Stanford MEDICINE

Stanford Neurology
POSTON LAB

Annual Research Report | Volume 9 | February 2024

ANNUAL RESEARCH REPORT

Resources

Recruitment for research studies
Join studies that are actively recruiting.

Patient support
A list of programs offering various types of support.

Research Spotlight

DLB drug development
Breakdown of Dementia with Lewy bodies clinical trials

Introducing: SYNTap ®
Early identification of and tailored treatments for synucleinopathies

Immune Response Spotlight
Elevated immune response in PD & PD immunosenescence

Imaging Spotlight
Brain volume assessment & Perivascular spaces

Dear members of our research community,

We at the Poston Lab and the Stanford Movement Disorders Center would like to take the opportunity to express our sincere gratitude for your time and participation in our research on Parkinson's disease and parkinsonian disorders. Your dedicated participation lies at the heart of our scientific research.

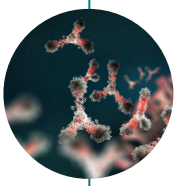
As a show of thanks, here is an update on our progress to date. We have been hard at work compiling and interpreting valuable information given to us by you, our research participants. The fruits of our efforts will soon be available for shared access in the scientific community.

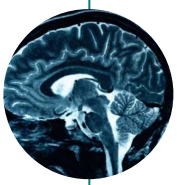
Sincerely,
The Poston Lab
and the Stanford Movement Disorders Center

We express our sincere gratitude to our project sponsors and collaborators.

Much like our participants, the invaluable support from these groups is indispensable, rendering our research endeavors possible and impactful.

Annual Research Report



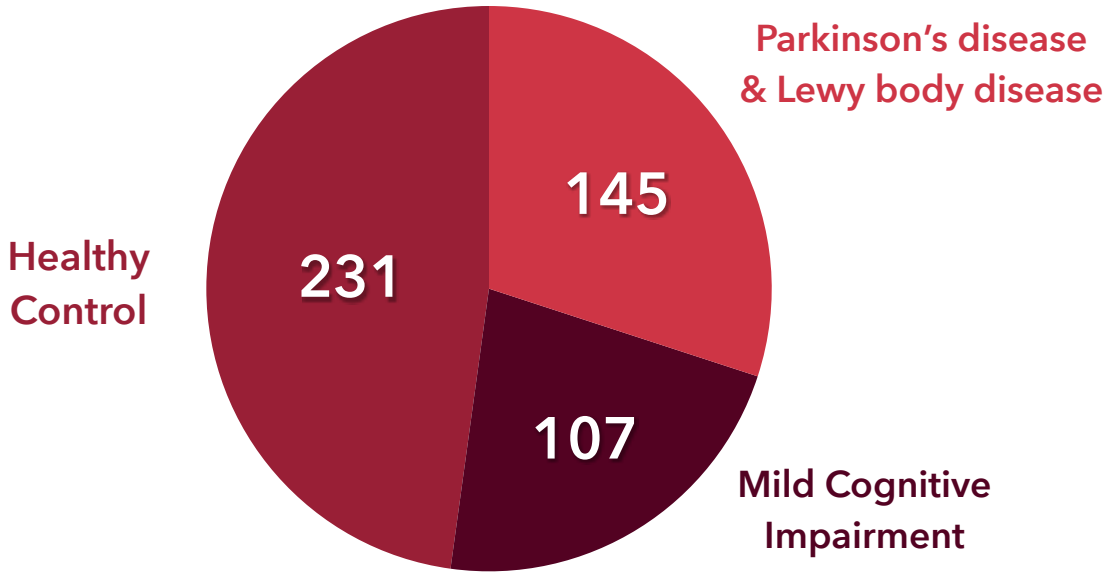


Parkinson's Foundation
CENTER OF EXCELLENCE

We are proud to be named a Parkinson's Foundation Center of Excellence. Centers of Excellence must demonstrate exemplary multidisciplinary care, with Centers of Excellence playing a vital role in leading the PD field in advancing clinical research. These designations recognize medical centers that excel in utilizing a specialized, multidisciplinary team-based approach to provide the highest level of evidence-based, patient-centered care; demonstrate leadership in professional training; and conduct impactful patient education and community outreach.

Recruitment for Research Studies

Our studies are possible thanks to patients and caregivers who participate in our research studies. We are grateful for your generosity as you are a key part of research.



With the help of our clinical research coordinators, we have considered over 438 individual cases for research this year. We are currently recruiting for the studies listed below. ***Join today!***

Amyloid & Tau PET Imaging Study

We are recruiting volunteers to participate in a PET imaging study of the brain to determine the impact of amyloid and tau protein tangles on cognition. Study participants will be asked to come in for two 2-hour study visits, each including a 40 minute combined PET-MRI scan.

For more information, contact: Hillary Vossler (hvossler@stanford.edu) or Skylar Weiss (skweiss@stanford.edu)

Facial Expression Biomarker Study

We are looking for volunteers with Mild Cognitive Impairment due to Lewy bodies and Dementia with Lewy bodies to participate in a study looking at facial movements in neurodegenerative diseases. We hope to validate a diagnostic tool developed by Stanford Undergraduate, Erin Smith, for early detection of Parkinson's disease. Study participants will be asked to come in for one 30 minute study visit.

For more information, contact: Alena Smith (alenaa@stanford.edu)

Mind & Memory Changes Study (LB-SPARK)

The Lewy Body Scientific Partnership for Advancing Research and Knowledge aims to understand mind and memory changes in Parkinson's disease. LB-SPARK is recruiting individuals with Parkinson's disease, Dementia with Lewy bodies, and healthy volunteers.

This is a longitudinal study looking at Parkinson's disease over time. You will be contacted once per year by phone or visit at Stanford. Study participation includes neurological exams, neuropsychology testing, a blood sample, gait & balance tests, collecting cerebrospinal fluid (optional), and collecting PET/MRI scans (optional).

Compensation: You will be given a parking and lunch voucher, $200 if you agree to a lumbar puncture collecting cerebrospinal fluid, and $100 for a PET/MRI scan.

For more information, contact: Hannah Schmitz (hschmitz@stanford.edu)

LB-SPARK
Lewy Body Scientific Partnership for Advancing Research and Knowledge

LB-SPARK will be replacing the Pacific UDALL Center (PUC). Please contact hschmitz@stanford.edu for more details.

Stanford Healthy Brain Aging Project

The Healthy Brain Aging Project, sponsored by the NIH Alzheimer's disease research center (ADRC) is still actively recruiting people with Parkinon's disease, Lewy body dementia, and healthy older adults for longitudinal study.

A·D·R·C for healthy brain aging

For more information, contact: Veronica Ramirez (vramirez1@stanford.edu)

Stanford Brain Donation Program

Science has taught us that aging, dementia, and neurodegenerative disorders happen at the cellular level. While our research in diagnosing living participants is becoming more promising every day, Stanford investigators aim to use microscopic brain tissue analysis to learn more about brain disorders and improve our diagnostic ability. Autopsy and postmortem brain donation will help doctors move from a "best-guess" approach to one of concrete evidence-based diagnosis. Using this valuable information, we will be able to refine our approach to clinical diagnoses for future patients and families.

If you or a family member are interested in brain donation, please contact: Gabriel Hergenroeder at (650) 721-5247 or ghergenroeder@stanford.edu

Shimmer

Cognition Therapeutics is conducting a Phase 2 research study on a potential new treatment for Dementia with Lewy Bodies and are looking for qualified participants between the ages 50 to 85. Participants must have been diagnosed with mild to moderate Dementia with Lewy bodies (DLB), have a caregiver or study partner who is willing and able to attend all study visits and participate in some study assessments. Health insurance is not required to participate.

For more information, contact: Stephanie Tran (trans@stanford.edu)

Decision-Making in Parkinson's Disease

Decision-making impairment is especially associated with the early stages of Parkinson's disease. This study endeavors to show how much of of the decision-making impairment in Parkinson's disease patients is due to memory problems, attention, or visual processing. Also, it will assess how these cognitive processes affect your gait. These results can provide early detection of Parkinson's disease by analyzing decision-making. Moreover, it can show the effect of dopamine on decision-making. Patients eligible for this project must be diagnosed with Parkinson's Disease with no cognitive impairment. To participate, you will need to be able to come onsite to Stanford for two consecutive Fridays, for approximately 2.5 hrs each day. You will also receive an apple watch to participate.

