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 research participants. The fruits of our efforts will soon be available for shared access in the scientific community. More information can be found starting on page 3.

Research Recruitment

With the help of our research assistants, we have considered over 612 individual cases for research. We are actively recruiting participants with diagnoses of Parkinson’s disease and healthy controls.
Recruitment for Research Studies!

- **NEW FacePrint Study** – We are looking for volunteers to participate in a 30-minute 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. Volunteers with Parkinson’s disease, REM sleep behavior disorder, multiple system atrophy, progressive supranuclear palsy, corticobasal syndrome, or healthy controls are invited to participate.

  For more information, contact: Anna Newman
  (650) 269-0484
  anewman7@stanford.edu

- **Stanford Alzheimer’s Disease Research Center (ADRC) & Pacific Udall Center (PUC)**
  We are still actively recruiting for our longitudinal research studies at Alzheimer’s Disease Research Center and Pacific Udall Center. For more information, contact:

  Christina Wyss-Coray or María-Lucia Campos
  (650) 721-2409
  ADRCstanford@stanford.edu
  (650) 721-5351
  udallcenter@stanford.edu

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**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 Christina Wyss-Coray at (650) 721-2409 or ADRCstanford@stanford.edu
Facial Expression: An Early Diagnostic Tool for Parkinson’s Disease?

After watching a video by the Michael J. Fox Foundation, Erin Smith noticed that whenever Michael J. Fox or another Parkinson’s disease patient smiled or laughed, it came across as less expressive. She spoke with caretakers and clinicians, and they reported similar observations in their loved ones and patients, even years before diagnosis. By reading papers on research studies, she found that the often-overlooked sections of the brain that undergo the earliest changes in Parkinson’s patients are the same parts involved in the formation of facial expressions. She became captivated, and wondered whether observations of facial expressions could be used to objectively monitor changes in the brain and detect the onset of Parkinson’s disease.

Erin’s interest in facial expressions in Parkinson’s disease inspired her to develop the FacePrint study to investigate changes in facial movement associated with Parkinson’s disease. The initial technology was developed and validated through two pilot studies and adapted for the FacePrint study. The study includes a series of brief video clips (Figure 1) designed to evoke an emotional response in viewers. As participants observe the visual stimuli, a computer records facial expression changes and reactions. Currently, the study includes participants with Parkinson’s disease, including atypical cases, as well as a cohort of healthy controls. Understanding more about the effects that Parkinson’s disease has on facial expression may lead to the development of an early diagnostic tool.

With the Poston Lab, Erin has received grant support for the FacePrint Study from the Michael J. Fox Foundation for Parkinson’s Research.

Figure 1: Videoclip images from the FacePrint study.
Our memory of the events that occurred in our lives, at specific times and places, is called 'episodic memory.' Episodic memory problems sometimes arise in people with Parkinson’s disease, and these kinds of memory problems can predict which patients are at risk for developing more serious cognitive problems. Episodic memory is complex and involves multiple processes, and one of the challenges for Parkinson’s disease researchers has been finding a test that is sensitive enough to detect subtle and early changes in episodic memory. Researchers have used the Mnemonic Similarity Task (MST) to study episodic memory changes in healthy older adults and people with other types of neurodegenerative diseases, but not yet in Parkinson’s disease.

We wanted to find out whether the MST was feasible to use in this population, so we tested whether people with Parkinson’s disease without cognitive impairment could perform the task similarly to healthy controls. Participants were asked to remember a set of images during an “encoding phase” (Figure 2, top row). Then, in a “test phase” (Figure 2, bottom row) participants were shown a new set of images, which consisted of images that were exact repeat images, images that were similar to those seen earlier (called lure images), and completely new images, and were asked to respond if they were “repeat,” “similar,” or “new.”

