



**Brain Support Network**

## **Conference Notes**

### **PSP/CBD Research Update and Practical Conference**

**Saturday, October 28, 2017**

**Crowne Plaza Hotel in Foster City, California**

**Hosted by Brain Support Network**

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These notes were prepared for Brain Support Network by medical writer Alexandra Aszklar who attended the conference. Notes are organized chronologically, by agenda speaker.

## **Advances in Therapeutic Development for CBD & PSP**

**Adam Boxer, MD, UCSF MAC**

### Clinical Research Updates

- There are some treatments being tested in patients that really have a chance to make a difference
- Can ultimately present us with a standard treatment in the long run

### Advancements in PSP publishing's

- Multidisciplinary intensive rehab therapy (MIRT)
  - Rehab in PSP is extremely helpful
  - Improvements that people saw over a month of intensive rehab was greater than any drug anyone has ever tried
- Tau Therapeutic Targets
  - We don't know exactly why, but in PSP & CBD, the tau protein has a large part in these diseases
  - Chemistry of tau protein is being researched more
  - Most advance testing are therapies that block the spread of abnormal forms of the tau protein, from one nerve cell to another.
    - Think that antibodies may be of help in blocking this spread

### Current clinical PSP Therapies

- Microtubule stabilizing agents (Epothilone, Davuntide, Abeotaxane)
- Post-translational modification/aggregation (Methylene blue, Tideglusib, O-glc-NACase inhibitors, Salsalate)
- Anti-sense oligonucleotides
  - Immunotherapies to tau or phosphor-tau (mAbs, active vaccines)
- Other approaches
  - Young plasma infusions
  - Hypnotics (Suvorexant and Zolpidem) (sleep medicines)

### Challenges for PSP therapeutic development

- Late diagnosis
- Clinical heterogeneity (need a tool to measure the effects of the drug for people with different types of symptoms)
- Rare disease (are there enough patients?)
- Narrow pipeline (we need more drugs to test)
  - Richardson's (PSP-RS/NINDS-SPSP) Most clinical trials formulate around this form of PSP.
  - Other variants of this are PSP, PSP-P, PSP-CBS, PSP-SL, and PSP-F

- If we can diagnose people reliably during psychiatric and earlier phases, we can be more certain on how to treat
- Treat people that can benefit from early treatment, and detect people very early. First symptom might be a single fall, (suggestive of PSP), but what we want to do is get to test clinical trials at this stage, or even before. (Prevention trials)
- Looking at different features of the disease within different people, looking at eye movement, falls, movement capabilities, behavior, language, and cognitive function. By rating people on each different domains, we think we can detect PSP better and diagnose people easier
- ARTFL research, LEFFTDM, 4RTNI (Clinical research networks) are recruiting patients all over the country. (4 in California). Recruiting about 900 people, goal is about 1500 people. Studying people to develop new tools to measure disease progression.

## Tau PET Imaging in Corticobasal Syndrome

*Richard Tsai, MD, UCSF MAC*

### PET

- Pet scans are useful in helping identify the underlying pathologic protein in dementia
- Inject a tracer that can track different proteins in your brain (attaches, gives off a signal, and you can see where that signal is in your brain)
- B-amyloid PET imaging has altered the diagnostic and clinical trials landscape in Alzheimer's
- More and more new investigational drugs are targeting tau.
- F-AV-1451 development in Alzheimer's
  - Initially developed to study tau in Alzheimer's
  - Actually working well in identifying location and severity of Alzheimer's disease tau
  - The tau protein in CBD is different than Alzheimer's tau
  - Hard to predict what the underlying pathology is in CBD
    - Can be associated with CBD, PSP, AD, TDP-42, and a mix of the above
- F-AV-1451 in Corticobasal syndrome
  - 3 Different types coming up
    - Different levels of protein build up
    - Took all the scans for CBD patients, about half have PSP/tau pathology
  - Can a tau pet measure how severe your disease is?
    - Signal strength correlates with motor symptoms severity
  - Does FAV1451 actually bind to CBD-tau?
    - Not sure yet, but there have only been two patient studies
    - Areas with high populations of tau seen in the autopsy are often associated with areas associated with CBS/CBD
  - Trouble with nonspecific binding – not exactly sure what it's binding to, so we can't be sure that it is 100% accurate. There are a lot of nonspecific signals in neurodegenerative syndromes that are not expected to have tau
    - More work needs to be done...
    - More imaging needed in autopsy cases to be sure