For more information, contact: Stephanie Tran (trans@stanford.edu)

Aging with HIV infection and Parkinson's disease, a collaborative SRI-Stanford Study

We are recruiting volunteers to participate in a sleep, cognition, and imaging study of the brain to determine the impact of normal aging, HIV infection, and Parkinson's disease on cognition, motor function, and sleep. We are recruiting healthy volunteers, those with HIV infection, and those who have been diagnosed with Parkinson's disease. Eligible participants must be 50 years or older.

This longitudinal study involves: two separate day-long study visits (including a 60-minute MRI brain scan), two weeks of at-home sleep recording between study visits, and a follow-up study visit after 24 months.

For more information, contact: Alena Smith & Nicole Arra (hivpd23@gmail.com)

A STATEMENT ON

Our Commitment to Inclusive Clinical Research

The Poston Lab understands that excellent clinical research represents us all. We recognize the importance of including diverse populations in our research studies, as the neurodegenerative disorders we investigate impact various races, ethnicities, and genders differently.

Historically, medical institutions have disproportionally catered to certain demographics, resulting in a lack of knowledge in disease-specific differences between groups. The Poston Lab is committed to simplifying study enrollment procedures, connecting with underrepresented communities, and equitably providing support and information resources. We collaborate with the Alzheimer's Disease Research Center Justice, Equity, Diversity, & Inclusion Committee (ADRC JEDI), which endeavors to foster an inclusive culture of collaboration, training, education, mentoring and outreach across the multiple cores and components of the Stanford ADRC, the Stanford University community, and the greater Bay Area community and beyond. We believe these steps towards inclusivity in our studies will help generate more comprehensive research outcomes that benefit everyone.

We want to thank you for your contribution to our goal. Your participation is crucial in improving treatments outcomes for all.

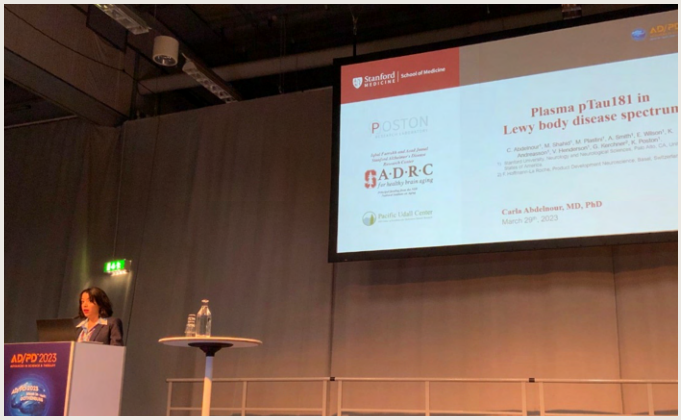
Presentations

This past year, the Poston Lab traveled near and far to share knowledge and present our research findings. Here are some highlights!

Alzheimer's & Parkinson's Diseases Conference

AD/PD | Gothenburg, Sweden | March 2023

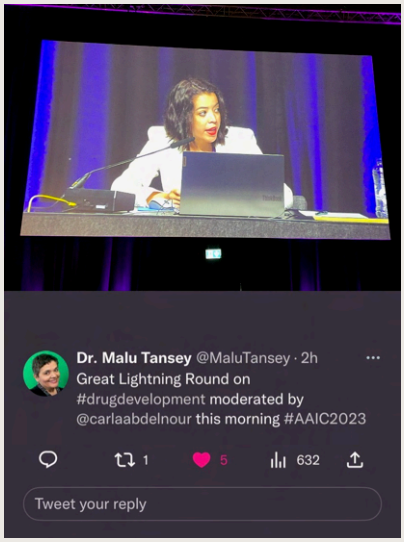
Dr. Poston (top right), Dr. Abdelnour (top left, bottom right), and Dr. Plastini (bottom left) gave presentations at AD/PD.

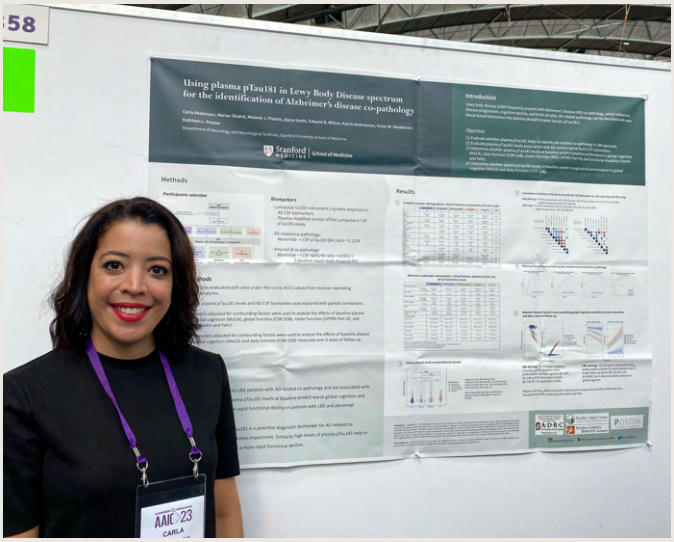


Alzheimer's Association International Conference

AAIC | Amsterdam, Netherlands | July 2023

Dr. Abdelnour presented her plasma pTau181 biomarker data at AAIC.

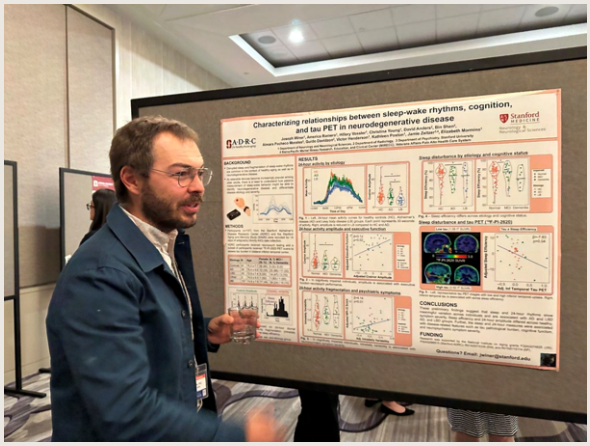




Alzheimer's Disease Research Center (ADRC) Meeting

Washington, DC | May 2023

Dr. Winer presented his actigraphy data at the Spring 2023 ADRC Meeting.



Lewy body Caregiver Symposium

Stanford, CA | October 2023

Dr. Poston gave a talk about Lewy body pathology at the Stanford I&R Center's Lewy Body Caregiver Symposium.

Meet our new lab members

Dimuthu Hemachandra, PhD, MSc

Postdoctoral scholar

Dr. Dimuthu Hemachandra, originally from Sri Lanka, kickstarted his academic journey with a BSc. in Physics from the University of Peradeniya. He later moved to Canada, where he earned an M.Sc. in Astrophysics from the University of Western Ontario, focusing on studying the Andromeda Galaxy using infrared spectroscopy and space-based telescopes.

With an aim to apply his scientific skills to improve human well-being, he transitioned from Astrophysics to Biomedical Engineering and Neuroscience. Dimuthu joined the Robarts Research Institute at the University of Western Ontario in 2018 as a Researcher. where he completed his Ph.D. at the Khan Computational Imaging Lab. Dimuthu's research interests focus on utilizing machine learning techniques to investigate subcortical brain structures and connectivity, aiming to detect neurodegenerative diseases early on.

Passionate about open and collaborative science, Dimuthu believes in the power of sharing knowledge and working together for progress. In his free time, he enjoys exploring new places, capturing moments with his camera, social dancing, and playing the guitar.

Hannah Schmitz, BS

Clinical Research Coordinator

Hannah Schmitz earned her Bachelor of Science degree in Cell Biology from the University of California, Davis in 2020. Prior to joining the ADRC and PUC, she

conducted research in molecular biology and genetics, most recently studying genetic retinal diseases in the Vollrath Lab at Stanford. Previously at UC Davis, she volunteered through the National Alzheimer's Buddies program to provide companionship and social support to Alzheimer's patients. She is excited to combine her passion for research with her joy of working with patients and to make progress towards better understanding and treating neurodegenerative diseases.

