

MIND MATTERS

Fall 2024–Winter 2025

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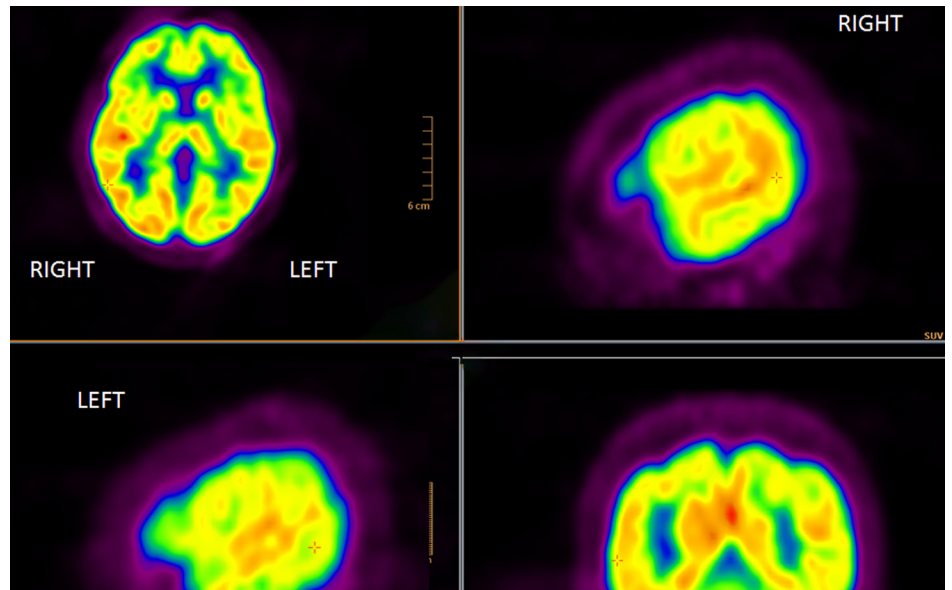
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SECTION 1

Donanemab: Approved for Treatment of Early Alzheimer's Disease

By: Alison Pietras, PA, and Arjun Masurkar, MD, PhD



On July 2, 2024, the US Food and Drug Administration approved donanemab, making it the second disease-modifying therapeutic holding traditional approval for the treatment of early Alzheimer's disease (AD). Donanemab is an antibody that is directed against amyloid plaques. It is administered intravenously every 4 weeks for 18 months, although it can be discontinued prior to 18 months if amyloid has been successfully cleared from the brain.

The results of the clinical trial that led to its approval were published in July 2023 in JAMA. Donanemab treatment resulted in significantly reduced brain amyloid plaque, as well as a ~22% slowing of progressive loss of cognition and function over an 18-month period, with additional evidence suggesting a ~37% reduced risk of disease progression over 18 months. Side effects included transient focal brain swelling or bleeding in the brain, discovered on MRI and termed amyloid-related imaging abnormalities, or ARIA. ARIA occurred in ~37% of trial participants receiving donanemab, compared to ~15% in the placebo group, and the majority were without symptoms. ARIA led to serious outcomes in 1.6% of participants receiving donanemab. Carrying an e4 variant of the APOE gene put patients at higher risk of ARIA. These potential side effects tended to occur at the beginning of the protocol.

Long-term benefits of donanemab remain unknown and are currently being investigated. The NYU Langone Pearl Barlow Memory Center is working diligently with the Pharmacy and Therapeutics Committee to safely add this medication to our formulary in the near future.

SECTION 2
What Is Vascular Dementia?

By: Emma Kaye, DNP, AGACNP-BC, FNP-BC, and Arjun Masurkar, MD, PhD



While Alzheimer’s disease (AD) is the most common cause of dementia (~70%), vascular dementia is the second most common cause (~20%). Vascular dementia causes impairment due to brain injury as a result of disease of the brain’s blood vessels. The brain relies on an extensive network of blood vessels, millions of tiny highways that deliver oxygen and nutrients to the brain’s neurons for optimal function. When this network is disrupted, for example, through gradual stiffening of the vessels or a sudden blockage, the impaired blood flow can damage the health of neurons. While vascular dementia can impact memory, it can more commonly be associated with difficulties in problem-solving, organizing, and planning.

What causes vascular dementia? While this is a question still being explored, unhealthy lifestyle choices, such as poor diet, lack of exercise, or cigarette smoking, can over time lead to atherosclerosis and other biological changes that can damage both the blood vessels and the neuronal network they support. People with heart disease caused by other factors may also be at risk for these changes. Others may have genetic risks for blood vessel problems in the brain. Through any of these pathways, damage may manifest as sudden loss of blood flow, experienced as strokes, or can gradually build up silently over many years until the cumulative effects become evident with noticeable cognitive symptoms.

