Immunotherapies targeting alpha-synuclein in Parkinson’s Disease
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Parkinson’s disease (PD) is a progressive neurodegenerative disorder characterized by loss of dopamine neurons in substantia nigra and accumulation of abnormal protein, alpha-synuclein in the form of Lewy bodies and Lewy neurites. Alpha-synuclein is a small 140 amino acid protein with N-terminal region that can interact with cell membranes and a highly acidic unstructured C-terminal region. It is present in the presynaptic terminals of neurons, involved in synaptic plasticity and vesicle trafficking. Alteration in aggregation properties of this protein is believed to play a central role in the pathogenesis of PD. It exists in insoluble forms that can aggregate into oligomers and fibrillar structures. Lysosomal dysfunction may promote accumulation of insoluble alpha-synuclein. In addition, alpha-synuclein aggregates may be released into extracellular spaces to be taken up by adjacent cells where it can cause further misfolding and aggregation of protein. Due to these observations, there had been huge interest in developing antibody based therapies for PD. These antibodies can potentially prevent the formation of toxic variants of alpha-synuclein, facilitate degradation of existing toxic proteins or prevent them from being immunogenic thus inhibiting inflammatory response.

Several studies have tested immunotherapies in PD animal models with aim to target alpha-synuclein. Immunotherapies can be instituted in two ways: active immunization in which immune system is stimulated to produce antibodies against alpha-synuclein or passive immunization in which antibodies against alpha-synuclein are directly administered. Once alpha-synuclein antibodies have crossed the blood brain barrier, they are hypothesized to clear the existing alpha-synuclein. Animal studies have demonstrated the presence of these antibodies within the neurons. Exact mechanism of entry is unknown but once inside the cells they can activate the lysosomal clearance, hence affecting intracellular accumulation. Extracellularly, they can bind to receptors on scavenger cells, mainly microglia, thus activating them to facilitate uptake of extracellular alpha-synuclein. Immunotherapies against alpha-synuclein could directly block the toxic effects of the misfolded protein. Binding of the antibodies to alpha-synuclein directly will prevent the uptake of toxic protein by the cells, hence blocking the transfer and spread of PD pathology.

Active immunization against alpha-synuclein was demonstrated by Masliah and colleagues almost a decade ago. They administered recombinant human alpha-synuclein in transgenic mice expressing alpha-synuclein under the control of platelet-derived growth factor β. Reduction of accumulated alpha-synuclein in neurons with mild microglia activation was noted. Over time, other animal studies have been able to expand on these results. A biotechnology company AFFIRiS has developed two peptide vaccines PD01A and PD03A. Both peptides when administered to PD
animal models, caused antibody based immune response against aggregated alpha-synuclein. Humoral autoimmune response was not observed in these studies, hence no neuroinflammation or neurotoxicity was noted.

The first human phase 1 study recruited 32 subjects with early PD. 12 subjects each were included in low and high dose treatment group and eight were recruited in the control group. This study confirmed the tolerability and safety of subcutaneous administration of tested vaccine, PD01A. These subjects are now part of phase 1b follow-up extension study. AFFiRiS presented results of phase I randomized, placebo-controlled trial in 2017, confirming safety of PD03A in PD patients. It showed a clear dose dependent immune response against the peptide itself and cross-reactivity against alpha-synuclein targeted epitope. AFFiRis recently presented results of another phase 1 clinical study assessing the safety and tolerability of vaccines PD01A and PD03A in early MSA patients. Both vaccines were well tolerated and PD01A induced an immune response against the peptide itself and alpha-synuclein epitope.

Passive immunization against alpha-synuclein was first reported by Masliah and coworkers in 2011. A monoclonal antibody against C-terminus of alpha-synuclein, 9E4, was injected into a transgenic mouse model of PD. There was reduction in alpha-synuclein aggregates in the brain along with improvement in motor and cognitive impairment. Since then, few other immunization studies have reproduced favorable results in animal models of PD. Prothera BioSciences Inc. designed a phase 1, double-blind, randomized, placebo-controlled clinical trial (NCT02095171), in normal subjects. Testing agent, PRX002, was based on antibody 9E4. The results showed that it was well tolerated and there was dose-dependent reduction in the levels of free alpha-synuclein in plasma.

Prothera conducted 6-month phase 1b trial (NCT02157714) to evaluate the safety, tolerability and immune system response to multiple ascending doses of PRX002. 64 patients with PD received PRX002 via intravenous infusion once every 28 days. The drug was found to be safe and levels of free serum alpha-synuclein was reduced, up to 97%. Roche is currently recruiting participants with early PD for a multicenter, randomized, double-blind phase 2 trial to evaluate the efficacy of PRX002 vs placebo (NCT03100149). Another antibody, BIIB054, from Biogen was studied in 40 healthy subjects. It was well tolerated with favorable safety profile and could cross the blood-brain barrier. Like PRX002, this was also an ascending-dose study to assess safety and tolerability. Finally, BioArctic Neuroscience AB has developed antibodies, BAN0805, that are selective for oligomeric forms of alpha-synuclein.

Immunotherapy against alpha-synuclein has provided a new therapeutic avenue in the field of neuroprotection. Results from first human clinical trial are promising and provide a basis for the development of improved antibodies against alpha-synuclein. As the understanding of PD pathogenesis and therapeutics continue to evolve, it will become clear whether immunization targeted against alpha-synuclein will modify the disease progression.

References

VA Parkinson’s Specialists Gather in Los Angeles

On Friday, April 20th, 58 Parkinson’s disease specialists from across the nation gathered in Los Angeles for the 2018 VA PD Consortium Conference. Participants represented all 6 of the VA Parkinson’s Disease Research, Education and Clinical Centers (PADRECs) and numerous VA PD Consortium Sites. A full day of educational presentations and discussions focused on relevant advances in the diagnosis and management of Parkinson’s disease and related disorders, with a focus on topics relevant to Veterans care. Dr. Indu Subramanian, welcomed the participants as the Director of the host Southwest PADRECC in West LA. A full morning agenda started with a review or recently revised guidelines for the diagnosis of progressive supranuclear palsy by one of the leader authors of the report, Dr. Irene Litvan. Three more clinically focused presentations followed with two reviews of recently approved medications including one focused on medications for tardive dyskinesia by Dr. Walter Dunn and a second discussion of other new therapeutics by the Director of the Houston PADRECC, Dr. Aliya Sarwar. In his discussion of the management of tardive dyskinesia, Dr. Dunn discussed his own clinical experience and the literature regarding the use of the recently approved therapeutics, deutetrabenazine and valbenazine. The third presentation involved advances in the diagnosis and management of functional movement disorders that included a discussion of how the diagnosis of these disorders is becoming a diagnosis of inclusion rather than exclusion as well as the various studies supporting management strategies with psychotherapeutic and physiotherapeutic approaches.