Leah Varghese, BA

Clinical Research Coordinator

Leah graduated from University of California, Berkeley with a B.A. (Honors) in Molecular and Cell Biology with an emphasis in Neurobiology. During her time at UC Berkeley, she worked for 2.5 years as a student research assistant in William Jagust's lab. There, under the guidance of Dr. Xi Chen, Leah investigated the behavioral effects of prior knowledge on memory across the adult lifespan. For her honors thesis, she expanded this project to include fMRI analysis to additionally examine the neural effects of prior knowledge on memory across the adult lifespan. Her experience in the Jagust lab fostered a deep passion for aging, cognitive decline, and neurodegenerative diseases. Leah is eager to pursue graduate studies, where she aims to explore the structural and functional changes in the brain during both normal and pathological aging, with a particular emphasis on how basic cognitive mechanisms change with age. Outside the lab, Leah enjoys biking, exploring San Francisco with her friends, attending concerts, and baking.

SAVE THE DATE

February 29th, 2024: Introduction to Synuclein Biomarkers – How Researchers are "Seeing" Lewy Bodies in the Living Brain

Dr. Kathleen Poston will be speaking at the Lewy body Dementia Association (LBDA) webinar to discuss the recent advances in the development of biomarkers for alpha-synuclein, how they are changing research in Lewy body dementia, and how they may change clinical practice in the future. Dr. Poston will also describe the two synuclein biomarkers that are currently available to physicians and provide a sneak peek into the potential for future biomarkers that may provide even more information to researchers and clinicians about the development and progression of Lewy bodies.

WHEN: February 29th at 1pm PT

WHERE: Virtual webinar, via Zoom.

Register today! https://us02web.zoom.us/webinar/register/WN_GNPq5LL-Tz29GZyWtg2CPQ or email Rose Heithoff (rheithoff@lbda.org) for assistance.

More events on next page

February 28th, 2024: Demencia por enfermedad de Parkinson | Spanish Language Webinar on Lewy body dementia (LBD)

El Brain Support Network y Stanford Neurology organizarán un seminario gratuito en español sobre la demencia por enfermedad de Parkinson y por demencia con cuerpos de Lewy (DCL). La doctora Carla Abdelnour, becaria postdoctoral de la Universidad de Stanford, brindará una descripción general de los síntomas y el tratamiento de la demencia de ambas enfermedades. El seminario será moderado por Linda Higueras del Brain Support Network, cuyo padre padeció demencia por cuerpos de Lewy. Los asistentes podrán hacer preguntas a la presentadora a través del cuadro de preguntas y respuestas o del chat. El seminario será grabado.

CUANDO: 28 de febrero a las 6pm (hora del Pacífico)

DÓNDE: Seminario en Zoom

Registrar hoy! https://stanford.zoom.us/webinar/register/4417058960961/WN_G6amjJT8QDC-OwOhCb2Seg#/registration o envía un correo a la Dra. Carla Abdelnour (carlaab@stanford.edu).

April 20th, 2024: Parkinson's Moving Day

Moving Day is an inspiring and empowering annual fundraising walk event that unites people around the country living with Parkinson's disease, their care partners and loved ones to help beat Parkinson's disease. Moving Day is more than just a walk. It's a celebration of movement – proven to help manage Parkinson's symptoms. *Please visit us at the Stanford Booth!*

WHEN: April 20th at 9am PT

WHERE: Lake Cummings Regional Park in San Jose, CA 95125

Register to walk today! https://movingdaywalk.org/event/moving-day-san-jose/

FACULTY SPOTLIGHT

Meet **Dr. Andrea Fuentes**, Clinical Assistant Professor and member of the Stanford Alzheimer's Disease Research Center team.

Dr. Andrea Fuentes first moved to the Bay Area to complete her bachelor's degree in Human Biology at Stanford University.

During a semester abroad in Paris, France as a Stanford student, she had the opportunity to work at the Pitié-Salpêtrière hospital, an institution that was integral in the foundation of modern neurology and recognition of Parkinson's disease. This clinical experience first inspired her path towards becoming a neurologist as she learned from kindhearted physicians using their expertise to help improve the quality of life of patients with movement disorders.

She then went on to obtain her medical degree from the UCSD School of Medicine, completed her neurology residency at the UPENN and movement disorders fellowship at the UCSF. In 2023, she joined the faculty of the Stanford Department of Neurology and Neurological Sciences.

She provides comprehensive care for patients with different types of movement disorders, including Parkinson's disease, atypical parkinsonian disorders, essential tremor, ataxia, dystonia, and Huntington's disease.

Dr. Fuentes' research interests include the identification of biomarkers for neurodegenerative disorders, evaluating novel treatments for movement disorders, and addressing health disparities to improve health outcomes for medically disinvested populations affected by Parkinson's disease.

She is also dedicated to community outreach to raise awareness about Parkinson's disease and medical education, teaching the next generation of neurologists.

Outside of work, she enjoys traveling, exploring new restaurants, baking, reading and spoiling her dog.

Dementia with Lewy bodies Drug Therapies in Clinical Trials: A Closer Look at Drug Development

Written by:
Dr. Carla Abdelnour

Research often takes around 17 years to transition from theory to practice.

While it is crucial to conduct thorough studies and validate research findings, we must acknowledge the need to expedite this process. To address this, we need to evaluate the current situation and identify areas for improvement.

In our paper entitled: "Dementia with Lewy Bodies Drug Therapies in Clinical Trials: Systematic Review up to 2022" we reviewed all clinical trials performed until 2022 *(figure 1, page 13)*. Our aim was to understand the current situation of drug development in dementia with Lewy bodies and identify areas of improvement that will inform the design of future clinical trials.

What did we discover?

Over the last decade, there's been an increased interest in drugs that might improve symptoms and slow down disease progression in dementia with Lewy bodies. This promising shift signifies a hope for therapies that could make a difference in the lives of those affected.

Researchers are exploring various paths, investigating drugs initially designed for other conditions, like cancer or Alzheimer's disease, to see if they could be repurposed to treat dementia with Lewy bodies.

However, the journey isn't without challenges.

Many trials are using measures not specifically designed for dementia with Lewy bodies, which might not fully capture the disease's effects. But there's encouraging progress in developing new ways to accurately measure the impact of treatments on dementia with Lewy bodies.

A crucial focus is catching dementia with Lewy bodies earlier, to test treatments that could slow or halt its progression. Additionally, there's a need to ensure these studies include diverse groups of people, so that future treatments are effective for everyone affected by dementia with Lewy bodies.

