FTD DISORDERS REGISTRY®

The VOICE of FTD

WINTER 2019

Meet Dr. Christine M. Walsh

Assistant Professor of Neurology at the University of California, San Francisco

Christine M. Walsh, Ph.D., assistant professor of neurology at the University of California, San Francisco (UCSF) uses a variety of behavioral and neuroimaging techniques in studying sleep in both healthy older adults and individuals with neurodegenerative disease, in particular progressive supranuclear palsy (PSP). Currently she serves with the UCSF's Memory and Aging Center within the Weill Institute for Neurosciences.

FIRST STEPS TO RESEARCH PATH

A grandfather diagnosed with Parkinson's Disease and an interest in studying the brain led Dr. Christine Walsh down a research path that began with learning and memory, drifted into brain modification, and recently merged with sleep patterns.

"In college this was interesting, and I thought, 'I want to try and make a difference with what I do,' " she said.

Dr. Walsh received her BA degree in physiology from Trinity College Dublin, University College Dublin in Ireland. Then she completed her doctoral work at the University of Michigan studying the effects of REM sleep modulation on learning and memory. She also has studied the neural correlates of cognitive aging.

"For my undergrad thesis I focused on inflammatory markers and how to regulate those in light of learning and memory," she explained. "Then for my graduate work I took a two-fold approach where I was working with older adults and how aging affected their skill acquisition, their memory, and their learning ability, both spatial and sequence learning. I jumped into sleep to try and understand how sleep modifies our ability to learn and change what we've learned as well. Once you've learned something, what does your memory look like and how do you switch it?"

An ah-ha moment came while Dr. Walsh was attending an aging conference and noted that the graphs being shown on cognitive aging were similar to those she had seen at a different conference talking about cognition in sleep deprived young adults.

MEMORY, AGING & SLEEP

In 2011 Dr. Walsh joined the UCSF Memory and Aging Center where she has been studying sleep in both healthy older adults and in individuals with neurodegenerative diseases. The neuroscientist is particularly interested in the relationship between sleep disturbance and cognitive decline.

"I started out trying to understand habitual sleep patterns in healthy older adults and how that related to their cognition. After only a few months, I had a meeting with Dr. Bruce Miller, and we started talking about

Continued on Page 2

FTD Disorders Registry LLC
637 Carolina Street
San Francisco, CA 94107

www.facebook.com/EndFTDregistry
@EndFTDregistry
youtube.com/channel/UCQU8ZEx-eueiDPLIFXzfhPQ
www.linkedin.com/company/ftd-disorders-registry

Continued from Page 1

progressive supranuclear palsy because the brain areas that are earliest affected in PSP are the same brain regions that regulate the brain wake-on system," she said.

After that conversation, she took her first steps into the world of progressive supranuclear palsy, a rare brain disorder that affects movement, control of balance and walking (a person's gait), speech, swallowing, vision, mood and behavior, and thinking. The disease results from damage to nerve cells in the brain.

According to the National Institute of Neurological Disorders & Stroke (NINDS), this disorder's long name indicates that the disease worsens (progressive) and causes weakness (palsy) by damaging certain parts of the brain above nerve cell clusters called nuclei (supranuclear). In particular, these nuclei control eye movements. A telltale sign of this disease occurs when someone is unable to aim and move their eyes properly.

PSP is considered a tauopathy. Tauopathies are a group of progressive neurodegenerative disorders that are defined by the presence of tau protein aggregates in the brain. Tau can form tangles in neurons in the brain and leads to neurodegenerative disorders that also includes Alzheimer's disease and more recently, Parkinson's disease.

SLEEP & PSP

Dr. Walsh has collaborated with several other researchers as they seek to understand brainstem nuclei and how they affect sleep in person's with PSP as well as sleep and rest activity rhythms in those with PSP compared to healthy older adults.

"We also started looking at corticobasal syndrome (CBS), another tauopathy, to try to understand whether the sleep associations that we're seeing in PSP sleep deficits are specific to PSP or is it a factor of the presence of the tauopathy?" she said. "We use the CBS or CBD cohort to help us understand what is specific to PSP."

This past summer Dr. Walsh said they added comparing the sleep of people affected by chronic traumatic encephalopathy (CTE), a progressive degenerative disease of the brain found in people with a history of repetitive brain trauma (including athletes).

Research has shown that sleep loss increases amyloid in the system and increased amyloid poses greater sleep disruption. In addition, recent studies have confirmed an association between tau and sleep.

"Now at the Memory and Aging Center and throughout UCSF's Parkinson's Spectrum Disease Center we are collecting sleep measures in those individuals" with Parkinsonisms, the neuroscientist said.

"I've looped back to my original reasons for getting into research. Soon we will be able to start seeing how sleep in PSP differs from Parkinson's since people with PSP are often first misdiagnosed with it," Dr. Walsh noted. "We may be able to find a sleep difference that could help identify if an individuals who is initially diagnosed with Parkinson's more likely has early PSP."

A new study, on which Dr. Walsh is a co-investigator, is the Treatment in Disturbed Sleep in persons with PSP. This is a remote, six-week clinical trial sponsored by UCSF where researchers hope to answer the question: "Can We Improve Sleep in PSP?"

"Our hope is to improve sleep for the participant, and in turn for the caregiver too. Maybe by improving sleep, we can also improve general wellbeing, improve

Continued on Page 3

FTD Disorders Registry LLC
637 Carolina Street
San Francisco, CA 94107

www.facebook.com/EndFTDregistry
@EndFTDregistry
youtube.com/channel/UCQU8ZEx-eueiDPLIFXzfhPQ
www.linkedin.com/company/ftd-disorders-registry

Continued from Page 2

some of the global effects of this disease, and we'll see stability in disease symptoms," she said.