Researchers, including those at the NYU Alzheimer’s Disease Research Center, are investigating the relationship between vascular health and cognitive decline, as well as the interaction between vascular dementia and AD. These studies aim to discover new approaches to identify those who may

be at risk and methods to mitigate this risk. The ultimate goal is to halt vascular dementia progression in its early stages and safeguard the crucial blood vessel network before it is damaged beyond repair.

SECTION 3
All About Exercise Boosting Brain Health: Cardiovascular Endurance vs. Resistance Exercise
By: Joshua Gills, PhD



Exercise isn’t just about building muscles or shedding pounds—it’s also a powerful tool for enhancing brain health. Both cardiovascular (cardio) and resistance exercises offer unique benefits that can improve cognitive function, mood, and overall mental well-being.

Cardio Exercises
Cardio, such as walking, running, swimming, or cycling, involves continuous movement that speeds up your heart rate and breathing. This type of exercise increases blood flow to the brain, delivering oxygen and nutrients essential for brain health.

Brain Health Benefits of Cardio:

- **Enhanced Memory:** Regular cardio can increase the size of the hippocampus, the part of the brain responsible for memory and learning.
- **Improved Cognitive Function:** Cardio has been linked to better attention, processing speed, and executive function.
- **Mood Boost:** Cardio can trigger the release of endorphins and reduce stress hormones, helping to alleviate symptoms of anxiety and depression.
- **Neuroprotection:** Cardio reduces neuroinflammation and strengthens neural connections, potentially lowering the risk of cognitive decline and dementia.

Resistance Exercise
Resistance exercise includes strength building activities like weightlifting, body-weight exercises, and isometrics. These exercises are not only great for building muscle but also offer significant brain health benefits.

Brain Health Benefits of Resistance Exercise:

- **Increased Focus and Mental Clarity:** Resistance exercise can boost the production of neurotrophic factors, which support brain plasticity, enhancing focus and cognitive flexibility.
- **Stress Relief:** High-intensity workouts help reduce stress levels, improving mental resilience and reducing the impact of stress on the brain.
- **Improved Mood:** Like cardio, resistance exercise also stimulates the release of endorphins, promoting a positive mood and combating mental fatigue.

Incorporating both cardio and resistance exercises into your fitness routine can significantly benefit your brain. Whether you’re aiming to sharpen your memory, improve your mood, or protect your brain from aging, a balanced mix of these exercises can keep your mind as fit as your body.

Joshua Gills, PhD, is a post-doctoral fellow at NYU Grossman School of Medicine and is a current NYU ADRC REC Scholar.



Want to Start Exercising and Maintain It? Exercise for Mood!
By: Kristin Szuhany, PhD

Physical Activity and Cognition
Physical activity is associated with better cognitive functioning, including processing speed, memory, and executive functioning, and can reduce risk of age-related cognitive decline. Physical activity is defined as any bodily movement that expends energy. Exercise is a type of physical activity that involves planned and repetitive activity to improve physical fitness. Physical inactivity, defined as not meeting recommended guidelines of 150 minutes of moderate intensity activity per week (~21 minutes per day), is a known modifiable risk factor for Alzheimer’s disease and related dementias.

The Gap Between Intention and Action
Though physical activity improves brain health and is also associated with positive benefits to physical and mental health (such as reducing depression, anxiety, stress), most people do not meet physical activity guidelines. The rates of people who meet the guidelines decline with age, with only 10-21% of midlife to older adults meeting recommendations. Only 56% of adults who *intend* to exercise actually do ANY exercise!

Theories of physical activity motivation suggest that intentions and values associated with physical activity (e.g., thinking, “I want to be a healthy person”) are only one piece of the puzzle. We also need to consider the expectations about the pleasure related to physical activity, enjoyment of activity, and mood changes experienced during and immediately after physical activity.

To better highlight these mood and enjoyment expectations, we may need to shift the way we think about why we exercise. We should not just focus on exercise to improve weight, fitness, or reduce the risk of poor health—all delayed benefits that do not provide immediate reward. Instead, we should pay attention to the immediate mood benefits we get now—right after exercising! This framing has been shown to improve mood and to keep people more motivated to continue exercising.

The Best Strategy to Start and Maintain Exercise
Find something that you enjoy doing—be creative! Exercise doesn’t mean just running or going to the gym; it can be taking a walk, dancing, or playing your favorite sport. Pay attention to how your bodily movement makes you feel in the moment and do the things that uplift your mood and reduce your stress. Use those good feelings to motivate you the next time you plan to exercise. Exercise for your mood and those health and brain benefits will come!