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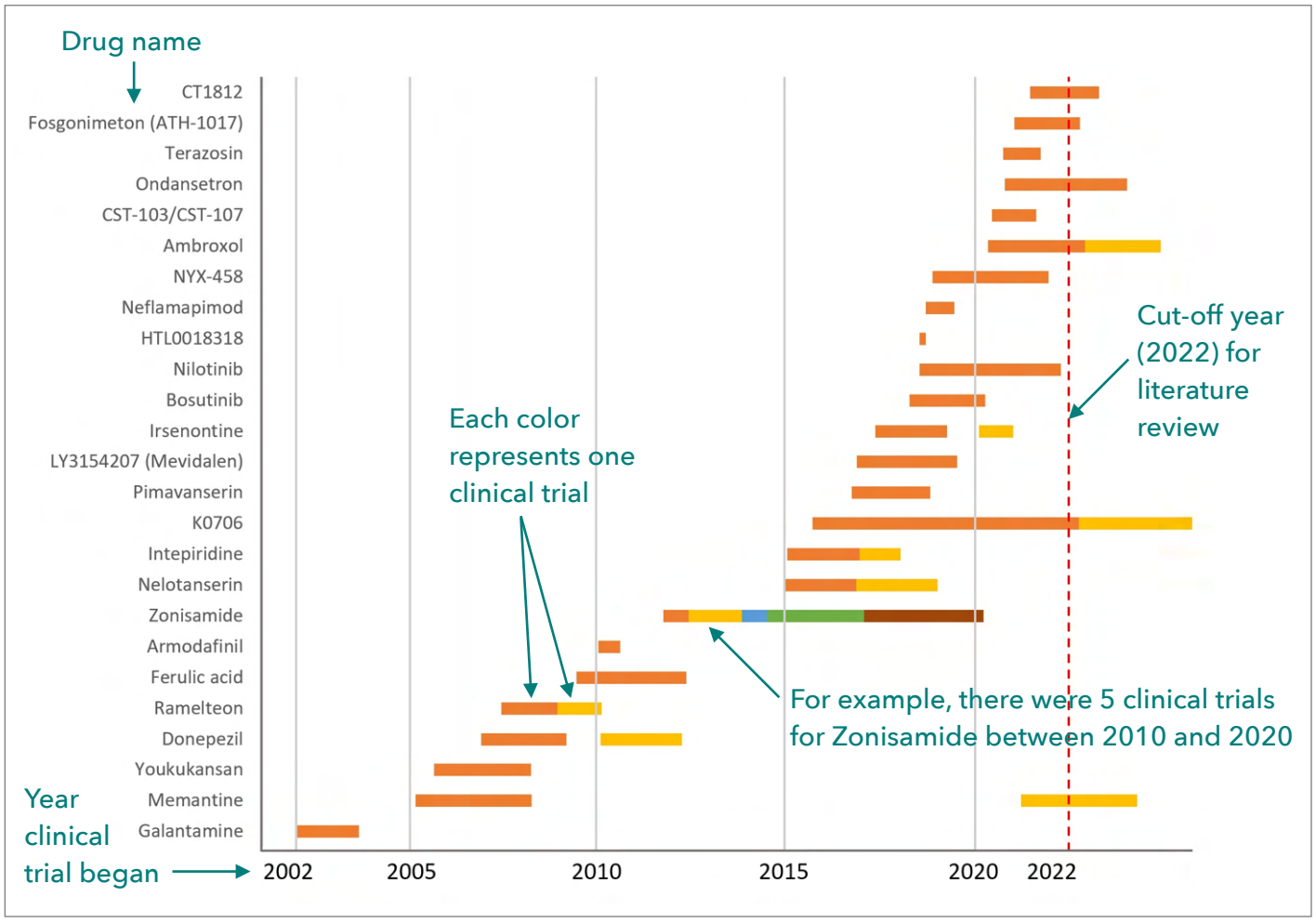


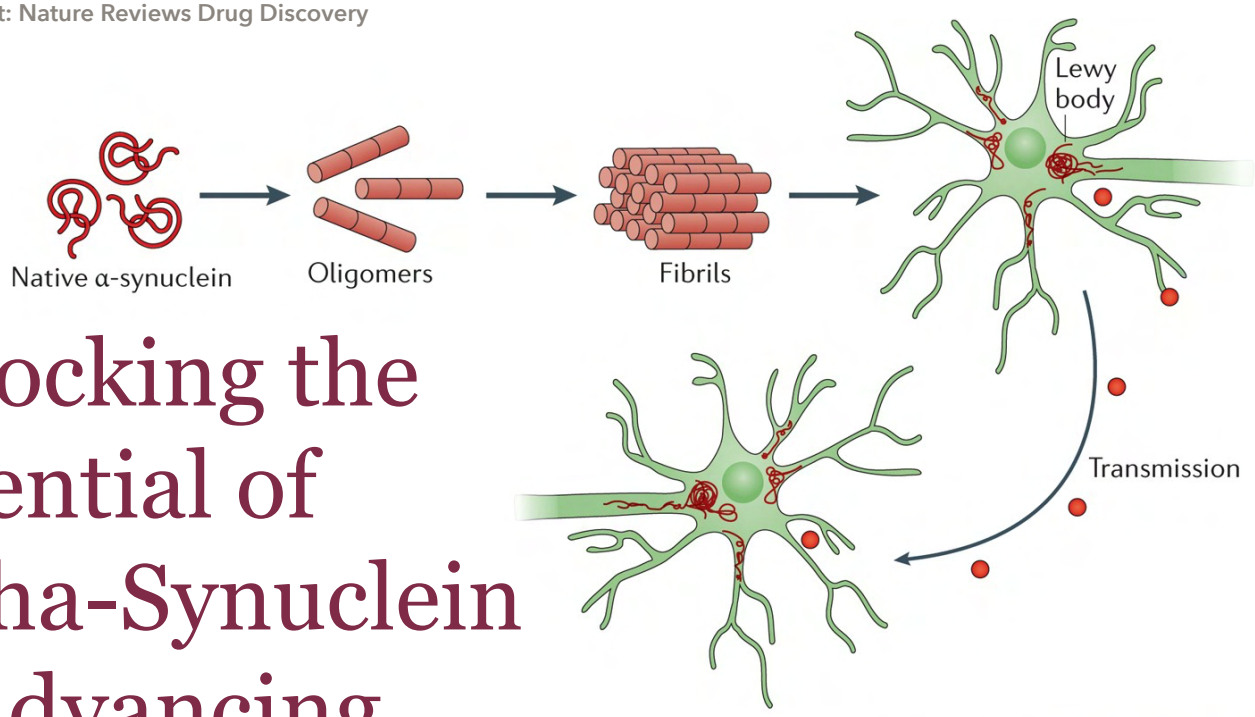
Figure 1. Evolution of clinical trials for DLB, showing all the agents investigated in DLB clinical trials from 2002 to 2022.

While there's optimism in understanding and treating DLB, there's still much ground to cover. Innovations in trial designs and involving diverse populations worldwide hold the key to unlocking more effective treatments.

During the pandemic, the rapid development of vaccines was made possible by the participation of thousands of volunteers in clinical trials. Similarly, the discovery of treatments for dementia with Lewy bodies relies on the collaboration between scientists and research participants.

Participants' involvement is *crucial* in the journey towards finding effective treatments. If you're interested in contributing to our efforts to advance treatments for this condition, you may be eligible to participate in our research studies and clinical trials. For more information, visit **page 3.**

Image credit: Nature Reviews Drug Discovery



Unlocking the Potential of Alpha-Synuclein in Advancing Parkinson's Disease Research

DR. MELANIE PLASTINI

discusses our research collaboration with Amprion® Inc., explaining how the SYNTap® Biomarker Test's early detection of alpha-synuclein paves the way for early identification of and tailored treatments for synucleinopathies.

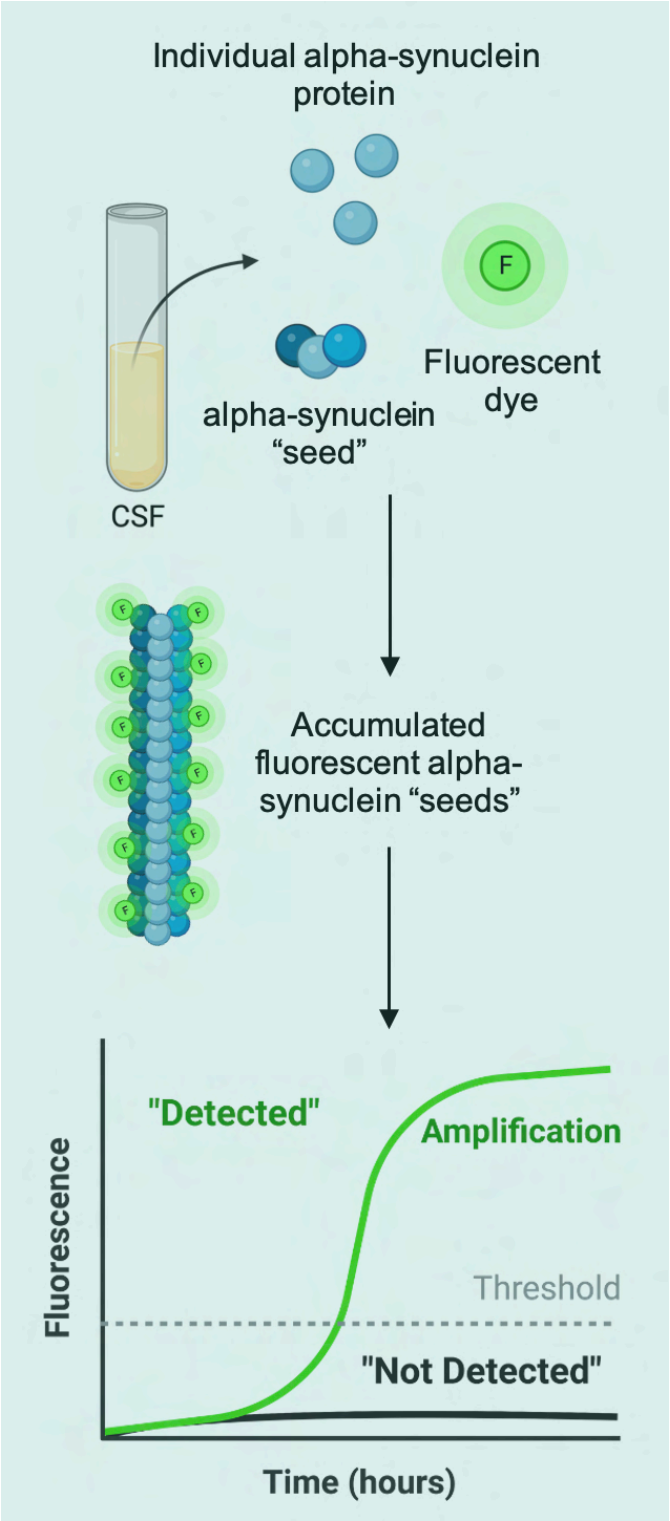
The identification of misfolded alpha-synuclein protein in the cerebrospinal fluid (CSF) represents a pivotal breakthrough in our understanding of Parkinson's Disease (PD), Parkinson's Disease with Dementia (PDD), and Lewy Body Dementia (LBD). These diseases are collectively called alpha-synucleinopathies and are characterized by aggregates of misfolded alpha-synuclein in the brain tissue of people who have died of PD, PDD, or LBD. (cont. next page)