Dr. John Duda, The VA PD Consortium Chairperson, provided an update of the state of the VA PD Consortium, highlighting the new Consortium sites that have recently joined the Consortium as well as several upcoming opportunities for collaboration among the Consortium. Dr. Adrienne Kenner continued the theme of updated management of common movement disorders by providing an update of tremor disorders and Dr. Caroline Tanner, the San Francisco PADRECC Director, wrapped up the morning session by reviewing our understanding of environmental risk factors for the development of PD, with a focus on Veteran relevant topics including Agent Orange, traumatic brain injury and toxicant exposures from residence at Camp Lejuene.

The early afternoon session highlighted our growing understanding of the role of lifestyle modifications for the management of PD by focusing on exercise. Dr. Giselle Petzinger began the discussion by reviewing her own research into the changes in neuroplasticity seen with physical exertion and Dr. James Morley complimented that with a discussion of his own research into overcoming the barriers to implementing an exercise program for Veterans with PD including a discussion of the importance of making specific prescriptions for physical activity. Two more presentations reviewing recent updates to the management of two more movement disorders, chorea and dystonia, followed by Drs. Ruth Walker and Maya Katz respectively. The final presentation was given by another invited speaker, Dr. Michele Tagliati, who lead a comprehensive review of recently completed and ongoing clinical trials in movement disorders as well as a discussion of his own and other research investigating anti-diabetes medications in the management of PD.

Finally, the day’s activities concluded with a reception and poster session highlighting the research being conducted by other Consortium members. Lively discussions followed most sessions and the collegiality shared by all was a highlight of the meeting. Attendees agreed that the program was highly informative, engaging, and particularly relevant to their practices involving the management of Veterans with PD and related disorders within the VA Healthcare system.
VA staff at any facility in the VHA system now have a new tool to use for obtaining information on movement disorders patients seen within that facility. At the request of the PADRECCs, a Movement Disorders Registry has recently been added to the list of conditions in the Clinical Case Registry (CCR).

The Clinical Case Registry is a software application that works within the VHA’s electronic medical record system, (the VistA system that underlies the Computerized Patient Record System [CPRS]) to extract a wealth of information. The CCR was initially developed as a registry for HIV and hepatitis C patients. Once it was realized that the CCR was a very useful tool, other conditions were added. There are now forty different medical conditions supported by CCR with more in development.

When a new registry is under development, first a collection of diagnostic codes is gathered. Some conditions, such as multiple sclerosis and amyotrophic lateral sclerosis only utilize one ICD code. For the Movement Disorders registry, instead of requesting a Parkinson’s disease registry and a separate registry for Essential tremor and other conditions, a decision was made to include multiple diagnostic codes in one registry as the Movement Disorders registry.

The CCR application contains a group of “Reports”. Each report is preconfigured to extract only certain items (variables), but with the option of customizing the various portions of the report. A partial listing of the available reports includes: BMI by Range, Clinic Follow Up, Combined Meds and Labs, Current Inpatient List, Diagnosis Report, General Utilization and Demographics Report, Inpatient Utilization, List of Registry Patients, Outpatient Utilization, Patient Medication History, Pharmacy Prescription Utilization, Procedures, Radiology Utilization, and Renal Function by Range.

Nightly, the CCR compiles a listing of patients with the designated diagnostic codes who have been seen at that facility. These diagnostic codes have been assigned during medical care. Only the HIV and Hepatitis C registries have the diagnosis of each individual within that registry verified by a clinical case coordinator.

With the Diagnostic Report, it is possible to find how many patients with a particular diagnosis have been seen overall since January 1, 1985, or seen during a specified time, or seen in a certain clinic, or seen by specific providers. Using the Combined Meds and Labs Report, for example, a provider can look for how many Parkinson’s disease patients seen in his or her clinic have, or have not had, vitamin D levels tested, along with whether the test results were abnormal or not and whether the patient received treatment or not. The List of Registry Patients Report can be run in summary mode to give patient group totals for diagnostic codes or can be run in detailed mode to include patient-specific information, (Patient name, Last 4 of Social Security Number, Date of death, Date of selection). Date of selection is the earliest date that the selection rule or code was found. So, when there is a need to find people who already have a condition, this information can be utilized.

The report information can be exported to Excel. With approval, the CCR can be used for research. An investigator can query the registry in summary mode to see if there is an adequate number of patients for a proposed study. The CCR can be used to supplement a chart review by first extracting some information from the registry, exporting it to Excel/Access and then reviewing the subject’s medical record to find information not included in the registry reports.

It is possible to find individuals lost to follow up, those on a particular combination of medications, those with a body mass index in a certain range, and to combine registries to find patients who have received diagnostic codes for both conditions. Due to the concern that Parkinson’s disease patients are at increased risk of melanoma, a provider or researcher could search for patients who are in both the Movement Disorders and Melanoma Registries within CCR.

Additionally, being able to extract the information from the current local VistA/CPRS system and export it without having to individually search on a patient by patient basis will provide a better means of managing and organizing clinical care. These are just a few examples. The new Movement Disorders registry provides many opportunities for optimizing clinical care as well as facilitating research. The PADRECC centers and their consortium members can look forward to the benefits of utilizing this newly established Movement Disorders Registry within the Clinical Case Registries.
A Winning Therapy Approach for Veterans with Parkinson’s Disease
Debra Gleeson, Ph.D., CCC-SLP, Battle Creek, Michigan VAMC

For Veterans with Parkinson’s Disease, using their voice effectively in a communication-driven society can be challenging. Tapping into creative options for stimulating recovery and improvement, Dr. Debra Gleeson, Ph.D., CCC-SLP worked in harmony with the Cheff Therapeutic Riding Center in Augusta, Michigan to obtain funding for a program using horses as the foundation for therapy. Their funding answer came by way of the Professional Association of Therapeutic Horsemanship International (PATH Intl), which awarded Cheff Center a grant through the Equine Services for Heroes (ES4H) program to provide the opportunity for Veterans with Parkinson’s disease to participate in therapeutic riding lessons.

