. Here is a list of activities that seniors might enjoy to help them take their minds off COVID-19 while also still making them feel connected with society!

Online Museum Tours:

- National Museum of Natural History: <https://naturalhistory.si.edu/visit/virtual-tour>
- The British Museum: <https://britishmuseum.withgoogle.com/>
- The Taj Mahal: <https://www.youtube.com/watch?v=665AHTNpf2o>
- The MoMA: <https://artsandculture.google.com/partner/moma-the-museum-of-modern-art>
- Versailles: <https://artsandculture.google.com/project/versailles>
- Street Art: <https://streetart.withgoogle.com/en/online-exhibitions>

Online Concerts/Live Performances:

- NPR Music is compiling a list of live audio and video streams from around the world

- The Metropolitan Opera: <https://www.metopera.org/user-information/nightly-met-opera-streams/>
- Improv Comedy: <https://magnettheater.com/calendar/?-date=2020-03-21#schedule-holder>

Mediations and Podcasts:

- Mindful App: <https://www.mindful.org/free-mindfulness-resources-for-calm-during-covid-outbreak/>
- Headspace provides free meditations: <https://www.headspace.com/covid-19>
- Lovingkindness Meditation from OnBeing: <https://onebing.org/blog/sylvia-boorstein-a-lovingkindness-meditation/>
- Calm: free meditations, music and calm body exercise routines: <https://www.calm.com>

Virtual Book Clubs:

- Virtual book clubs list: <https://time.com/5809322/social-distancing-book-clubs/>
- Tolstoy Together: read War and Peace only a few pages a day: #TolstoyTogether. <https://apublicspace.org/news/detail/tolstoy-together>
- Reese's Book Club: monthly club with a woman at the center of the story. <https://hello-sunshine.com/book-club> <https://www.instagram.com/reesesbookclub/?hl=en>
- TweetSpeakLive: A virtual poetry and storytelling reading. Events are held on Zoom. https://twitter.com/hashtag/TweetSpeakLive?src=hashtag_click

Section 4: The Effect of Mindfulness and Meditation on Cognitive Functioning

By: **Tanya Spruill, PhD**



As researchers continue to work towards effective treatments for Alzheimer's disease (AD), there is an urgent need to identify strategies that can prevent or delay disease onset. In light of growing evidence of the benefits of meditation and mindfulness for both psychological and physical health, the impact of these approaches on cognitive function is being actively explored. Mindfulness-based interventions have been shown to improve attention, memory, executive function, processing speed and

general cognition in older adults with subjective cognitive decline and mild cognitive impairment.

Mindfulness is defined as a non-judgmental awareness of present-moment experiences, including thoughts, emotions and bodily sensations. One way to develop mindfulness is through meditation. Formal practices such as guided body scans and sitting meditations are used to train the mind to attend to the present moment. The breath is often used as an anchor, and when the mind wanders, attention is redirected back to the breath. Meditation fosters awareness and acceptance of thoughts and emotions, including negative ones, as non-threatening, temporary experiences. This leads to an enhanced ability to recognize and disengage from escalating patterns of negative thinking (i.e., rumination) and reduces emotional reactivity. Mindfulness can also be practiced informally by bringing focused attention to activities in routine daily life, which helps disrupt the tendency to be on automatic pilot.

Mindfulness-based interventions improve attention control and emotion regulation, and reduce depression, anxiety and stress. These psychological factors are associated with cognitive decline as well as AD risk factors such as physical inactivity, poor sleep and high blood pressure. In addition, there is emerging evidence of direct effects of mindfulness and meditation on the brain. For example, observational studies have found larger hippocampal volume and reduced age-related hippocampal atrophy in experienced meditators compared with controls. Several small trials have also shown positive changes in brain structure and function in regions that are sensitive to aging and AD after mindfulness-based interventions.

Though still preliminary, current evidence suggests that meditation and mindfulness may hold promise for slowing age-related cognitive decline and preventing AD. Studies to date have been limited by small sample sizes, inadequate controls and brief follow-up periods. Additional research is needed to address these limitations, identify the best ways to teach mindfulness to older adults, and understand the mechanisms by which mindfulness and meditation can preserve cognitive function. In the meantime, improving psychological well-being is reason alone to promote these strategies to support successful aging.