Early detection of these aggregates in the CSF allows for a more precise diagnosis, an earlier diagnosis, and more tailored treatments to slow down the progression of the disease.

This capability is invaluable and can potentially enable us to identify people years before they develop clinical symptoms, and eventually develop therapies that slow or halt the disease progression.

The SYNTap® Biomarker Test, developed by Amprion® Inc., is at the forefront of this revolutionary approach. As a Seed Amplification Assay (SAA), this test detects misfolded alpha-synuclein in living patients using CSF taken from a lumbar puncture procedure. This assay is able to amplify trace amounts of misfolded alpha-synuclein aggregates (called "seeds") in the CSF and therefore is capable of increasing protein signals by a billion times or more! This is facilitated by a specific fluorescence-tagged molecule that illuminates when attached to alpha-synuclein. If aggregates are present in the sample, the fluorescence lights up, allowing for accurate detection of the signal.

One of the most significant implications of this research lies in its potential to address the challenges of misdiagnosis, which can occur in up to 20% of PD and LBD patients. (cont. next page)



The SYNTap® Biomarker Test amplifies trace amounts of misfolded alpha-synuclein in CSF, and detects these proteins with a fluorescent tracer.

Image credits: Amprion® Inc.

This is most important for clinical trials where the treatment directly targets alpha-synuclein, thus underscoring the importance of tests like the SYNTap® Biomarker Test in certain research protocols.

Moreover, this groundbreaking test not only aids in the early detection of alpha-synucleinopathies like PD, PDD and LBD, but also identifies people with other neurodegenerative diseases like Alzheimer's Disease, who also have alpha-synuclein as an underlying pathology. This knowledge is critical for tailoring treatment options and managing the complexities that arise when alpha-synucleinopathy complicates other conditions.

Through our research and collaboration with Amprion® Inc., we have demonstrated the capacity of the SYNTap® Biomarker Test to identify misfolded alpha-synuclein aggregates years before the onset of symptoms in some cases. Notably, we have detected such aggregates in patients previously diagnosed with other neurodegenerative diseases, highlighting the broad utility and diagnostic potential of this test.

None of this progress would be possible without the invaluable contributions of our research participants, their loved ones, and caretakers. Their time, dedication, and commitment to advancing scientific knowledge are the driving force behind our ability to uncover new possibilities in the early detection and treatment of alpha-synucleinopathies. We express our deepest gratitude to all those who have played a part in this transformative journey – thank you for making a difference in the fight against debilitating diseases.

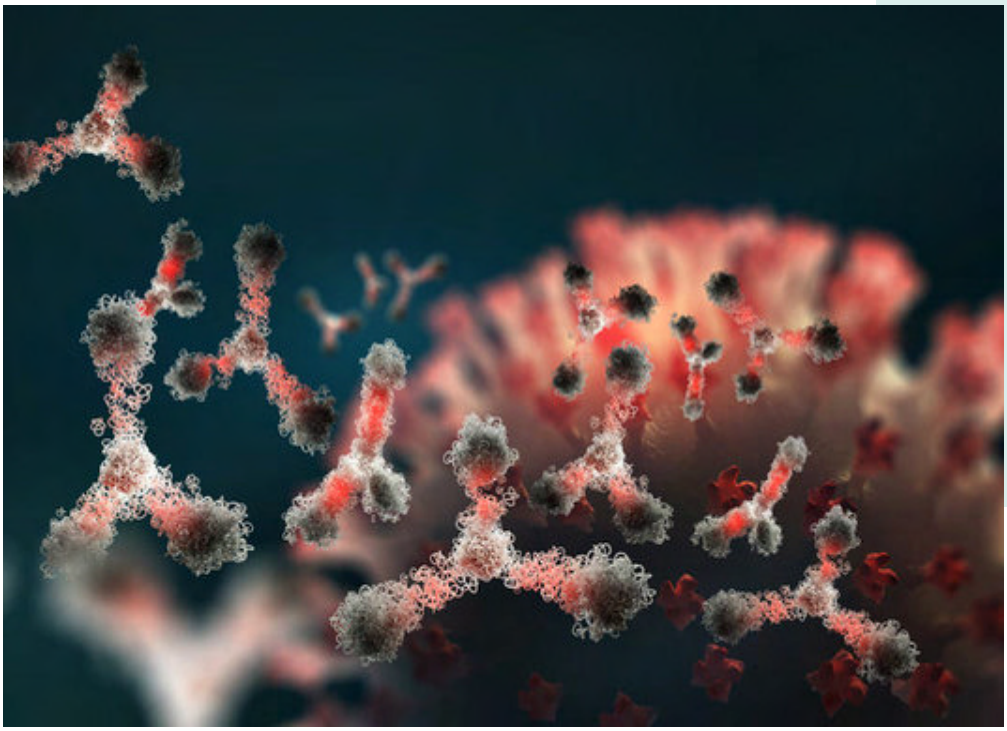


Image credits: Adobe Stock

The image above shows immunoglobulin antibodies attacking a virus.

Elevated Immune Response in Parkinson's Disease

Written by: Marian Shahid-Besanti, MSc

Antibodies are proteins made by the immune system to fight viruses, bacteria, and other foreign substances.

Immunoglobulin G (IgG) is a type of antibody, and high levels of IgG may reflect an infection, an inflammatory process, or an autoimmune disease that involves the central nervous system (CNS). Previous studies have suggested that there may be an inappropriate immune response in the brain in people with some of the symptoms of Parkinson's disease.

We aimed to examine the body's immune response in Parkinson's disease by quantifying IgG production in the CNS. We calculated the IgG index, quantified by running a standard laboratory test on cerebrospinal fluid (CSF) collected through lumbar puncture as well as plasma through a blood draw, in three independent cohorts: (1) the Parkinson's Progression Markers Initiative (PPMI) which included Parkinson's disease participants within two years of diagnosis; (2) the Parkinson's Disease Biomarkers Program (PDBP); (3) and the Pacific Udall Center (PUC). *Figure 1* below shows CSF and blood composition under healthy circumstances, during CNS antibody production, and when the blood-brain barrier is impaired. (cont. next page)

Albumin is the most abundant circulating proteins found in plasma, and the presence of albumin in cerebrospinal fluid (CSF) may indicate blood contamination.