Kristin Szuhany, PhD, is a clinical psychologist at NYU Langone and is a current NYU ADRC REC Scholar.



Exercise and the Prefrontal Cortex
By: Emma Kaye, DNP, AGACNP-BC, FNP-BC

As a dedicated triathlete and marathoner, I’d like to share with you the secret that helps me strive to perform, compete, and succeed. It’s all about harnessing the incredible power of the prefrontal cortex. This brain region regulates our thoughts, actions, and emotions through extensive communication with other brain regions. It helps with complex functions, from judgment and decision making to impulse control and attention.

Each workout floods your system with oxygen and nutrients, ramping up circulation and giving your cognitive function a turbo boost. Exercise sparks the growth of new synapses, boosts brain plasticity, planting seeds that keep your brain sharp and resilient. Plus, it releases proteins that help nerve cells survive and grow new connections, which helps you adapt to new challenges and bounce back from setbacks.

How does this knowledge help me compete in triathlons and run marathons? I use it to enhance my training: by visualizing my successes and feeling the synergy between my mind and body, I turn each stride into a quest for precision. As with many other pursuits in life, consistency and mindful effort often lead to continuous improvement. Each race offers new insights that help me refine my approach for the next challenge. I take time to reflect and mentally prepare in the days leading up to the race. When we train with mental intention, it shapes who we become and ultimately builds mental resilience to take on any life challenge outside of exercise.

The next time you hit the gym or go for a run, keep in mind that you’re not just working out your body. You’re throwing your brain a party that sharpens your mind, boosts your cognition, and keeps you alert and energized.

SECTION 4
The Effect of Childhood Adversity on Cognition
By: Sunnie Kenowsky, DVM



Adverse Childhood Experiences (ACEs) are traumatic circumstances experienced during the first 18 years of life such as abuse, neglect, and family dysfunction. These experiences can profoundly impact cognitive development and overall health. Prolonged exposure to ACEs, especially multiple types, can cause a toxic stress response in the child and structural and functional changes during development. Early life adversity can impair the hypothalamic pituitary adrenal axis which is a communication system that helps the body manage stress and maintain hemostasis.

Nelson et al. in *BMJ* (2020) reported various negative behavioral, neurobiological and physical developmental

consequences of ACEs, among them development of aggressive and violent behavior, post-traumatic stress disorder, depression, suicidal thoughts and attempts, eating disorders, and differences in brain development, such as decreased brain size and decreased brain electrical activity, which are associated with a decrease in thinking abilities. These include a set of higher-level cognitive skills that help people set and achieve goals, manage their emotions, control their impulses, pay attention, and obtain educational achievements. Additionally, the researchers reported associated adult outcomes of cardiovascular disease, stroke, asthma, COPD, diabetes, obesity, depression and risky health behaviors, such as substance abuse and poor health choices. Most of these outcomes are recognized risk factors for the development of Alzheimer’s disease and related dementias as reported by Livingston et al. in *The Lancet Commissions* (2020).

Brain health can be optimized by consistently making healthy choices on a daily basis. Healthy choices include: learning and employing stress management, seeking treatment for trauma, anxiety, depression, mental and physical illnesses, quitting smoking and stopping substance abuse, obtaining regular medical checkups and following medical guidance, maintaining health insurance, building a supportive social network, engaging in aerobic, endurance and other types of exercise, consuming the MIND diet (Mediterranean DASH Intervention for Neurodegenerative Delay), obtaining adequate sleep and fostering brain resilience by doing such things as practicing mindfulness, developing grip strength, and learning new things such as a new skill set, playing a new musical instrument or learning a new language. Making daily healthy choices can help counteract the negative impacts of ACEs and promote better long-term health and cognitive outcomes.

SECTION 5
Dawn, Dusk, and Dark
By: Dianne Mack, PhD, MS, LCSW



It’s fall. The darkness arrives a bit earlier than it did at the start of summer. Dawn, dusk, and dark are experienced daily—yet differently—in all seasons. During this time of changing temperatures, the dusk hours creep by for some of us and hurry by for others. Do you miss the summer days and yearn for those months when the sunset was further away?

If you are a caregiver of a person with cognitive changes or dementia, or if you are a patient yourself, the shifting seasons and light, may remind us of times when brains were healthier, memories were easier to recall, and less help was needed to do everyday things.