Section 5: Music and Our Memories

By: *Mary Mittelman, DrPH, and Christina Madera*



Music is an important part of our everyday lives. Music helps us express our feelings and emotions. Music can be a powerful tool in helping improve overall mood and listening to music from our past can help bring back memories. One immediate benefit of music is that it can improve our emotional wellbeing. Have you ever noticed that you can't be sad listening to Pharrell Williams "Happy"? The song's infectious beat and catchy lyrics make you want to smile your problems away even if it's just for a moment. Music-related activities and music therapy can improve the well-being of people with dementia—and caregivers. For those caring for someone with dementia, it can be especially challenging to communicate with them. One way you can bridge the gap and feel closer to the person with dementia is through music.

Memory for music is relatively preserved among people with Alzheimer's disease because key brain areas linked to musical memory are relatively undamaged by the disease. Even in the late stages of Alzheimer's disease, a person may be able to tap a beat or sing lyrics to a song from childhood, even when they can no longer speak. Creating playlists for your loved one with dementia can help with managing stress levels, promoting relaxation and improving their quality of life. Each person's playlist should be personalized, based on individual preferences, culture, and social and behavioral needs, avoiding songs that will cause more agitation to a person with dementia who may be struggling with this already.

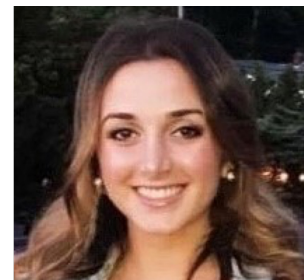
Music activities in groups have many benefits. In 2011, our ADRC's Dr. Mittelman founded a chorus, The Unforgettables, for people with dementia and their caregivers, which continues to rehearse and perform in concerts in 2020. Our research demonstrated that participants can enjoy and learn from rehearsing and performing in concerts that also engage the wider community. Chorus participants reported significant improvement in quality of life, social support, communication and self-esteem. Participants also noted positive effects of belonging to a group, sharing a normal activity and learning new skills.

Music therapy is not a cure for Alzheimer's disease or related dementias, but can alleviate some of the behavioral symptoms. Results of a recent study conducted by Drs. Ray and Mittelman at NYU suggest that widespread use of music therapy in long-term care settings may be effective in reducing symptoms of depression and agitation.

- Garrido, S., Dunne, L., Chang, E., Perz, J., Stevens, C. J., & Haertsch, M. (2017). The use of music playlists for people with dementia: A critical synthesis. *Journal of Alzheimer's Disease* : JAD, 60(3), 1129-1142. doi:10.3233/JAD-170612 [doi]
- Jacobsen, J. H., Stelzer, J., Fritz, T. H., Chetelat, G., La Joie, R., & Turner, R. (2015). Why musical memory can be preserved in advanced Alzheimer's disease. *Brain : A Journal of Neurology*, 138(Pt 8), 2438-2450. doi:10.1093/brain/awv135 [doi]
- Mittelman, M., & Papayannopoulou, P. (2018). The Unforgettables: A chorus for people with dementia with their family members and friends. *International Psychogeriatrics*, 1-11. doi:10.1017/S1041610217001867
- Thomas, K. S., Baier, R., Kosar, C., Ogarek, J., Trepman, A., & Mor, V. (2017). Individualized music program is associated with improved outcomes for U.S. nursing home residents with dementia. *The American Journal of Geriatric Psychiatry* : Official Journal of the American Association for Geriatric Psychiatry, 25(9), 931-938. doi:S1064-7481(17)30285-3 [pii]

Section 6: Counselor's Corner: How do I deal with stress and anxiety during COVID?

By: *Marissa Jacobi, LMSW*



Are you feeling stressed or anxious about the current coronavirus pandemic? You are certainly not alone...

As society attempts to adjust to a new normal, most of us are uncertain of just how to feel or respond to the global pandemic that we are currently faced with.