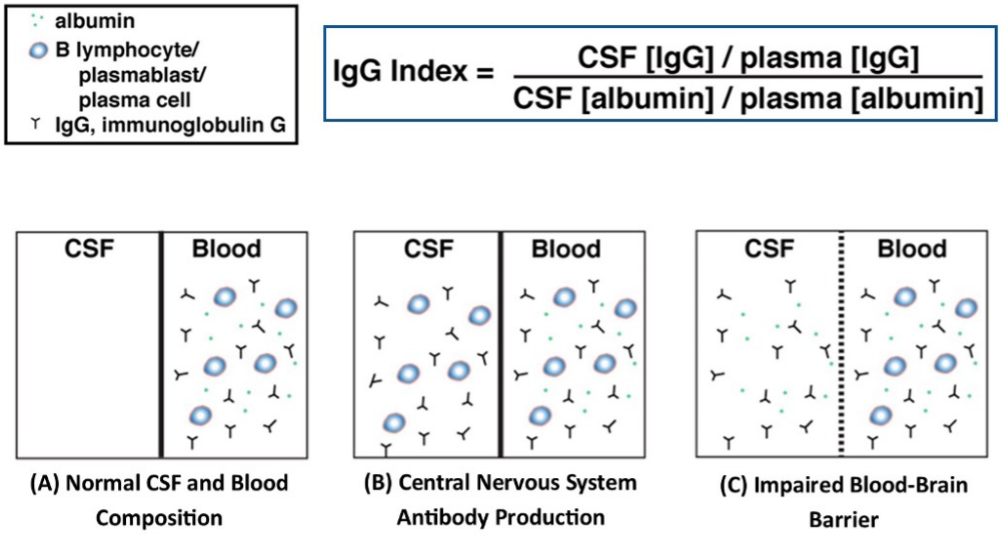


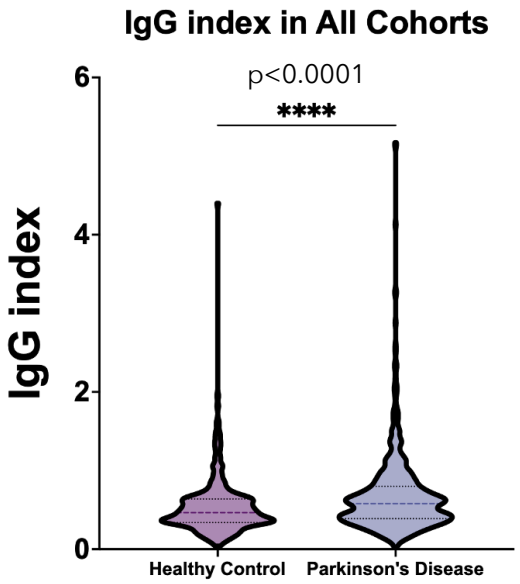
Figure 1 shows (A) the normal composition of CSF and blood in which blood has IgG, albumin, B cells (which are immune cells that create antibodies such as IgG) and the absence of these proteins, cells, and antibodies in the CSF; (B) CNS antibody production or an immune response in which B cells and IgG are found in the CSF, and albumin is only found in the blood; (C) an impaired blood-brain barrier in which albumin and IgG are found in the CSF due to the compromised blood-brain barrier that has lost its ability to prevent these proteins from entering the CSF.

What did we find?

IgG index is elevated in people with Parkinson's disease compared to healthy older adults around the same age (*Figure 2*). In addition, IgG index elevation in people with Parkinson's disease appears later, rather than earlier, in the disease course. Thus, elevated IgG index in people with Parkinson's disease supports the idea that there is some immune response associated with the disease.

Further research will determine whether this immune response is causing some of the problems in Parkinson's disease or if it is just a reaction to the symptoms of the disease.

Figure 2 below shows that IgG index is elevated in Parkinson's disease compared to healthy older adults around the same age.



Aging with HIV infection: A comparison with Parkinson's disease and healthy aging

Written by:
Dr. Eva M. Müller-Oehring

Dr. Müller-Oehring discusses her comparative study of aging with HIV infection, Parkinson's disease (PD), and healthy aging. Her study illustrates the implications of aging on the immune system and the resulting higher risk for age-related neurodegenerative disorders.

As people age, the immune system undergoes changes and its ability to protect against infections and diseases declines, a process called immunosenescence.

This age-related immune system change, together with diseases that impact the immune system, can lead to a higher risk for age-related neurodegenerative disorders. For example, people living with human immunodeficiency virus (HIV) infection are now aging and reach normal life expectancies due to very effective antiretroviral pharmacotherapy (ART).

Yet, despite successful immunosuppression with ART, neurodegeneration occurs in people living with HIV and the prevalence of mild to moderate neurocognitive disorder is high. The cognitive deficits are more often consistent with age-related diseases that affect subcortical regions such as in Parkinson's disease (PD) than those that affect cortical regions, such as Alzheimer's disease (Scott et al. 2011).

To assess the brain-cognition relationships, we utilized MR brain imaging and assessed cognition such as executive functions and memory in 42 older people living with HIV and 41 people with PD.

Executive function and memory are crucial for various aspects of daily life as they entail the ability to learn and retain new information, to solve problems and make decisions, as well as time management and social interactions.

Older people living with HIV and people with PD had lower executive function scores than the neurologically normal older adults and showed a graded effect with older adults (cont. next page)

showing the best executive function and people living with HIV showing most impacted executive function (Figure 1). Testing memory, people living with HIV and people with PD showed similar deficits in the slope of learning (Figure 2) and memory compared to older healthy controls. Despite the similar types of executive and memory function, people living with HIV and people with PD exhibited different patterns in the brain imaging (Fama et al., 2023).

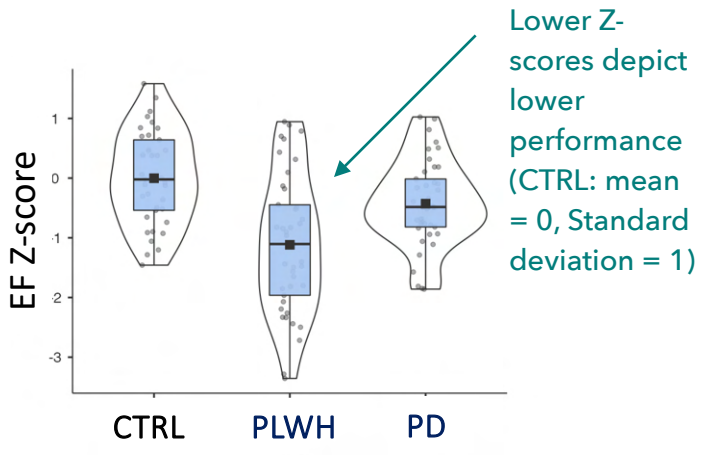


Figure 1. Group differences in executive function in people living with HIV (PLWH), PD, and controls (CTRL).

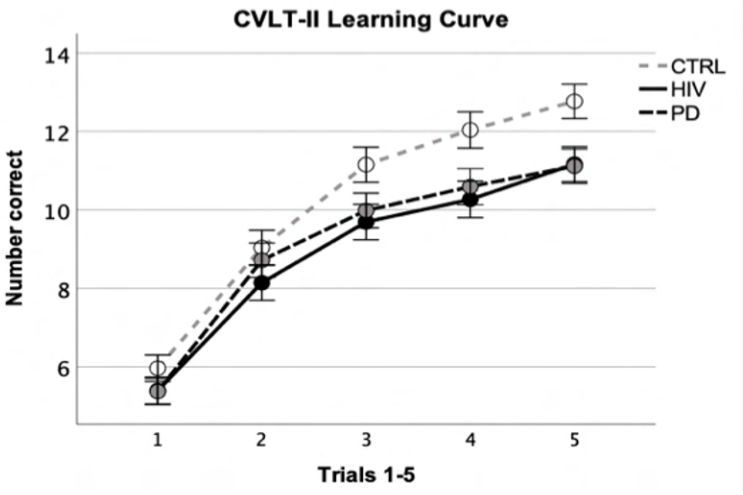


Figure 2. Graph depicting the learning curve (number correct items) over 5 trials (CVLT-II, California Verbal Learning Test)

Studying these relationships is important as they highlight how aging, immune function, and neurodegenerative disease affect the complex interplay of brain circuits underlying executive function and memory.

Identifying and understanding the risk factors for functional impairment can help to develop lifestyle interventions, cognitive training programs, or pharmacological treatments to slow the decline of brain structure and function.

To expand on this, our collaborative SRI-Stanford study, led by Drs Tilman Schulte and Kathleen Poston, is further investigating the role of sleep and daytime activity on brain structure and function in normal aging, aging with HIV infection, and Parkinson's disease.