## **FTD Disorders Registry: A Patient & Caregiver Registry**

***Dianna Wheaton, MS, PhD, CHES, FTD Registry***

FTD Disorders Registry – A patient and caregiver registry to advance science

- Secure online database designed to be the home of all individuals wishing to participate in FTD research
- Community where you can share your experience of FTD to help us understand these diseases better and support the development of new treatments
- Fully independent entity with the patient/caregiver registry as a sole non profit mission
  - Funded by grants
- Contact & Research registry (Restricted to US & Canada)
  - Have access to information updates and emails
  - Focused to help do outcome research and support clinical trial and research study recruitment
  - Data collection tool uses surveys and questionnaires that are administered online, 3 intake surveys (demographics, disease impact, and research readiness)
  - Client partner surveys are also administered (ARTFL clinical network)
- Why join?
  - Your experience can improve our knowledge of FTD, impact care, and help others
  - Participating in research surveys will provide data to advance the science
  - The registry will be the go-to site to recruit for FTD clinical trials
- Who can join?
  - Persons impacted by any FTD disorders
  - Half enrollees are spouse/caregiver/friends
- What can we do with the data?
  - Tabulate who, where, and how many
  - Build a clearer picture of the impact of FTD from a patient, caregiver, and family perspective
  - Assess research study/clinical trial feasibility
  - Use the data to raise awareness, and advance research and facilitate more meaningful connections

## **A Cluster of PSP in Northern France: Is This the Key?**

**Larry Golbe, MD, Rutgers Robert Wood Johnson**

There is a cluster of people with PSP in Northern France

- Dominique Caparros-Lefebvre, MD (Wattrelos)
- Arrived in 2005, had done research in PSP before that, noticed there were a lot more people there with PSP than expected
- Incidence of PSP in Wattrelos and nearby towns
- 98 patients studied, symptom onset measured
- Discovered that it took about 3-4 years for someone to reach medical attention after their symptoms arose
- PSP incidence over the 5 years – 27 cases with onset during those 5 years (A lot!)
- PSP incidence measured in Olmsted County, MN and estimated in London, Newcastle, and Yonago 1.1/100,000
- Population of Wattrelos (2007) 42,077 (i.e., there was a high number of patients there with PSP)
- Large piles of metal ore behind the canal/factories, all patients with PSP diagnosed lived within very close proximity to this location
- Another factory that used dyes made from arsenical are there too
- Only 2 things that differentiated these patients from PSP in general, and that is that their onset age was a bit later, more likely to lose sense of smell, and ration of classic Richards to less common PSP was reverse to what it is with regular PSP
- No molecular difference
- Could this be a genetic founder effect? No. None of their families were related to each other as far as they knew
- Are metals causing this? People would grow vegetables in their yards with this. Metals such as arsenic, nickel, and chromium. Vegetables have a high percentage of these metals, so yes there is a very good chance that these metals played a part in this disease.
- Analyzing samples of metals, trying to compare addresses of where people worked/lived, trying to collect blood/urine/household dust/nail to test, genetic analysis, genetic testing, and testing for PSP
- Trying to test which metals are most toxic (PSP wise)

## Understanding the Role of Polyamines During Tauopathies

*Daniel Lee, PhD, University of South Florida, Tampa*

### Tau Filaments

- Stabilizes structures called microtubules which support neuronal function
- Tau can misfold, fall off of microtubules, and can clump or aggregate that are hard for the cell to digest
- Tau therapies approaches include trying to stabilize and trying to decrease clumping
- Polyamines Increase protein clearance, regulate genes, promote cell growth, and regulate neuronal activity and stability

### What are polyamines?

- We get them from plants and fruits, and our body synthesizes them as well
- Goes through a process that makes little molecules (polyamines)
- Our body has a very good way of regulating these levels of polyamines.
  - Converts it to an inactive form and can either be removed from the cell, or be recycled back in the body
- Often times, there's an excess of these inactive tau products

### Trying to understand why this is happening...

- How can we decrease the amount of inactive tau and boost amount of active
- Tau Aggregation Assay
- Microtubule Polymerization Assay
  - When you add polyamines to the system, you decrease the clumping
  - If you add inactive products, you promote more tau clumping