The connection between speech therapy and horseback riding is based on the principles of hippotherapy. Hippotherapy is an evidence-based clinical treatment practice used by speech-language pathology professionals focusing on the purposeful manipulation of equine movement to engage sensory, neuromotor, and cognitive systems to achieve functional outcomes. There are numerous influences of a horse’s movement on speech and language. By normalizing muscle tone and postural support, Veterans with speech and voice problems associated with Parkinson’s disease can attain improved respiratory function, breath support, and sustained phonation as an energy source for speech. They can benefit from enhanced proprioceptive input to the oral motor mechanism to improved speech timing and rhythm and achieve improved oral-motor control.

Veterans selected for this program participate in the Parkinson’s Speech Education Group at the Battle Creek VA Medical Center and completed the necessary forms and clearance from their primary care provider. Four Veterans were selected to participate in speech therapy sessions simultaneously with their group therapeutic riding lessons. The program began in April 2018 and will continue through July 2018. The emphasis is on merging the principles of LSVT BIG and LOUD with Hippotherapy to create a platform for enhancing respiratory function, breath support, sustained phonation, speech timing, and oral-motor control. The results of the first two sessions has been promising and the outlook for future gains is bright.

For more information on speech therapy and implementation of hippotherapy treatment principles for Veterans with Parkinson’s disease, please contact the Speech Pathology program at the VA Medical Center in Battle Creek, Michigan.

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References

1. Funded through the Adaptive Sports Programs for Disabled Veterans and Disabled Member of the Armed Forces Grant, through the U.S. Department of Veteran Affairs.

**Philadelphia PADRECC Update**

**Education Update**

**Monthly Video Case Conference:** Monthly video case conference calls are held with service area Consortium Centers to share case studies and discuss diagnosis and treatment of difficult cases.

**Patient & Caregiver Education/Support Group Program:** This program runs from April-December and meets once a month for one hour to provide support and education on topics related to PD. To increase accessibility, some groups are broadcasted to two local CBOCs using tele-health technology.

**PD 101:** This 2-hour program was held on April 13, 2018 and provided an overview of Parkinson’s disease symptoms, treatment options and the Philadelphia PADRECC Team. Participants also had the opportunity to ask questions. This program was held in-person at the Philadelphia PADRECC and broadcasted to 2 area VAMCs and 4 area VA Community Based Outpatient Clinics (CBOCs) to increase accessibility.

**Community Outreach:** Clinical Staff continue to attend local community health fairs and present at local support groups providing information and education on the PADRECC program and services available as well as information on topics related to PD.

**Workshop for Veterans with Parkinson’s Disease at The Philadelphia Museum of Art:** In June 2017, the Philadelphia PADRECC partnered with The Philadelphia Museum of Art to offer a unique workshop designed for Veterans with Parkinson’s disease and their care partners. The program included a private guided tour and an art lesson by a teaching artist. The exercises in this workshop were fun and created a camaraderie that encouraged people to go beyond self-imposed limitations. The Philadelphia PADRECC is looking forward to continued collaboration with the Philadelphia Museum of Art.

**Walk to Stamp Out Parkinson’s:** Last October, several members of the Philadelphia PADRECC Team and their families walked alongside patients, families, and other healthcare professionals in The Parkinson’s Council’s Annual Walk to Stamp out Parkinson’s. The walk was held at The Philadelphia Zoo and was a fun day had by all raising awareness for Parkinson’s disease.

**Clinical Update**

**Expansion of Telehealth Services:** The Philadelphia PADRECC has expanded telehealth to 7 VA Medical Centers and 16 CBOCs within VISN’s 2 and 4. Telehealth is used to provide consultative services, follow up care, DBS stimulation adjustments, and medication management. VA Video Connect into the home is a modality used to reach Veterans who find traveling to a VAMC or a CBOC too difficult and is a great tool for clinicians to follow up on the most vulnerable Veterans. With the expansion of their telehealth program, the Philadelphia PADRECC recently converted an old storage room to a telehealth clinic room freeing up valuable clinic space needed by other providers.

**Research Update**

**Drug-induced Parkinsonism (DIP): A canary in the coal mine?:** DIP associated with dopamine receptor blocking drugs (most often antipsychotics) is the second most common cause of Parkinsonism and can be clinically indistinguishable from PD. In some cases, when symptoms persist after drug withdrawal, DIP may represent “unmasking” of prodromal PD with the offending drugs acting as a “stress test” for dopaminergic pathways. In two studies funded by a VISN 4 pilot award, we found that hyposmia, severe non-motor symptoms or the appearance of DIP with low-intensity dopamine blockers may signal underlying neurodegeneration. We are continuing to study the relationship between DIP and underlying PD using clinical and radiologic biomarkers.
The Immune System and Parkinson’s Disease: Dr. Morley and the PADRECC are collaborating with a local biotech company (Longevity Biotech) on a project recently funded by the Michael J. Fox Foundation to study whether the immune system plays a role in PD. The team will recruit pairs of patients and their caregivers to study whether immune cells and other blood markers are different in PD and are associated with disease severity or other PD characteristics. This study will begin recruiting subjects in June 2018.

Bacteria and Parkinson’s Disease: Dr. Fullard and Dr. Duda, in collaboration with Dr. Noam Cohen from the Ear Nose and Throat Department, continue to study how bacteria that colonize our body might contribute to the risk of Parkinson’s disease. This study is trying to understand if there are genetic reasons why some people with PD have certain types of bacteria in the hopes of developing new therapies in the future. Once recruitment is complete, we will examine differences in the genetics of the taste receptors and in the bacteria of the nose and gut between those with Parkinson’s disease and those without.

Traumatic Brain Injury: Dr. John Duda, PADRECC Director and his colleagues, Drs. Kacy Cullen, Isaac Chen and John Wolf, from the Department of Neurosurgery at the University of Pennsylvania, continue studies funded by the Rehabilitation Research and Development Service of the Department of Veterans Affairs to study the relationship between brain trauma and neurodegeneration. The researchers have published several studies that have shown how the brain reacts to trauma and how that could possibly lead to chronic neurodegenerative disease development. It is hoped that these studies will lead to treatments to prevent the development of these neurodegenerative diseases in Veterans and others who have suffered head injuries.