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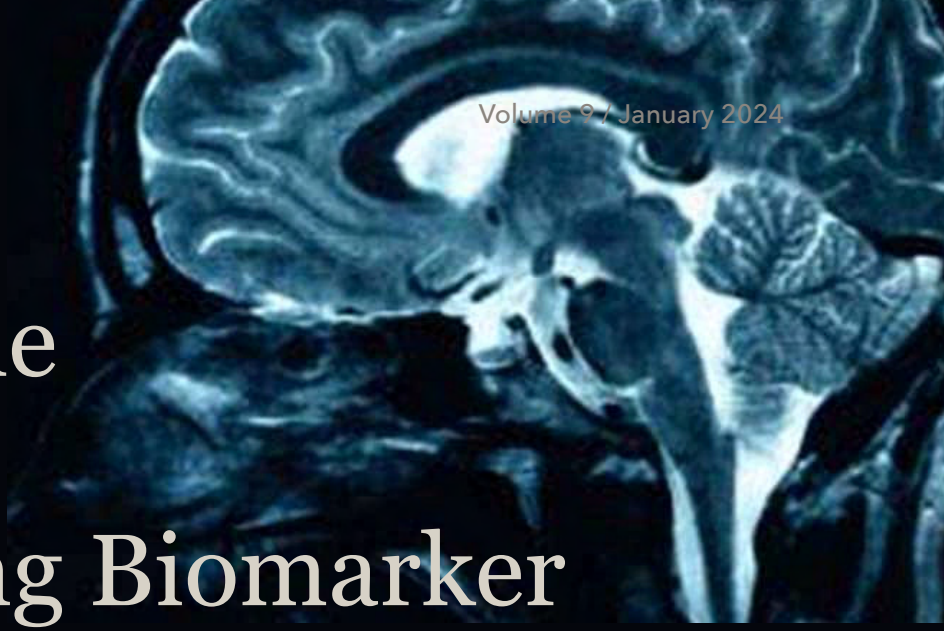
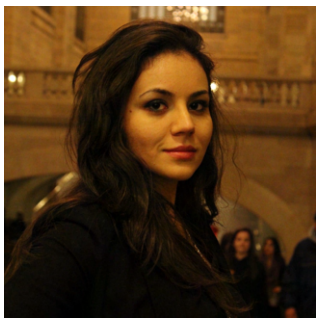


Brain Volume Assessment as an Imaging Biomarker in Parkinson's Disease

Image credit: Echelon Health

Written by: Elnaz Ghasemi



It is recognized that clinical symptoms of Parkinson's disease are quite varied, with no two people experiencing the disease in the same way. Individuals with PD experience diverse motor and non-motor symptoms that contribute to their overall function and impact their quality of life.

New treatments for PD symptoms can only be achieved through robust and accurate biomarkers (biological measurements) that can identify different stages of disease, as well as track the progression of disease and a person's response to therapy.

In recent years, magnetic resonance imaging (MRI) of the brain has been increasingly used as an imaging biomarker by clinicians and researchers to diagnose and track changes in disease. MRI is very safe and can obtain detailed images of the precise anatomy of the brain by using a powerful magnetic field, without using any radiation.

This medical imaging technique can be used to study brain changes associated with the motor and cognitive symptoms experienced by people with PD.

Our research team has recently collaborated with Icometrix, a healthcare technology company in Belgium, to investigate the association between brain volume in specific brain regions and overall motor and cognitive function in people with PD. (cont. next page)

For this investigation, we used several computational neuroimaging tools and techniques on MRI scans of 614 people, with PD for non-motor analysis and 670 people with PD for motor analysis. The scans were collected from Stanford University research participants and Parkinson's Progression Markers Initiative open-access data.

Icobrain, an FDA-approved, AI-based image analysis software, developed by Icometrix, was one of the computational tools we used to quantify clinically relevant brain structures and to establish the pattern of brain atrophy on MRI of individual people with PD (figure below).

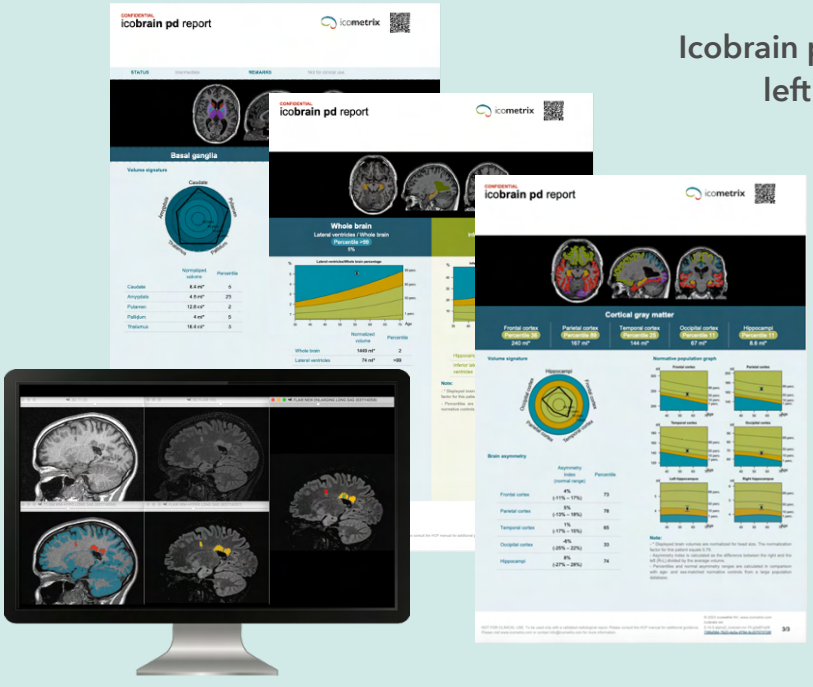
Results of our study demonstrated an association of both motor and cognitive disabilities with lower brain volume in specific cortical brain regions.

Specifically, an association between the volume of specific brain regions, such as hippocampus, putamen, caudate, temporal lobe, and cerebellum, and changes in a test of cognition.

An association between the volume of specific brain regions, such as the putamen, caudate nucleus, and occipital lobe, and changes on a test of movement.

This study underscores a role for brain volume assessment as a potential imaging biomarker for predicting longitudinal motor and cognitive changes in people with PD, providing a practical alternative to PET or cerebrospinal fluid biomarkers.

We truly appreciate and thank our research participants for their generous contribution and for helping to move the field of Parkinson's disease research forward.



Icobrain produces a MRI report (sample pictured on left) with an individual's brain quantifications…

… which then is used by clinicians and researchers.

The Brain Waste Clearance System

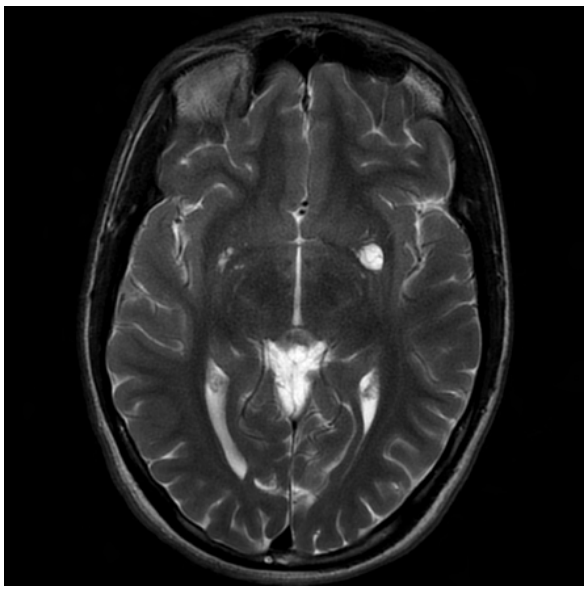
Written by: Drs. Eva M. Müller-Oehring, Eric T. Peterson, and Dimuthu Hemachandra



The glymphatic system, also termed the brain waste clearance system, has recently received increased interest for its potential role in the pathogenesis and progression of neurodegenerative diseases and dementias.

First described in 2012 (Iliff et al.), there is growing evidence from studies performed in animals that failure of the glymphatic system could contribute to the buildup of toxins and proteins such as amyloid-beta and tau, characteristic of Alzheimer's disease, and other neurodegenerative disorders such as Lewy body and Parkinson's disease.