### Polyamines decrease tau aggregation and promote microtubule

### SRM-Gene therapy –memory recall

- Make proteins and overexpress the enzymes that promote production of tau
  - Tested on mice, inject right into the brain, testing memory
  - Mice with tau learn much slower than mice with boosted polyamines
  - Leads us to think that we need to boost polyamines

### Using in vivo microdialysis to measure tau

- Samples the environment of the brain, so we're able to see what's in there
- Can get real time measurements of how tau is moving in the brain
- During activity they are being released, and that doesn't seem to be a good thing
- Can be used as a good therapeutic for future targets

## **Panel of Previous Five Speakers**

***Moderated by Alex Klein, PhD, CurePSP***

### **For Dr. Larry Golbe:**

**Q:** For the cluster in France, did they really exclude any genetic causes for this cluster?

**A:** Can't say they excluded it, but hopes to collect DNA from all the people and get genetic commonalities between them. It is hard to gather information from interviewing patients, and none new of any relatives with PSP.

**Q:** There are geographical areas with high clusters in France, but are there anywhere else?

**A:** We don't know of any clear-cut PSP clusters anywhere else, but there is one in Guadalupe (not PSP). Has heard of other smaller clusters in the US that are of mining/rural areas. Can't confirm that these are statistically significant.

**Q:** What is the difference between PSP Richardson's and PSP Parkinson's?

**A:** PSP Richardson's is somewhere between 40-50% of all PSP. Classic description where eye movement problems occur in the middle, falls are the earliest signs, person doesn't respond much to Levodopa. PSP Parkinism is 30-40%, usually respond to Levodopa, and don't develop eye movement problems and falls until later. More tremors, and less likely to develop cognitive problems.

**Q:** Are there any other environmental risk factors for PSP? What does this mean for us?

**A:** People with PSP are less likely to have advanced education; this could be due to many different things. People who have less education are more likely to have a job that exposes them to more toxins, or makes them more likely to live in rural places.

### **For Dr. Adam Boxer:**

**Q:** PSP sleep symptoms – what are they and what trials are underway?

**A:** People with PSP tend to not sleep very well at night, don't get restful (REM) sleep. Normally, that would make people sleepy the next day, but people with PSP who don't sleep well are not that sleepy the next day, and can't fall asleep the next day either. Many different sleep medicines that are approved/marketed already. Trying to get to know if there is one sleep medication that is better for people with PSP.

**Q:** Salsalate vs. Aspirin – Which is better?

**A:** It's been determined that on the tau protein there's a chemical modification that makes it stickier and more toxic to cells. Salsalate is an inhibitor of the protein that modifies tau groups. Aspirin doesn't do this and most likely doesn't help much.

**Q:** Regarding the rehab study – what is the exercise regimen?

**A:** Don't remember but it was very intensive multi-disciplinary, in-patient program, over the span of two months. Journal article can be found here:

<http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0170927>

**For Dr. Richard Tsai:**

**Q:** Regarding identifying PSP early without symptoms – how is this done?

**A:** Would have to rely on biomarkers (imaging, measuring proteins in the blood or CSF). Biomarkers help detect diseases early, and looking at donated spinal fluid is very helpful in finding protein abnormalities in both symptomatic and asymptomatic patients.

**Q:** The tracer you mentioned is radioactive – can you comment on its level of danger?

**A:** Yes, it is usually made in a lab, but the radioactivity is very low and doesn't usually last for very long. The strength is much lower, and the increased risk for cancer is <1%.

**For Dr. Dianna Wheaton:**

**Q:** 50/50 split between contact and research registry – is there an automatic flow for what you are contacted for?

**A:** Yes, you will get access for trials and general access, but less targeted contact if you were participating in the research registry. Additional consent to participate in research allows them to collect specific information that allows them to send the targeted email that help determine more. (if you want more interaction, you have to consent to participate in research.)

**For Dr. Daniel Lee**

**Q:** Any food science in this?

**A:** Not a lot of research on polyamines and neurodegenerative diseases as far as tau. Typically, you get a lot of polyamines in your diet (plants, fruits, salads etc..) The problem is that the pathway of metabolism becomes disrupted during this disease, but they are not quite sure why.