Neurorestoration in Parkinson’s Disease: Dr. John Duda and his colleagues Kacy Cullen, PhD, and Isaac Chen, MD, PhD from the Center for Neurotrauma, Neurodegeneration, and Restoration (CNNR) at the Crescenz VA Medical Center, continue to investigate whether one of the main brain pathways affected in Parkinson’s disease, the nigrostriatal pathway, can be generated in a petri dish and transplanted in animal models to reverse the motor symptoms in PD. While studies are early, the success of their efforts to date have led to several publications and special recognition at several different scientific meetings.

Exercise in PD: Identifying early or prodromal PD that has been “unmasked” by DIP allows intervention at the earliest stages of disease. Dr. Morley continues his VA Rehabilitation R&D service Career Development Award entitled “Effect of exercise on recovery in drug-induced Parkinsonism and Parkinson disease.” Subjects with suspected DIP who are found to have abnormal DAT-SPECT are randomized to exercise (aerobic walking) or no intervention. We are examining the short term effects of exercise after 8 weeks and a potential disease modifying effect of exercise using serial DAT-SPECT and biochemical markers after 52 weeks.

If exercise can benefit our PD patients, how can we make sure they are getting enough? Dr. Sneha Mantri, PADRECC fellow, is finishing a study to better understand exercise and activity levels in PD. She is examining PD patients’ attitudes and barriers to exercise and comparing them to activity levels using both a self-reported survey and objective monitoring in the community using wearable devices. Dr. Mantri hopes to use this information to identify potential interventions to increase exercise and activity levels in PD patients.

Philadelphia PADRECC–Parkinson’s Disease Consortium Center
West Haven, CT
Director: Diana Richardson, MD
The West Haven Parkinson’s Disease Consortium has had an active year celebrating our 10 year anniversary. We remain active in promoting good health, well-being, fitness and education for our Veteran patient with Parkinson’s disease and other movement disorders. Currently we continue to hold an annual PD Lectures & Support series throughout the year. We also continued traditions in April for Parkinson’s Awareness month with the Annual Parkinson Fair, the annual Parkinson’s Disease Symposium; and, team representation at the Parkinson’s Unity Walk in NYC Central Park. This year, we sponsored and conducted an Agent Orange Information, Research and Education support group to help Veterans with Agent Orange Exposure and other environmental exposure understand their conditions. We have been able to assist Veterans in enrollment in the exposure related registries and also help with pursuit of compensation.
Southeast/Richmond PADRECC Update

Clinical News

Telehealth Update: The Richmond PADRECC continues to expand telehealth (TH) services to those Veterans unable to travel to the Richmond PADRECC for face to face clinical visits. TH services have been provided to Veterans living in 9 different states, The District of Columbia and Puerto Rico. Richmond PADRECC has consistently seen over 400 TH visits/year for the last 2 years. We are currently projected to increase by 10-15% for this fiscal year. Our Neurosurgery DBS Team continues to utilize TH as part of the preliminary evaluations for DBS as a treatment option. An introduction to the DBS team, on/off medication testing, DBS educational overview, review of the Veterans medical history and discussion of any medical clearances that may be needed all take place utilizing TH prior to a face-to-face evaluation.

Richmond PADRECC - Moving forward with Speech Therapy – Adding CVT to Home, Pre- and Post DBS evaluation and Utilizing the Speech Vive: Catie Kane, M.Ed CCC-SLP, has recently transitioned to serve as the primary speech-language pathologist for the Richmond PADRECC where she treats patients with Parkinson’s Disease who have impairment in speech, voice, swallowing, or cognition. Catie is certified in LSVT LOUD treatment and Speech Vive calibration. She has established pre- and post-operative speech screening tools for patients undergoing deep brain stimulation (DBS) surgery, is experienced with assistive technology, and has presented on the Role of Speech Therapy for the National Parkinson’s Education and Support Telephone Conference.

Collaborative efforts from the speech pathology department and PADRECC team have recently brought the Speech Vive to the Richmond VAMC. This evidence-based device outputs white noise into the ear which elicits an automatic response of louder and clearer speech production. The Speech Vive has yielded positive results since its introduction to our facility with more than 65% of patients selecting it as their preferred therapy option for improved speech and voice.

In addition, Catie is working with the Richmond PADRECC to increase utilization of interdisciplinary therapy through an electronic medical platform (Clinical Video Telehealth). This medium for patient-therapist encounters enables the individual to be seen and treated in the convenience of their own home, with an overall goal to increase access and quality of care to Veterans in need.

Education News

MDS: The Richmond PADRECC continues to participate in the MDS (movement disorder series) that is held 5 times/year. Jessica Lehosit DO, Interim Director of Richmond PADRECC presented “Initial Therapeutic Choices for Management of Parkinson’s Disease” and Lori Stuart KT at McGuire VAMC presented on “The role of Kinesiotherapy in the treatment of Parkinson’s Disease and other Movement Disorders”.

PD Self: Richmond PADRECC participates in identifying Veterans who are interested and qualify for PD SELF. PD-SELF stands for Parkinson’s disease Self Efficacy Learning Forum. PD SELF is a national pilot program of the Parkinson’s Foundation which is designed to provide people with PD (PWP) an in-depth understanding of the disease and self-efficacy tools to manage PD.

Patient and Caregiver Support Group: The group continues to meet 8 times per year offering assorted topics related to Parkinson’s Disease. The goal of the group is to help Veterans with PD and their families learn how to adapt to the physical, emotional and psychosocial challenges associated with Parkinson’s Disease.

Wellness Workshop: Richmond PADRECC Providers collaborated with a community Assisted Living facility offering a Wellness Workshop to PD patients in the community. Topics included a Holistic Approach to Managing Parkinson’s, atypical Parkinsonism, fatigue and GI complications. The wellness workshop was well attended.

Rehabilitation Services: During Parkinson’s Awareness month in April, the Richmond PADRECC and PM&R held an educational awareness event covering Rehabilitation services available at the Richmond VA for our Parkinson’s patients. Physical Therapy, Occupational Therapy, Speech Therapy, Kinesiotherapy and Music Therapy presented information about their discipline, demonstrated equipment and answered questions.
Parkinson’s Disease Educational Forums: Richmond PADRECC continues to collaborate with Regional, State and National external professional health care provider groups. The Richmond PADRECC physicians, APP and RN’s have presented on various Parkinson’s Disease topics. The audiences reached have been physicians, Advanced Practice Providers, Nurses and Therapist. Topics have included PD 101, Diagnosis and treatment of motor and non-motor sequelae of PD, research and biomarkers.