We found that Parkinson’s disease participants performed similarly to older adults whether they were on or off dopaminergic medication, showing that Parkinson’s disease-related motor symptoms did not interfere with their test performance. These results suggest that the MST is feasible to use for people with Parkinson’s disease, opening the opportunity for researchers to learn more about episodic memory in Parkinson’s disease. We presented these findings at the Cognitive Neuroscience Society Annual Meeting of 2019 in San Francisco (Figure 6, page 7), and the manuscript is currently being prepared for publication.

**Figure 2:**
Encoding and Test Phases of the Mnemonic Similarity Task. 
*ITI = inter-trial interval.*
We are just beginning to understand what factors cause thinking and memory problems in individuals with Parkinson’s Disease. For instance, we know that Lewy body pathology (Figure 3) in the brainstem causes most of the motor symptoms experienced by people with Parkinson’s disease. However, if Lewy body pathology is found in other parts of the brain (limbic and cortical regions), it can cause problems with thinking and memory.

They found that the type of thinking problems differed depending on which pathology was found. Specifically, the people with Lewy body pathology and co-occurring Alzheimer’s pathology demonstrated more memory problems, whereas individuals with just Lewy body pathology demonstrated more problems with executive functions, like problem solving and organizing. Understanding these relationships will be critical to developing treatments to improve memory and thinking in individuals with Parkinson’s disease.

Most recently, evidence has shown that some people also have Alzheimer’s disease pathology (Figure 4) at the same time as Lewy body pathology, and this co-occurring Alzheimer’s disease pathology may be responsible for some of the thinking and memory problems experienced by patients. Dr. Kathleen Poston and Dr. Sephira Ryman examined thinking and memory tests from research patients who had passed away and donated their brains to research. The goal was to understand how the combination of Lewy body and Alzheimer’s disease pathology related to their thinking and memory problems while they were alive.
People with Parkinson’s disease are at risk of developing cognitive impairment and dementia. Multiple studies have shown that lower amyloid protein concentration in the cerebrospinal fluid (which is collected from lumbar punctures) is associated with more cognitive problems in people with Parkinson’s disease. However, there are few studies on the relationship between cognitive impairment and amyloid protein build-up in the brain, as measured by positron emission tomography (PET). For example, sometimes we can see the buildup of amyloid on a PET scan, as shown in Figure 5 in the “amyloid positive” picture.

In this study, we used PET to determine whether amyloid protein build-up in the brain is associated with cognitive problems in Parkinson’s disease – specifically, with processing speed, as measured by the Symbol Digit Modalities Test (SDMT). This is a test in which participants are instructed to report the correct numbers associated with unique symbols in empty spaces as fast as they can. Previously, Ms. Marian Shahid demonstrated that lower amyloid protein concentration in cerebrospinal fluid is associated with worse SDMT performance in Parkinson’s disease. In this study, we found that higher amyloid protein build-up in the brain is associated with worse SDMT performance in Parkinson’s disease. Therefore, our findings from this study show a relationship that is similar to what we found when investigating amyloid protein concentration in the cerebrospinal fluid, and thereby furthers our understanding of abnormal amyloid (i.e., higher amyloid protein build-up in the brain as measured by PET and/or lower amyloid protein concentration in the cerebrospinal fluid) in Parkinson’s disease.

Of course, this does not mean that the amyloid is causing the cognitive problems. Our findings just show an association. Therefore, the Poston Lab researchers are working to better understand the interaction between amyloid protein build-up in the brain and more extended domains of cognitive impairment in Parkinson’s disease. Ms. Jeehyun Kim presented the initial findings from this study in October 2019 at the 144th Annual Meeting of the American Neurological Association in St. Louis, Missouri (Figure 7, page 7).

**Figure 5:** Amyloid protein build-up on a PET scan.
Figure 6:

Figure 7:
Dr. Kathleen Poston and Ms. Jeehyun Kim at the 2019 American Neurological Association (ANA) Annual Meeting in St. Louis, Missouri.
Scientific Papers