You may find yourself preoccupied with worries about your health or the health of your friends and family. You may be spending hours consuming media filled with upsetting images and statistics. Or, you may find that you are experiencing changes in sleep or appetite, worsening of chronic health conditions, or increased consumption of alcohol, tobacco, or other drugs. Though each individual responds to stressful situations differently, the examples listed above are all common manifestations of stress and anxiety.

It is important to be mindful of your personal needs during these difficult times. By answering the following questions, you may be able to better understand and meet your needs:

What might make me feel grounded during a time of chaos?

Explore what types of activities bring you a sense of peace. Some are comforted by social interaction, spending time with family, or keeping in touch with friends virtually. Others require more personal space and alone time to feel recharged. Could any of the following activities help you find a sense of purpose, or provide a therapeutic outlet: scheduling a daily walk outside, reading a book, doing an art project, cooking or baking, practicing meditation or yoga, watching a funny television show, listening to music, etc.

Which activities invigorate me? Which make me feel drained?

Consider how aspects of your daily schedule and functioning are affecting your mood. How does exercise and maintaining healthy eating habits impact the way your body is feeling? Is increased sugar intake or use of substances making you feel sluggish? How is the media that you are consuming connected with some of the stress and anxiety you feel? Consider limiting media intake to one hour per day.

How can you effectively communicate your needs to those around you?

Remember that each individual has their own unique personal needs. Try not to expect those around you to be aware of your set of personal needs in absence of communication. If you let your family, friends, coworkers, and managers know about these needs, they will be better able to understand how to interact with you during this difficult time.

As per CDC.gov recommendations, if you or someone you care about are feeling overwhelmed with emotions like sadness, depression, or anxiety, or feel like you want to harm yourself or others: Call 911, the New York State COVID-19 Emotional Support Helpline at 1-844-863-9314, or the Disaster Distress Helpline, 1-800-985-5990, or text TalkWithUs to 66746.

Section 7: Discovery of a New, Very Early Stage of Eventual Alzheimer's Disease

By: *Barry Reisberg, MD, Professor Emeritus for the Alzheimer's Disease Research Center Clinical Core*

In 1978, the term "Alzheimer's disease," was applied only to a rare condition occurring before 65 years of age, also referred to as, "presenile dementia." The generally used term for what we now call Alzheimer's disease was "senility." Using the available clinical rating scales at that time as a starting point, I began to study symptoms in my patients. In my first book, "Brain Failure: An Introduction to Current Concepts of Senility", published in 1981, I noted three phases of the condition, which was not a novel observation.

In 1982, we published the Global Deterioration Scale (GDS) in the *American Journal of Psychiatry*. The GDS describes seven major stages in the evolution of Alzheimer's disease. The first stage of the GDS is where individuals have neither subjective complaints nor objective evidence of cognitive impairment. Those with a GDS of 1 are referred to as being cognitively "normal." In GDS stage 2, persons have subjective complaints of cognitive decline in their thinking ability. Most commonly, in this stage, individuals complain of not recalling names as well as they previously had. Another frequent complaint is that they forget where they have placed familiar objects, such as their keys. Our subsequent research has confirmed our initial (1986) estimate that, in otherwise healthy persons, this 2nd GDS stage of Subjective Cognitive Decline lasts an average of about 15 years before the onset of the next stage (see the figure).

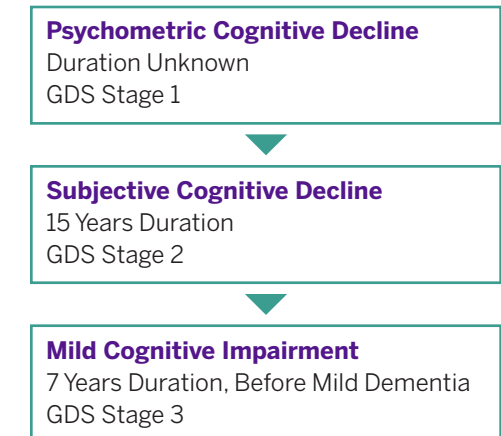
The next stage, stage 3, is where a person's performance in demanding employment and social situations begins to decline. In addition, performance on psychological testing also declines

in comparison with prior abilities. In 1988, we showed that individuals in stage 3 performed significantly worse than those in stage 2, who had subjective complaints only, on 15 of the 16 test measures that we studied. We coined the term, "Mild Cognitive Impairment", or MCI, widely used today for describing this condition. We estimated in 1986, and we subsequently confirmed, that the MCI stage lasts about 7 years in otherwise healthy persons (see the figure). Our 1988 publication showed that Mild Cognitive Impairment was followed by the stages of dementia, defined as a generalized decrease in thinking capacities.