Research News

Oculomotor functions in movement disorders: This ongoing study has been enrolling subjects for 10 years, and has become a part of every willing participant’s initial visit to our clinic. Specific, unique, repeatable eye movement abnormalities have been correlated with different movement disorders, strongly suggesting the ability to assist in differential diagnosis. George Gitchel PhD, Mark Baron MD, and their collaborator have filed for a patent on the technology, and have licensed the intellectual property to a company. Royalties from this collaboration have already come back into the VA system. The company announced the release of this new product at the Consumer Electronic Show (CES), where it was awarded as an Innovation Awards Honoree, for “Tech for a Better World” (https://www.businesswire.com/news/home/20180107005112/en/Eyes-Health-CES-2018-Innovation-Awards-Honoree).

Eye movements as a clinical and prodromal biomarker in Parkinson’s disease: Funded by the Michael J Fox Foundation for $1M, this study expands upon our longstanding aforementioned protocol investigating the oculomotor behavior of movement disorders. This blinded multisite study (Richmond PADRECC, VCU, Emory, University of Iowa) continues to recruiting controls, PD subjects, those with “Other” movement disorders, and subjects with REM behavior disorder (RBD). Preliminary data suggesting that blinded eye movement recordings could potentially effectively differentiate clinically manifest disease states. Preliminary data from RBD subjects strongly suggest the ability to detect preclinical stages of PD, perhaps a decade or more before clinical conversion.

BOSS-PD: The Richmond PADRECC is serving as a site for this MERIT funded study at the Atlanta VA. The purpose is to investigate the equivalence (or at least non-inferiority) of behavioral therapy versus Solifenacin for urinary incontinence in PD subjects.

TMS for cognition in TBI subjects: George Gitchel (PI) was awarded $500k for this study to investigate the possibility of improving cognition in a population of TBI subjects with cognitive complaints.

Bile Acids and Gut Microbiome: This is a MERIT funded study at the Richmond VAMC in the hepatology clinic. PADRECC is a collaborative partner, recruiting and assessing PD subjects to compare with other conditions affecting the gut.

AP2-3000: Richmond PADRECC has been selected as a site for this study involving the Apokyn subcutaneous continuous infusion pump. Currently pending IRB approval.

P2B001/003: Richmond PADRECC has been selected as a site for this study investigating this new drug that contains rasagiline and pramipexole in a single pill. Currently pending IRB approval.

Alpha-stim Cranial Electrotherapy Stimulation (CES):

Sleep disorders are very common in patients with Parkinson’s Disease. Dr. Qutubuddin and Dr. Carne are in the process of starting research using Alpha-Stim to treat sleep disorders in Parkinson’s patients, mainly insomnia. The Alpha-Stim CES is a device used in the treatment of depression, anxiety, sleep and pain. The Alpha-Stim’s microcurrent waveform activates groups of nerve cells that are located at the brainstem. These nerve cells produce serotonin and acetylcholine, which can affect the chemical activity of the nerve cells that are both nearby, and at a distant site. Alpha-Stim appears to amplify or diminish the activities of these cells called modulation, and occurs either because of, or together with, the production of a certain type of electrical activity pattern in the brain known as an alpha state. The neurological mechanisms occurring during the alpha state appear to decrease stress-effects, reduce agitation and stabilize mood, and control both sensations and perceptions of types of pain. These effects can be produced after a single treatment. Repeated treatments may increase the relative strength and duration of these effects, and in some cases may be permanent.
Northwest PADRECC Update

The Northwest PADRECC is comprised of the VA Portland Health Care System and the Puget Sound VAMC and Consortium sites.

Clinical Update:

Telehealth: NWPADRECC Portland has a very active Telehealth clinic seeing 12-15 patients per month as both New evaluations, follow up care, and Pre-DBS screening.

DBS: So far for FY 18 Portland has completed 17 DBS surgeries and 14 battery changes. We are currently all trained and are using the new St. Jude DBS system and just started using the Boston Scientific device for implantation. We are also continuing to do programming of Veterans who come to us for the surgery from outside our VISN via TH with the home provider with the patient to control the programmer. This has saved multiple trips for these folks back and forth to Portland.

Botox: Portland and Seattle continue to have very active botox injection clinics. We easily see over 500 visits per year. Staff was currently trained in the use of the ultrasound, useful for patient in need of injections for sialorrhea as well as spasticity.

Education Update:

Portland hosted 2 patient education events this past year. Both conferences were held locally in Portland as well as sent out by V-tel to 12 remote sites. We had a total of over 200 participants!

“Exercise and Parkinson’s Disease: A Powerful Medicine”, presented by Laurie King PhD, PT
“Sleeping Challenges in Parkinson’s Disease” presented by Amie Hiller MD

NWPADRECC Portland hosted its annual CME “Neurology Updates for General Practice”. This is offered locally as well as by V-tel to any health provider interested. The topics vary from year to year. This year the topic titles are: “NPH/What to Do?”, “Neuro-opth/What Am I Seeing?”, “Neuro Causes of Autonomic Dysfunction”, and “Cannibis and Epilepsy”. Registration for this event is in TMS.

Research Update:

The NW PADRECC strongly encourages and supports investigator-initiated research projects. Some of the projects in the past year have been:

Buspirone, in combination with amantadine, for the treatment of levodopa-induced dyskinesia (OHSU eIRB # 11875)
Dr. Kathryn Chung is conducting a research study looking at the effect and the safety (side effects) of buspirone in combination with amantadine on abnormal involuntary movements (dyskinesias) in Parkinson’s disease (PD).

Pacific Northwest Udall Center (PaNuC): Clinical Core and Specimen Collection (VA IRB # 2332; OHSU eIRB # 6154)
Dr. Joseph Quinn is conducting this research study to examine the changes in thinking and memory of Parkinson’s disease patients over time. A second goal is to determine the role genetics plays in cognitive impairment in Parkinson’s disease.

Using Multiplex Families to Map Genes that Modify Susceptibility and Age at Onset in Parkinson’s Disease (VA IRB # 2731)
Dr. Kathryn Chung is conducting this research study to identify genes that increase a person’s risk of developing Parkinson’s disease (PD) or related disorders. The goal of this study is to better understand and treat PD and other related disorders.
Measuring Cortisol Levels in Persons with Parkinson’s (PD) (VA IRB # 3794, OHSU eIRB # 15183)
Dr. Amie Hiller is conducting a research study looking at cortisol levels in Parkinson’s disease (PD). Cortisol is a hormone that is normally released in response to events and circumstances such as waking up in the morning, exercising, and stress.