READ MORE ABOUT DISTURBED SLEEP IN PSP STUDY

Dr. Walsh said that a benefit to working in the sleep field is how easy it is for people to relate to the research.

"When I'm giving a talk at a conference and I'm talking about sleep deprivation or just how little sleep people with PSP are getting, people can instantly relate to that," she said. "Perhaps they're not sleeping well or they're in a novel environment. The hotel's making all kinds of noises, or they've been socializing too much, or they're in a time zone change. A nice part about researching sleep is that you just start talking and people instantly are like 'Yeah, I know, this is pretty awful.' "

LIFE & DREAMS

So how does a sleep researcher sleep at night herself? Like most moms with youngsters, "Not well," she said as she laughed. "I've never been a great sleeper, but I also have three kids under the age of 5, so I've been sleep deprived for five years. So my tau and amyloid are just escalating higher and higher."

Before children Dr. Walsh estimated that she slept six to seven hours per night, less depending on deadlines for grants or the phase of graduate school she was in and the work that she needed to complete.

Her grandfather is the only relative to receive a formal diagnosis of Parkinson's, she said. It is unclear how environmental factors affect the risk for the disease, and Dr. Walsh's grandfather worked in the printing industry where trichloroethylene (TCE) used in the inks has been linked to Parkinson's Disease.

This sleep researcher is hoping that the results of this clinical trial will make a difference for persons with PSP, their families, and their caregivers.

"I'm starting to live some of my dreams. I would love that in helping sleep that we can slow down some aspects of the disease and maybe just maintain someone's quality of life," she said. "Even if someone is waking up less at night, it means that the caregiver is waking up less at night so it can improve the caregiver's resilience and health."

Caregivers are often tired and distraught dealing night and day with the person affected by PSP. To improve caregivers' sleep would mean that outcomes later in their lives might be better and perhaps their relationship with their loved one could improve.

"Even beyond that, if we could try and track how sleep changes throughout disease progression or maybe there's something that can help identify or be a stepping stone in identifying some of the early characteristic markers of these diseases that we can say, 'Oh, hold on, this person is more like _____. Let's try them on this medication that could give them a substantially longer and healthier life.'

"They are lofty goals," Dr. Walsh said, "but some of it may be attainable."

Perhaps her dreams will come true.

ACHIEVEMENTS

As a neuroscientist, Dr. Walsh's involvement in clinic is limited, but she will assist as needed with neuropsychological testing in the UCSF's Memory & Aging Center's clinic. In addition, she is a certified psychometric rater and has served at least six clinical trials. She also oversees and administers actigraphy sleep and circadian measures for two of these clinical trials.

She has been a member of the American Academy of Neurology, the Sleep Research Society, the Cognitive Neuroscience Society, and the Society for Neuroscience.

Dr. Walsh received the UCSF's Faculty Enrichment Award for Seminar Series Grant in 2018. She has re-

Continued on Page 4

FTD Disorders Registry LLC
637 Carolina Street
San Francisco, CA 94107

www.facebook.com/EndFTDregistry
@EndFTDregistry
youtube.com/channel/UCQU8ZEx-eueiDPLIFXzfhPQ
www.linkedin.com/company/ftd-disorders-registry

Continued from Page 3

ceived travel and training fellowships for the Alzheimer's Association International Conference and for Blue Cross Blue Shield of Michigan

She has presented numerous times at conferences across the United States. A short list of recent publications that discuss these revelations about sleep and PSP, which Dr. Walsh has co-authored, include:

- "The role of co-neurotransmitters in sleep and wake regulation" (2019 - Oh J, Petersen C, Walsh CM, Bittencourt JC, Neylan TC, Grinberg LT)
- "Selective Vulnerability of Brainstem Nuclei in Distinct Tauopathies: A Postmortem Study" (2018 - Eser RA, Ehrenberg AJ, Petersen C, Dunlop S, Mejia MB, Suemoto CK, Walsh CM, Rajana H, Oh J, Theofilas P, Seeley WW, Miller BL, Neylan TC, Heinsen H, Grinberg LT)
- "Sleepless Night and Day, the Plight of Progressive Supranuclear Palsy" (2017 - Walsh CM, Ruoff L, Walker K, Emery A, Varbel J, Karageorgiou E, Luong PN, Mance I, Heuer HW, Boxer AL, Grinberg LT, Kramer JH, Miller BL, Neylan TC)
- "Rest-activity rhythm disruption in progressive supranuclear palsy" (2016 - Walsh CM, Ruoff L, Varbel J, Walker K, Grinberg LT, Boxer AL, Kramer JH, Miller BL, Neylan TC)

Dr. Walsh has mentored individuals at various stages of their education, ranging from high school students, to research volunteers, research assistants, post-docs, and even junior faculty. Her research mentorship has focused on sleep and circadian rhythms, with some emphasis on cognitive aging and psychometric rating in clinical trials.

The overarching goal of Dr. Walsh's research is to understand how sleep and circadian rhythms affect healthy aging and neurodegenerative disease and are associated with the trajectory of both healthy aging and neurodegenerative disease. She has focused on the path of studying PSP and neurodegenerative diseases through her sleep research.

"If this trial is successful in its running, and we might not see any changes at all, but if there is, then we might be able to make a difference in our specific cohorts sooner," Dr. Walsh said.

READ MORE ABOUT TREATING DISTURBED SLEEP IN PSP STUDY

Join the Registry.
Tell Your Story.
Advance the Science.

"Together, we can make a difference!"

FTD Disorders Registry LLC
637 Carolina Street
San Francisco, CA 94107