Image credit: Radiopaedia



The mainstay of evidence on the glymphatic system comes from animal studies using histological methods and microscopy. These methods are not safe for human use, and thus, magnetic resonance imaging (MRI) protocols have been developed in recent years to enable non-invasive ways to study the glymphatic system in humans.

Perivascular Spaces (PVS)

One potential way to visualize and measure aspects of the glymphatic system in the human brain is through structural MR imaging of perivascular spaces (Figure 1 on next page). The blood vessels in the brain will pulse with the heartbeat, and these pulses drive an exchange between the blood vessels and the surrounding brain tissue, contributing to brain waste clearance (Figure 2 on next page). (cont.)

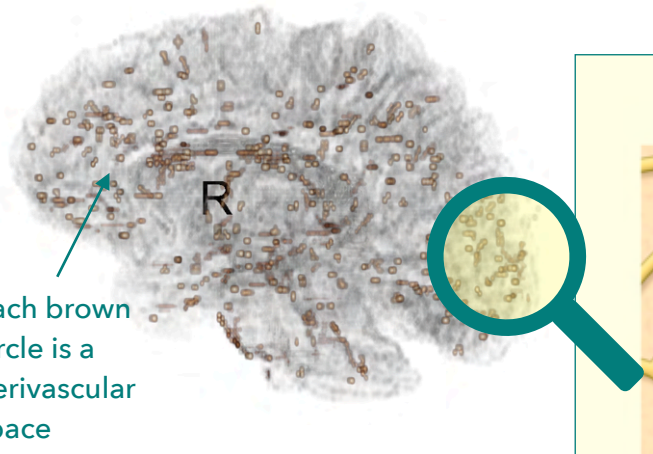


Figure 1: Perivascular Spaces in a 71-year-old man (3D rending of the whole brain).

Image credit: Kaur et al., 2020

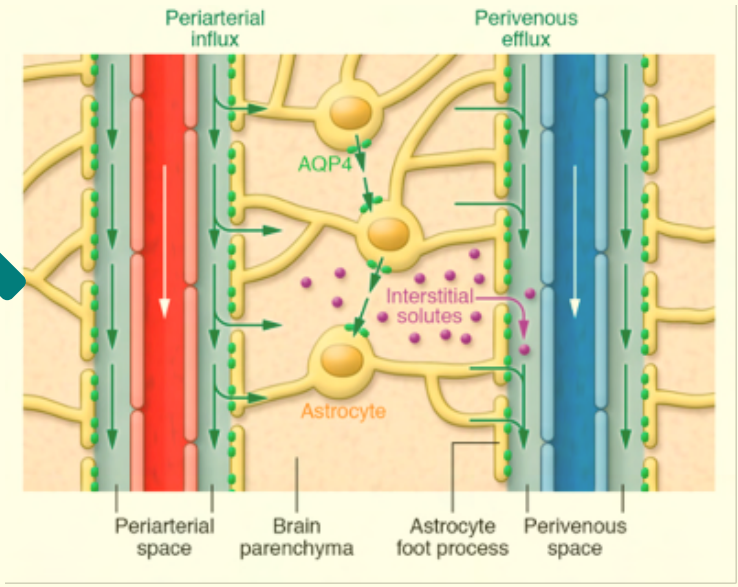


Figure 2: Illustration of glymphatic flow and interstitial waste solutes movement between the parenchyma and perivascular spaces surrounding the vasculature.

Perivascular spaces are normal anatomical features of the brain and can be seen on brain imaging studies such as MRI scans (Figure 1). Although the exact mechanisms are not fully understood, perivascular spaces may become enlarged with aging (Kress et al, 2014), in Alzheimer's (Gertje et al., 2021) and Parkinson's disease associated with changes in the cerebral spinal fluid which might be related to cognitive changes that can occur in some patients (Chen et al., 2022).

New developments

In a collaborative effort, the Poston lab at Stanford and Schulte lab at SRI are using a new MRI technique to assess glymphatic clearance. Using our next generation brain scanner that has both MRI and PET imaging capabilities, we can take pictures of the perivascular spaces and glymphatic flow with the MRI at the same time as we take pictures of brain proteins, such as amyloid and tau proteins, with PET imaging.

This new imaging approach allows to us analyze the glymphatic system, which is supposed to remove toxins from the brain, in relation to protein accumulation.

This proof-of-concept study will aid our understanding of the glymphatic clearance in living people and could enhance our ability to evaluate potential treatment strategies non-invasively.

Helpful Resources

If you or a loved one has Parkinson's Disease, the following resources may be useful.

Stanford Parkinson's Community Outreach

The Stanford Parkinson's Community Outreach team provides education, assistance, and resources to improve the quality of life for those with Parkinson's disease, caregivers, and the community. Materials are available in English, Spanish, and Chinese. The Stanford PD Community Blog produces a list of Parkinson's-related webinars and virtual meetings with speakers. Webinars are offered in English and in Spanish.

Medical Loan Closets

Loan closets provide medical equipment such as walkers, canes, wheelchairs, and bathroom equipment free of charge. Here is a list of a few loan closets available in the Bay Area:

- https://www.recares.org
- https://www.avenidas.org/medical-equipment-loan-closet-now-open/
- https://norcalsci.org/equipment-list

Support Groups

Being part of a support group can be one of the best ways to reduce stress and connect with others who can relate to your experience. Care partners and family members also benefit from sharing questions and concerns with like-minded others. Here are some resources available to help you find a support group in the Bay Area.

https://med.stanford.edu/parkinsons/northern-california-resources/support-groups.html

http://parkinsonssupport.weebly.com

Some sources of **online** support:

Stanford Grupo de Parkinson en Español is a support group which meets virtually each month, open to individuals with PD and caregivers. It is lead by Dr. Carla Abdelnour.

The Parkinson's Buddy Network is an online community of people impacted by Parkinson's, helping you build meaningful connections and relationships.

NeuroTalk has a robust Parkinson's disease community.

The Stanford APDA Information & Referral Center brings 2 new support groups to the Bay Area

The American Parkinson's Disease Association (APDA) Information & Referral Center, in partnership with the Poston Lab, are proud to share Grupo de EP and Connecting Through Art, two new support groups for the Bay Area PD community

GRUPO DE EP

En Español: El tercer miércoles de cada mes

El Centro de información y referencia APDA de Stanford y el Stanford Parkinson's Community Outreach han iniciado un grupo de apoyo para la enfermedad de Parkinson (EP) para la comunidad de habla hispana. Estas reuniones virtuales están abiertas a cualquier persona en el norte y centro de California, no sólo a las familias de Stanford. Este grupo está disponible a personas con enfermedad de Parkinson y sus familias. No se requiere RSVP.

Para más detalles visite: https://med.stanford.edu/parkinsons/northern-californiaresources/espanol.html. Si está interesado en participar envíe un correo electrónico a: carlaab@stanford.edu para recibir el enlace de Zoom.

Grupo liderado por:
Dra. Carla Abdelnour

CONNECTING THROUGH ART

In-person, group art therapy: every second Friday of the month at the Forum (Cupertino, CA)

Connecting Through Art is a creative arts program that offers people with PD the space and ability to express feelings, emotions, and daily concerns through drawing and painting. This program provides a supportive and therapeutic environment that encourages participant reflection as they participate in art activities that help strengthen fine motor movements. CTA is open to any adult who has been diagnosed with Parkinson's disease and their care partners. The program is free, however, registration is required. Participants do NOT need to purchase art supplies to participate.

Art instruction provided by Christine Hirabayashi, Ph.D., LMFT, ATR-BC. **Our next meeting will be on March 9th, 2024.**

To register or for additional information, please contact: Alena Smith at (310) 863-8108 or alenaa@stanford.edu

Artwork from CTA participants

Publications

We are proud to share 19 scientific publications from our lab this year. Your involvement in our research has allowed us to share findings to an international audience, contributing to important understandings in neurology and neuroscience.

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Publications, continued

Cerebellar Volume and Disease Staging in Parkinson's Disease: An ENIGMA-PD Study.
Kerestes R,… **Poston KL**, … **Smith V**, …**Young CB**,… the ENIGMA-Parkinson's Study. *Mov Disord*. 2023 Nov 14; https://doi.org/10.1002/mds.29611