A Phase 3, Open-Label Study of the Safety, Efficacy, and tolerability of Apomorphine Administered by Continuous Subcutaneous Infusion in Advanced Parkinson’s Disease Patients with Unsatisfactory Control on Available Therapy [infusiON Apokyn] (VA IRB # 4202)
*NEW Kathryn Chung MD PI, Susan O’Connor RN, Research Coordinator

Clinical Characteristics of Parkinson’s Disease Subjects with Severe Hypertension During Motor OFFs (VA IRB # 4202)
Dr. Kathryn Chung and Dr. Way are conducting a research study looking at blood pressure changes in Parkinson’s disease (PD).

Publications:


Active Grants:
Zabetian C- VA Merit Review Award, 1 I01 CX001702 (PI), “Genetic Movement Disorders: Etiologies And Pathogeneses”
Zabetian C - NIH/NINDS, 1 U01 NS100610-01 (Co-I), “Dementia with Lewy Bodies Consortium”
Samii A - Sponsor: CHDI Number: A-5807 (Site Investigator), “A Prospective Registry Study in a Global Huntington’s Disease Cohort”
Quinn J - NIH/NCCAM, R01AT008099 (Co-I), “Mechanisms and Active Compounds in the cognitive effects of Centella Asiatica”
Quinn J - NIH/NIA, P30 AG008017 (Biomarker & Genetics Core Leader), “Oregon Alzheimer Disease Center”
Quinn J - NIH/NINDS, P50 NS062684 (Site PI), “Pacific Northwest Udall Center”
Quinn J - NIN / NINDS, 5U10NS077350-03 (PI), “Comprehensive Oregon Neuroscience Network for Excellence in Clinical Trials CONNECT)”
Johnson S - Veterans Affairs Merit Grant 1 I01 BX002525 (PI), “Regulation of VTA dopamine neurons by AMP kinase”
Johnson S - USPH Grant 1 R01 DA038208-01 (PI), “Regulation of VTA dopamine neurons by AMP kinase”
Chung K - NIH/NINDS, P50 NS062684 (Site Co-I), “Pacific Northwest Udall Center”
Houston’s Parkinson’s Disease Research, Education and Clinical Center (PADRECC) housed in the Michael E DeBakey VA Medical Center provides state of the art medical and surgical services to Veterans with Parkinson’s disease and related movement disorders who reside in the South Central and Mid-Western United States. The area served by the Houston PADRECC includes all or parts of the following states: Texas, Louisiana, Mississippi, Oklahoma, Arkansas, Alabama, Florida, Kansas, Missouri, Indiana, Illinois, Wisconsin, and Kentucky (Houston PADRECC Consortium).

Consortium update:
Houston PADRECC has added the following new consortium sites and members in FY 18:

1. G.V. (Sonny) Montgomery VA Medical Center, Jackson, MS (Juebin Huang, MD, PhD)
2. Central Texas Veterans Health Care System - Austin Outpatient Clinic (Padma Kumar MD).

Clinical Update:
Dr. Paolo Moretti, a Houston PADRECC neurologist and movement disorder specialist, relocated to Utah at the beginning of FY18. Our nurse supervisor and clinic coordinator nurse positions remain un-filled due to SCS hiring freeze. Despite these limitations, Houston PADRECC has maintained its leadership position with respect to patient encounters amongst all 6 PADRECCs.

There has been a total of 2884 patient encounters to this date, approximately 105 less then FY17, however the activity in both procedure clinics i.e., Deep brain stimulation and Neurotoxin injection therapy clinics has increased by 1% and 8% respectively.

New Initiatives:
- Houston PADRECC’s Suzanne Moore spearheaded the implementation of Movement Disorders Clinical Case Registry. This registry would be an invaluable resource for our clinics both in operational and research purposes.
- The updated New and Follow up patient evaluation templates are now in use at the Houston PADRECC
- A New Clinic Initiative – focused on preventive and corrective measures to improve brain and overall health of the patients called “the BRAIN HEALTH Clinic” is being developed. It is expected to begin before the end of FY 18.
- Initiated the process to begin Video Connect service with PADRECC patients.
Education Update:

Houston PADRECC’s Associate Director for Education position remains unfilled due to SCS hiring freeze.

We have continued our 16 educational programs geared towards patients/caregivers, medical trainees and practicing healthcare providers.

These include 1) Clinic based patient/caregiver education, 2) Patient’s monthly educational support group, 3) Patient and Caregiver educational conference (Educational Forums), 4) Collaborative Patient Educational Programs with Community groups, 5) Patient and Caregiver based educational newsletter (PADRECC Pathways), 6) Medical Staff’s weekly educational conference, 7) Medical staff’s monthly journal club, 8) Physicians’ monthly Clinical Case Conference, 9) Medical staff’s monthly inter-disciplinary surgical case discussion series, 10) Monthly Consortium based tele-educational meeting, 11) PADRECC based BCM neurology residents monthly elective rotation, 12) PADRECC’s joint educational venture with Pharmacy residency training program, 13) In-patient medical student and medical residents hands on educational experience, 14) PADRECC physicians’ lectures (including grand rounds, invited lectures) at the VA, BCM, national and international locations, 15) Production of National PADRECC newsletter (VA Report), 16) Nurse lecture series.

New Initiatives:

- Initiation of formal PADRECC clinic based educational rotation for Baylor College of Medicine students.
- Nurse clinic based “Fall Prevention”, educational initiative
- Nurse clinic based bilingual (English and Spanish) caregiver “Stress Reduction” educational initiative

Research:

We currently have 12 active research projects. In FY18, we have continued recruitment in our Circadian Rhythm/Sleep Study and began screening subjects for a collaborative project with the GI department entitled “High Resolution Manometric Abnormalities of the Esophagus and Clinical Features of Gastroesophageal Reflux in Patients with Parkinson’s Disease”.

Renewal for our collaborative traumatic brain injury project has been submitted.