Last month, together with my colleagues at NYU and elsewhere, we published a scientific article demonstrating that decline in psychological test measures occurs even before the stage of Subjective Cognitive Decline.1 We followed 47 healthy, cognitively normal subjects over an average interval of 6.7 years. If the subjects showed worsening at follow-up to the stage of Subjective Cognitive Decline, or worse, we categorized them as "decliners." If the subjects remained free of subjective or objective cognitive decline, we categorized them as "non-decliners." After compensating for differences between the groups (age, gender, educational background), we found a very significant divergence between the two groups in the rates of decline. The two groups differed in the decline rate to the extent that there was a less than 1/1000 chance that the differences were accidental.1 Further, after compensating for differences between the two groups in age, gender, educational background, and follow-up time, the combinatorial test measure score was significantly lower at baseline in the future decliners.

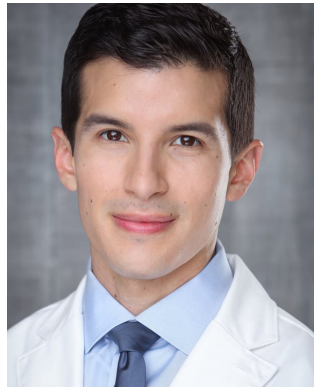
This appears to be the first study that directly links a decline in test measure scores to subsequent subjective loss in thinking abilities and, by extension, to MCI, and to the dementia of the Alzheimer's type continuum. These findings provide new opportunities for the identification and application of current and future strategies for the prevention of Alzheimer's related decline.

Figure: Stages of Changes in Thinking Abilities



1Reisberg, B., Shao, Y., Moosavi, M., Kenowsky, S., Vedvyas, A., Marsh, K., Bao, J., Buj, M., Torossian, C., Kluger, A., Vedvyas, G., Oo, T., Malik, F., Arain, F., Masurkar, A.V., Wisniewski, T. Psychometric cognitive decline (PCD) precedes the advent of subjective cognitive decline (SCD) in the evolution of Alzheimer's disease, *Dementia and Geriatric Cognitive Disorders*, 30th Anniversary: Research Articles, 2020.

Section 8:
Meet Our New Doctor



Dr. Joel Salinas
Joel (pronounced 'joh-EHL') Salinas has been appointed the Lulu P. and David J. Levidow Assistant Professor of Neurology at the Center for Cognitive Neurology. Dr. Salinas obtained his BA in Biology & Society from Cornell University. He earned his medical degree with research distinction at the University of Miami Miller School of Medicine as well as an MBA with a concentration

in Health Sector Management & Policy at the Miami Herbert Business School. He completed his neurology residency at Massachusetts General Hospital and the Brigham and Women's Hospital. He then subspecialized through a combined research and clinical fellowship in Behavioral Neurology & Neuropsychiatry at Massachusetts General Hospital and Neurostatistics & Neuroepidemiology at the Harvard TH Chan School of Public Health, earning a Master of Science degree in Epidemiology.

Most recently, he was Assistant Professor in Neurology at Harvard Medical School and the Massachusetts General Hospital Department of Neurology's division of Cognitive-Behavioral Neurology and was the Clinical Director of the McCance Center for Brain Health. He now specializes in practical clinical approaches to brain health and conducts research in social and behavioral epidemiology to understand social determinants of brain health and harness these insights to preserve healthy cognitive function at the population level. He also chronicles his experiences as a neurodivergent neurologist and the powerful stories of patients experiencing neurological conditions in his book, *Mirror Touch: A Memoir of Synesthesia and the Secret Life of the Brain*.