As dawn flows into dusk and fall turns to winter, let us rejoice in the here and now, the sweet memories of today or of times past. When it’s cold and dark outside, staying in touch with others is important for keeping our brains healthy and our hearts happy. Let us join with each other to celebrate our loved ones and live fuller lives. Let us remember that we are not alone. We are on this journey together. Let us celebrate the growing knowledge about brain health and new ways to prevent and treat dementia. So, each day let us spend time with one another, loving and caring for each other, and learning new things to prevent or slow down anything that may be harming or ailing our brains and minds.

So, the fall will fade into winter. Dusk will arrive earlier. Dark will come quickly and stay longer. Let us use this time to reflect and cherish what we have. Dawn will rise again—for many of us.

The Alzheimer’s Disease Research Center has resources to help you learn more about living a healthier life as you care for your brain and for others. Clinical and research trials, treatments, and caregiver supports are available for all.

Dianne Mack, PhD, MS, LCSW, is a member of the NYU ADRC Community Advisory Board.

SECTION 6
How Care Managers Support the Transition to Hospice Care
By: Komal Patel Murali, PhD, RN, ACNP-BC



Making the decision to transition to hospice care can be a challenging and emotionally heavy experience for families and caregivers. This experience is often also driven by decision-making factors that lie beyond the medical, like social and cultural practices, religious and spiritual beliefs, and values and preferences. The decision to transition to comfort-focused care like hospice usually involves shared decision making, where health care professionals and family caregivers come together to make a decision that is best aligned with goals of care. It is during these dynamic moments of communication where family members can express their unique views and needs and be met with the support and resources they need to make this significant end-of-life decision.

An important feature of dementia care involves care management that specifically helps individuals navigate care options and discuss the clinical status with a licensed social worker or nurse. These individuals are specially trained to provide tailored care management that focuses on the needs of people who are living with serious illnesses like dementia. When making critical decisions in dementia care, such as accessing home care, moving to a nursing home, or transitioning to hospice care, care managers can employ culturally sensitive and personalized communication to help you and those you care for in this process.

Additionally, care managers will focus on helping you to both understand how to manage dementia illness in conjunction with your healthcare providers while simultaneously navigating the healthcare system. They may also offer to conduct regular outreach to ensure that any decisions being made are aligned with your goals and wishes as your loved one moves along their illness trajectory. Therefore, when you find yourself needing an additional layer of support or assistance, consider contacting a care manager.

Komal Patel Murali, PhD, RN, ACNP-BC, is an assistant professor at NYU Rory Meyers College of Nursing and a recent NYU ADRC REC Scholar.

SECTION 7

What’s New at the Alzheimer’s Disease Research Center (ADRC)?

MEET THE NEW STAFF



Emma Kaye, DNP, AGACNP-BC, FNP-BC, has 2.5 years of experience in neurology, including a fellowship at the Neuroscience Institute of Northwell, covering Northshore and Southshore Hospitals. Specializing in cognitive and general neurology, she has built a strong foundation in the field. Her background, which includes a master’s, post-master, and doctoral degrees from Hofstra University, highlights dedication to advancing her knowledge in neurology.

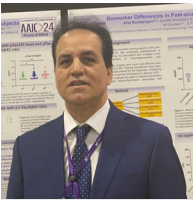
As an ambassador for CaringKind, she supports and advocates for families affected by Alzheimer’s and other dementias. She is excited to be publishing her upcoming book, *The Unmapped Terrain of Brain Health*, which provides insight into brain wellness through creative imagery.

Outside of neurology and community service, she travels to compete in marathons and triathlons. Her passion for these challenges has earned her top finishes and awards in her age group.



Brianna Vega has been with the NYU Alzheimer’s Disease Research Center (ADRC) as a student research intern since the Fall of 2021, and recently transitioned to the Research Data Associate position. Brianna recently graduated with a BS in Global Public Health and Biology from NYU. By working with the Data Core team on Neuropsychological testing, GAIT analysis, Actigraph, Biorepository, Brianna has gained invaluable experience and knowledge that will guide her in her new position. In her free time, Brianna enjoys baking, Pilates, traveling, and eating at new restaurants with friends. This will be her fifth year living in New York City, and she is excited for what’s to come!

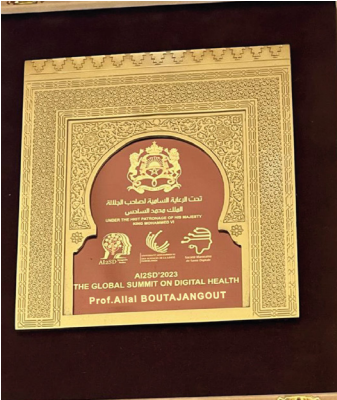
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Allal Boutajangout, PhD, focuses his research on Alzheimer’s disease (AD) and related disorders, with a particular interest in immunotherapy. He is currently in the process of testing the efficacy of generated antibodies in different neurodegenerative diseases, in addition to identifying novel blood biomarkers for the prediction and monitoring of disease progression, which is crucial for detection of early stage AD.