New Initiatives:

- P50 NIH grant. “P50 NS108720: Baylor College of Medicine Udall Center for Parkinson’s Disease Research” was submitted and scored, but not funded. A re-submission is planned for December 2018.
- A new collaborative protocol with Neurosurgery entitled “Analysis of Human Basal Ganglia Electrophysiological Recordings and Targeted Stimulation for Optimization of Deep Brain Stimulation” has been approved
- Protocol for an industry research project which is a “Phase 3, Open-Label Study of the Safety, Efficacy, and Tolerability of Apomorphine Administered by Continuous Subcutaneous Infusion in Advanced Parkinson’s Disease Patients with Unsatisfactory Control on Available Therapy” has been approved by the IRB and the site initiation visit has been completed.
- A new project to study the clinical characteristics of tremor in Veterans has been approved by the IRB and will utilize the Movement Disorders Clinical Case Registry to supplement a chart review for Essential tremor patients seen at the Houston PADRECC.

Publications and other research presentations:

- Abstracts/posters = 7 (4 presented, 1 submitted, 2 in development)
- Papers = 10 (6 published, 2 submitted, 2 in development)
Women and PD TALK

San Francisco PADRECC was honored to host this national forum attended by women advocates, neurologists, epidemiologists, biostatisticians, physical therapists, advanced practice nurses, social workers, and caregivers from California, Oregon, South Dakota, Illinois, Minnesota, Mississippi, North Carolina, Pennsylvania, and New York.

As part of the Women and PD Initiative, the Parkinson’s Foundation is leading the first national effort to address long-standing gender disparities in Parkinson’s research and care through the Women and PD Teams to Advance Learning and Knowledge or Women and PD TALK project. In this collective project, the Parkinson’s Foundation engages key stakeholders to ensure recommendations for women’s health are not only developed, but also implemented.

San Francisco and West LA PADRECCs presented four speakers on the agenda: Caroline Tanner, MD, PhD; Cameron Dietiker, MD; Susan Heath, RN, MS; and Adrienne Keener, MD.

QUERI Funded Project: PADRECC To CalVet Veteran Homes Telemedicine Expansion and Parkinson’s Disease Education

PADRECC San Francisco received a grant from the Quality Enhancement Research Initiative for a direct implementation project focusing on expanding telemedicine services from PADRECC-SF to California State Veteran Homes. PADRECC’s Annie Li Wong, NP and Susan Heath, RN, MS will pilot a two-part program that (first) expands its telemedicine services to rural Veterans living in the CalVet home, Fresno, utilizing Advance Practice Nurses; physicians will be consulted on an as-needed basis. The second part will pilot an education program aimed at teaching nursing home staff about Parkinson’s disease. The nurses piloted their first episode to the San Francisco VA Community Living Center and will share this knowledge at the CalVet Fresno July 2018.

New to San Francisco PADRECC:

Nijee Luthra, MD, PhD
Dr. Luthra is a Movement Disorders Neurologist who joined the San Francisco PADRECC team after completing her movement disorders fellowship as a PADRECC VA Special Fellow in the Spring 2017. Her research interests include Parkinson’s disease, tremor disorders and dystonia, with a focus on biomarkers of disease and treatment. Dr. Luthra is currently a co-investigator for multiple clinical trials for Parkinson’s disease and for essential tremor and has conducted secondary analyses on prospectively collected data from large cohorts to address novel questions.

Doris D. Wang, MD, PhD
The San Francisco VAHCS Neurosurgery department welcomes, Dr. Doris Wang, July 2018 who will perform deep brain stimulation surgery for the PADRECC. Dr. Wang is an Assistant Professor in Neurological Surgery at UCSF who completed her PADRECC fellowship in Stereotactic and Functional Neurosurgery under SF-PADRECC’s originating surgical director, Dr. Philip Starr. Dr. Wang’s research interests include mapping and testing the neural architecture of human motor learning using an implanted, bidirectional DBS device and develop targeted, closed-loop therapies to restore motor skill learning in patients with brain diseases and injuries.
San Francisco PADRECC Update (continued)

Research Update:

Paul Larson, MD

Dr. Larson is SF PADRECC’s Director of Surgery, the Chief of Neurosurgery at the SFVAHCS, and Vice Chair of Neurological Surgery at UCSF. Dr. Larson, fellow neurosurgeon Philip Starr, and imaging scientist, Alastair Martin (VA/UC) started the interventional MRI-guided surgery for deep brain stimulator placement and other MR-guided procedures. Their work resulted in San Francisco being the first VA in the country to offer iMRI-guided DBS surgery.

Dr. Larson’s research group has been at the forefront of gene therapy for PD, has a leadership role in 4 of the 7 human trials completed to date, and have performed more than one third of Parkinson’s gene therapy procedures performed worldwide. Dr. Larson is currently the Principal Investigator for a fifth gene therapy trial using iMRI-guided delivery, which is being done exclusively at the VA, and first Parkinson’s gene therapy trial to be performed in the VA system. A nationwide Phase II gene therapy will start this summer with Dr. Larson as the national surgical PI and the SFVAHCS as one of the surgical centers.

Philip A. Starr, MD, PhD

Dr. Starr was the founding surgical director in PADRECC-SF and continues to mentor our VA/UC Stereotactic and Functional Neurosurgery Fellowship; he is Professor of Neurological Surgery and holds the Dolores Cakebread Endowed Chair at UCSF. Dr. Starr’s clinical interests are in functional neurosurgery, particularly in the use of implanted devices to improve brain function. His lab is involved in the brain network disturbances underlying neuropsychiatric disorders. They introduced the technique of electrocorticography to the study of movement disorders in humans, and recently showed that primary motor cortex in PD has markedly elevated synchronization of population spiking activity to the motor beta rhythm. The lab is extending their work to the cortical areas mediating depression, anxiety, and impulsivity and utilize a variety of technical approaches in human neurophysiology, including single unit recording, field potential and electrocorticographic recording (acute and chronic), EEG, and task related activity. Starr lab hopes to increasingly focus on recording from totally implanted devices, and extend our analyses of motor circuits to other frontal lobe/basal ganglia circuits relevant to cognitive function and psychiatric disorders.

Southwest PADRECC Update

Greater Los Angeles Healthcare System

The West LA VA Medical Center is the center of excellence for the Southwest PADRECC Region. Providing subspecialty care to patients with Parkinson’s disease and other movement disorders, the medical center conducts evaluations and management of Deep Brain Stimulation for Parkinson’s Disease, Essential Tremor, and dystonia; and Botulinum Injection Clinic. In addition, we train two PADRECC Special Fellows in our field each year, as well as sponsor the PD @ Home national Parkinson’s telephone education/support conference for Veterans and/or Caregivers of Veterans. The teleconference is held the 2nd Tuesday of every month from 10:00 – 11:00 am PST, via toll free number 1.800.767.1750 code 5431# and is facilitated by our nurse coordinator, Patricia Pittman. The PADRECC Education Committee seeks out speakers who present diverse topics on Parkinson’s Disease.