Dr. Salinas's administrative office will be located at 222 E 41st Street, 14th floor. He will practice out of the Pearl Barlow Center for Memory Evaluation and Treatment and join the Alzheimer's Disease Research Center at 145 E 32nd Street.

Section 9:
Upcoming and Past Events

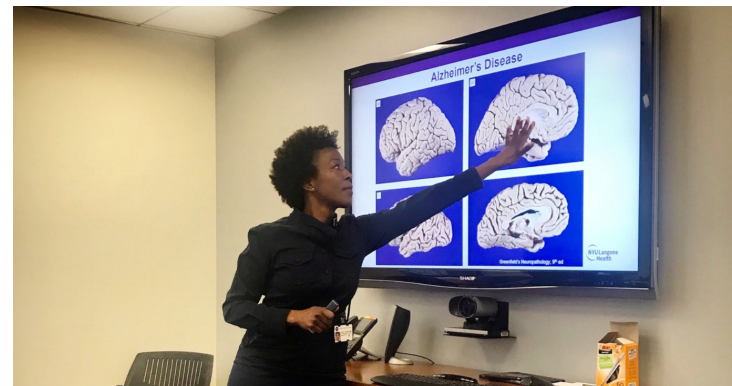
We are excited to continue our Alzheimer's Disease Research Center's, "Lunch and Learn" series, newly titled, "Learn at Home". This has been a great way to continue to discuss topics often brought up during study visits with some of your favorite clinicians via a virtual platform. The best part?? It's all done from the comfort of your living room sofa! At the center, we appreciate your continuous contribution and dedication to our study. This is a small token of our team's gratitude for your support in helping to find a cure for Alzheimer's disease and other related dementias.

Upcoming Events:

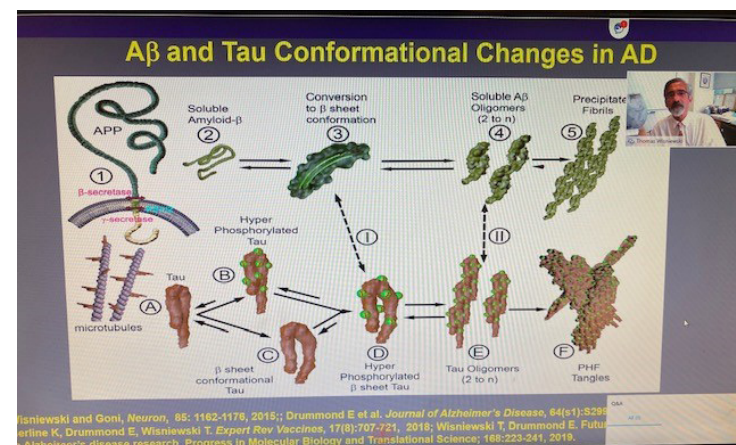
We have a number of events in the works for the fall and winter so be sure to keep an eye out for our ADRC email announcements.

Past Events:

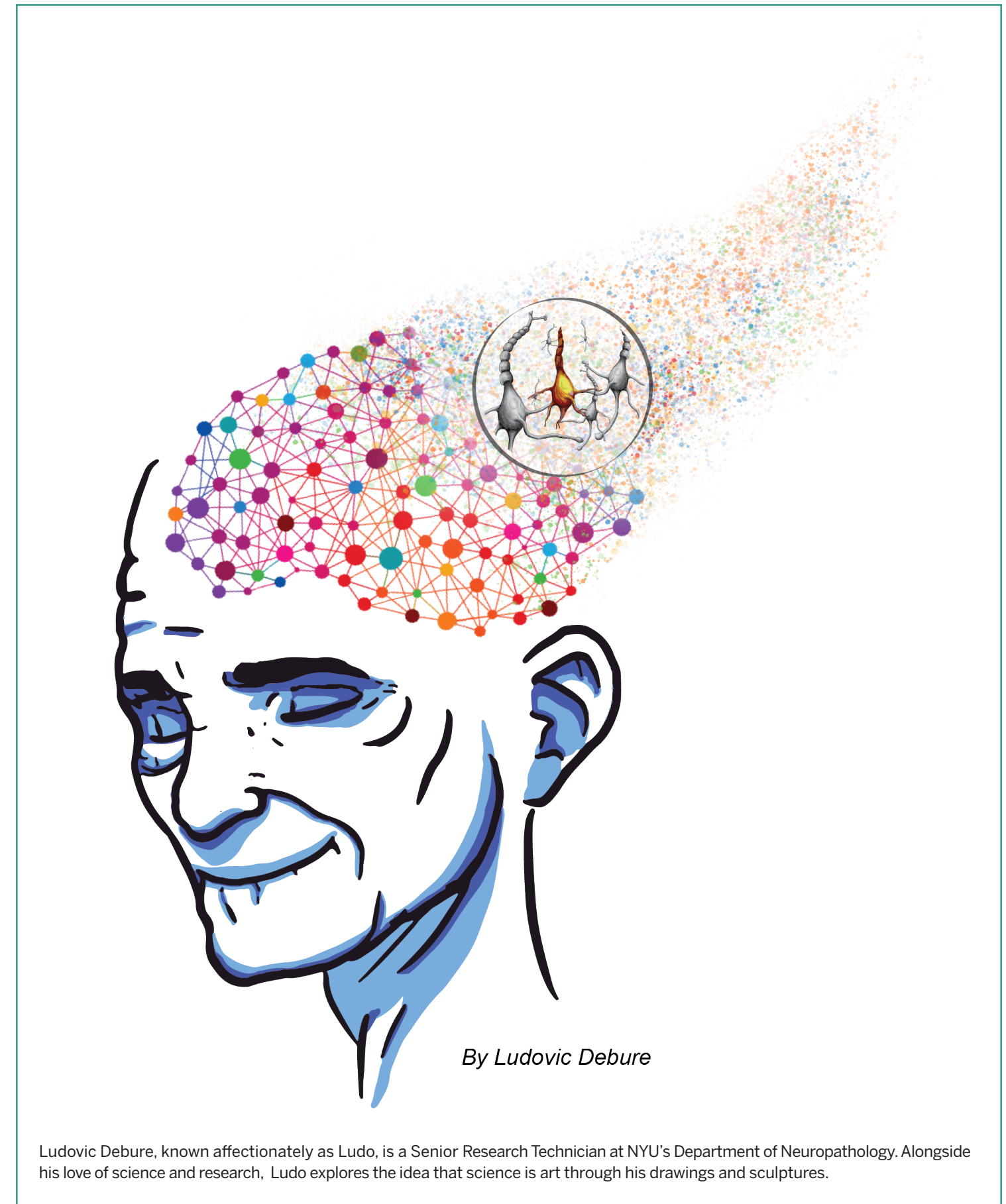
- Dr. Thomas Wisniewski, our Center for Cognitive Neurology Director and Principal Investigator for the ADRC study, presented on "Will There Be a Vaccine for Alzheimer's Disease" on July 31st. Over 80 people from both our ADRC and Barlow Clinic registered!
- Dr. Ricardo Osorio presented our very first Learn at Home series discussion "Sleep and Brain Health" on 5/29/20. It was a tremendous success with over 70 people in attendance!
- Winter Tea Dance: On February 12, 2020 some ADRC participants, Barlow Center patients, and research study staff visited the Intrepid Sea, Air & Space Museum for an afternoon of dancing with music from the Intrepid's years of service (1943-1974). Dancing was led by Rhythm Break Cares, an organization designed to provide the restorative power of music, movement, and touch to as many older adults living with Alzheimer's and dementia as possible, along with their families and caregivers. Everyone seemed to be having so much fun and could not stop dancing!



Our most recent Lunch and Learn with Dr. Arline Faustin on "What We Learn from Examining the Brain" took place on 1/31/2020.



Our most recent Learn at Home with Dr. Thomas Wisniewski.



By Ludovic Debure

Ludovic Debure, known affectionately as Ludo, is a Senior Research Technician at NYU's Department of Neuropathology. Alongside his love of science and research, Ludo explores the idea that science is art through his drawings and sculptures.

Section 10:
Contact Info

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