In May 2023, he was a member of the organizing committee of the Global Summit on Digital Health AI2SD 2023, under the patronage of King Mohammed VI of Morocco, where he received an honorable award.

He also served as a moderator and keynote speaker of the 2nd European Congress of Neurology and Neuropsychiatry that was held in London in February 2024.



THE ALZHEIMER’S ASSOCIATION INTERNATIONAL CONFERENCE (AAIC)

Biomarkers are measures of what is happening inside the body, shown by lab and imaging tests. They can help scientists diagnose diseases, evaluate health risks, see disease change over time, and monitor treatment. Researchers studying Alzheimer’s disease (AD) use biomarkers derived from blood, cerebrospinal fluid (CSF), and PET scans, to help detect brain changes in people who may or may not have noticeable changes in their memory.

The ADRC Biomarker Core helps to identify the biomarkers associated with AD through each stage of disease progression. Allal Boutajangout, PhD, who leads the Laboratory of Neurodegeneration and Drug Discovery Program at the Center of Cognitive Neurology, and also serves as Co-Director of the Center for Cognitive Neurology Biomarker Core at NYU, explained, “We detect many AD biomarkers, including markers of amyloid and tau, neurodegeneration, neuroinflammation, and others. Our goal is to find biomarkers that may be used for diagnosis of AD and other disorders. We measure these biomarkers using a technology called Simoa (Single Molecule Array). Plasma biomarkers are our top priority, because they are less invasive and less expensive to measure than CSF biomarkers.”

This summer, members of the NYU ADRC participated in the Alzheimer’s Association International Conference (AAIC) in Philadelphia, where they presented two talks and 28 posters. Dr. Boutajangout highlighted three of his posters focused on AD biomarkers.

Diagnostic utility of plasma biomarkers to differentiate controls, SCD, and MCI Subjects. The goal of this study was to identify candidate biomarkers for diagnosis of early AD. The study evaluated a total of 152 ADRC participants, including subjects with normal cognition (controls), subjective cognitive decline (SCD), and mild cognitive impairment (MCI). Eight biomarkers were measured from samples of participants’ blood plasma. Researchers observed that the levels of an amyloid beta 42 marker in MCI and a tau marker pTau181 in SCD were significantly different than in controls. These differences became even more pronounced when marker ratios were compared. For example, the ratio of the tau to amyloid levels was significantly different in both SCD and MCI. The next step is to correlate these candidate biomarkers with imaging and cognitive findings and thus further test the diagnostic utility of these biomarkers.

Biomarker differences in post-acute sequelae of COVID-19 patients compared to controls. Many COVID-19 patients experience neurological symptoms, including cognitive impairment. If these symptoms linger after the infection has subsided, they are referred to as post-acute sequelae. The goal of this study was to evaluate plasma biomarkers associated with cognitive impairment in patients recovering from COVID-19. The study included 131 ADRC participants with and without cognitive impairment, who tested positive or negative for COVID-19. Several biomarkers, including the amyloid level and the ratio of tau to amyloid, showed significant differences between COVID-19 participants with cognitive impairment and COVID-19 participants with normal cognition. Another study by the ADRC and its collaborators, also presented at the AAIC, showed that post-COVID-19 cognitive dysfunction may be linked to the damage of the blood-brain barrier due to inflammation.

Differences between high-precision Alzheimer’s disease plasma and PET biomarkers among cognitively normal older Black and White adults. Dr. Boutajangout collaborated with Dr. Omonigho Michael Bubu, MD, PhD, MPH, Associate Leader of the ADRC Clinical Core, who was the lead author on this study. Researchers compared plasma biomarkers and PET imaging biomarkers of AD in 203 cognitively normal ADRC participants, including 83 non-Hispanic Blacks and 120 non-Hispanic Whites. Compared to White participants, Black participants were found to have lower levels of plasma amyloid and tau, and also significantly lower levels of amyloid on PET. As these differences may impact diagnosis and clinical decisions, further studies are needed to compare biomarkers across racial and ethnic groups.

Dr. Boutajangout concluded, “Our team enthusiastically participated throughout the conference and received positive feedback, which validated the hard work and dedication we put in on a daily basis.”

UPCOMING EVENTS

RSVP here for ADRC events:
https://is.gd/CCN_EVENTS_RSVP

SECTION 8

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