Under the leadership of Southwest PADRECC Region Director, Dr. Indu Subramanian, the West LA VA Movement Disorders clinic continues to expand their services by adding EMG-guidance for chemodenervation procedures.

Adrienne Keener, MD is a Movement Disorders Neurologist who joined the team after completing her fellowship as a PADRECC VA Special Fellow in the Spring of 2016. She is an Assistant Professor at UCLA with an interest in epidemiology in Parkinson’s Disease, working with Drs. Jeff Bronstein and Beate Ritz on the longitudinal Parkinson’s Environment and Gene (PEG) Study. At the VA, she runs the botulinum toxin clinic and is working to bring telehealth to Veter-
Southwest PADRECC Update (continued)

ans in the Greater LA Healthcare System. She is also interested in medical education, and serves as the Associate Program Director for the UCLA Neurology Residency Program.

Denise Feil, MD, MPH is a Geriatric Psychiatrist and Associate Professor of Health Sciences at UCLA who joined the West LA VA Movement Disorders clinic in the Fall of 2016. She has extensive experience working in integrative care programs, including Greater Los Angeles VA’s GRECC (Geriatric Research, Education and Clinical Center), Memory Clinic, and HIV/Infectious Disease. She received a VA HSR&D Career Development Award and Diabetes QUERI RRP for research related to degenerative cognitive disorders and individualized care of vulnerable elderly patients. She is actively involved in training psychiatry residents and fellows in geriatric psychiatry. She joins the PADRECC to integrate targeted psychiatric services into the Movement Disorders program, support and build cross-disciplinary education and training of psychiatry and neurology residents and fellows on Movement Disorders, and to support PADRECC’s program development and health services research.

Patricia Pittman, RN, MBA joined the West LA VA team in June 2017 as a full-time Nurse Coordinator. She has a wealth of experience working in the VA and other health systems in areas including bed control, utilization review, and clinical outcomes. She brings an enthusiasm for working with neurologic patients with a prior background coordinating care for the Neuromuscular, ALS and Multiple Sclerosis clinics in the Greater LA Healthcare System.

Dessa Jones, MBA joined the West LA VA team in April 2018 as a full-time Administrative Officer. She replaces Karen Connor, RN, PhD, who retired January 2018. She has a wealth of experience working at the Greater LA Healthcare System in areas including Medical Support Assistant and as an Administrative Officer of the Day. She brings an enthusiasm for working with our Veterans. We are happy to welcome her to the team!

The West LA VA Neurosurgery department also recruited a new functional neurosurgeon, Dr. Ausaf Bari, MD, PhD, who joined Dr. Jean-Philippe Langevin in July 2016 providing surgical treatments for patients with movement disorders. Dr. Bari completed his fellowship training in Toronto with Dr. Andres Lozano, where he studied the relationship between the motor and reward systems of the brain, and the use of deep brain stimulation (DBS) to modify and enhance them.

NeuroPharmacy Pilot Program:
In collaboration with Sunita Dergalust, PharmD, who is the only pharmacist within the VA system that specializes in Neurology, we are integrating specialized pharmacy care in the PADRECC at the West LA VA. Patient records are reviewed and progress notes are entered indicating if a patient is compliant in refilling Movement Disorders related medications. If compliance is not met, the patient will receive a call from a pharmacy resident to obtain a more detailed account of how they are taking their medications, and assess for any barriers or concerns. Patients are asked to bring their medications to each appointment and a pharmacy resident counsels the patient, prior to checking out from their appointment, to provide education and ensure they are taking their medication as prescribed.

San Diego Healthcare System
Dr. Stephanie Lessig and Dr. Fatta Nahab serve as Attendings at the weekly Movement Disorder Clinics and monthly Parkinson’s Multidisciplinary Clinics at the San Diego VA Medical Center- La Jolla. The Neurology Clinic visits join neurology, nurse care manager, cognitive, speech therapy, pharmacy services into one clinic visit. Movement Disorder fellows and Neurology residents of the University of California, San Diego evaluate and treat patients at each Clinic visit. Nurse Care Manager, Marcy Tichacek, APRN, sees patients at clinic visits and follows patient progress and facilitates care by phone between appointments.

Drs. Stephanie Lessig and Fatta Nahab present an annual PD patient symposium, as well as an annual provider symposium directed at non-movement disorder providers such as primary care physicians and nurse practitioners.

Dr. Stephanie Lessig is the site Co-Principal Investigator at UCSD for the nationally recognized PPMI study by the Michael J Fox Foundation that targets newly diagnosed Parkinson’s patients throughout the community, including the VA. Dr. Fatta Nahab served as the site Primary Investigator for the SYNAPSE Study for evaluation of a new drug in treating Parkinson’s Disease Dementia.
## PADRECC National Directory

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<tr>
<th>Center</th>
<th>Medical Center</th>
<th>City, State</th>
<th>Director</th>
<th>Telephone</th>
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<tbody>
<tr>
<td>Houston</td>
<td>Michael E. DeBakey VAMC</td>
<td>Houston, TX</td>
<td>Aliya I. Sarwar, MD</td>
<td>713-794-7841</td>
</tr>
<tr>
<td>Southwest</td>
<td>West Los Angeles VAMC</td>
<td>Los Angeles, CA</td>
<td>Indu Subramanian, MD</td>
<td>310-478-3711 ext. 48001</td>
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<tr>
<td>Philadelphia</td>
<td>Corporal Michael J. Crescenz VAMC</td>
<td>Philadelphia, PA</td>
<td>John Duda, MD</td>
<td>215-823-5934 or toll free 888-959-2323</td>
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<tr>
<td>Southeast</td>
<td>Hunter Holmes McGuire VAMC</td>
<td>Richmond, VA</td>
<td>Jessica B. Lehosit, DO</td>
<td>804-675-5931 or toll free 800-784-8381 ext 5931</td>
</tr>
<tr>
<td>San Francisco</td>
<td>San Francisco VAMC</td>
<td>San Francisco, CA</td>
<td>Caroline Tanner, MD</td>
<td>415-379-5530</td>
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![PADRECC Service Areas Map](image-url)

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