## Removing Tau Protein Build-Up in Your Brain Cells

*Haung (Ho) Yu, PhD, Columbia*

Why does tau build up in your neurons in aging diseases?

- Tau was originally described as helping to facilitate function, but sometimes it gets disrupted in your brain cells and disrupts multiple types
- We want to see if we can reverse this
- With aging and disease, the regulation of these systems decline, we are trying to figure out why, and how we can boost them

What is autophagy? (Cell's way of self-eating) and why is it an important in removing "garbaging" cells?

- Proteasome – removes unfolded soluble proteins
  - Break down the cells so that they can be rebuilt
  - Identifying where this takes place is very important,
- Autophagy – remove aggregates following autophagic induction
- Lysosome – degrade most proteins – lysosomal acidification

Autophagy – the good and the bad

- In early stage diseases, the "garbage" collecting isn't happening fast enough
- Later on in disease, these processes become even more destructive, so we want to improve the pathways or the entry to recycling center
- If the "recycling center" itself is disrupted (in most neurodegenerative diseases), that can cause problems too

Can you see clearance of garbage in imaging and where it builds up, and are there patterns?

- Yes, some transport is probably being taken place but not efficiently
- Want to improve the entire process, most treatments work on early on disease, but with these diseases the onset happens quickly.

Goal is the bring the deliverers and recycling centers together

Does dependent reduction in aggregated and soluble tau levels matter?

- Trying to identify potential drugs that can enter the brain and start to treat the diseases
- Challenge is, can we improve the drug to enter the brain and last longer?

## **Progress Toward an Animal Model of PSP**

**Stewart Clark, PhD, University of Buffalo**

Having animal models in the lab – new model of PSP

Trying to find out where Tau's hideout is—Why do we need an Animal Model?

- To help reverse or stop the protein aggregation
- To improve longevity, and QOL
- Without a model specific to PSP, we cant look for drugs to help with these symptoms

Progressive model – take a healthy animal and “give them PSP”

What should this model look like?

- Postmortem brain characteristics
  - Pedunculo-pontine Tegmentum loss (pptg)
  - Ventricular enlargement
  - Substantia nigra loss
  - Abnormal protein aggregates
- Behavioral
  - Startle deficits
  - Motor deficits
  - Cognitive deficits

Hypothesized spread of tau in PSP

- As the disease progresses, we get higher concentrations in more areas
- We want to control the amount of areas it spreads to

Blunts Acoustic Startle Response (Multiple tests performed on the rats)

- When they are exposed to repeated loud stimulation, PSP patients seemed not to jump
  - Rats with this lesion (neurons remove) have different behaviors that are abnormal
- Substantia Nigra Loss
  - Overlap with Parkinson's
  - Overtime, pptg lesions produce a significant loss of SN neurons. Although at 14 months post lesion, the loss is not to the degree seen in PSP.

Still in the process of looking for cognitive deficits in animal models

- Produce abnormal tau and its spread
- Accelerate the progression of deficits

## **Cognitive, Behavioral, and Functional Aspects of PSP**

***Adam Gerstenecker, PhD, University of Alabama at Birmingham***

### Cognition in PSP

- #1 impairment is executive dysfunction which regulates things like multitasking, planning, organizing, etc., almost 75% PSP patients have at least one test impaired
- Executive dysfunction is major neurocognitive impairment even at early disease stage
- Relatively strong short and long delayed free recall and little additional benefit from cueing

### Behavioral abnormalities (can occur at any stage)

- Apathy and indifference were one of the biggest findings, similar with depression, and sleep/nighttime behaviors, eating behaviors, agitation, irritability, and disinhibition

### Education about apathy is important

- Particularly distressing for family members and caregivers and lead to symptoms being misinterpreted as depression
- It's depression, it's more "not caring" – it's being wrongly prescribed
- Families may believe that the patient is not as interested in family
- Depression was high in comparison to prior estimates
- There aren't that many depression studies in PSP

### Depression may not be solely a function of brain changes, but also related to functional consequences (what the disease is doing to a person)

- Therapy and behavior activation may be able to help

### Functional ability

- 2 types – basic daily activities of daily living and instrumental activities of daily living
- ADL – related to self care
- IADL – related to autonomy and independence (financial management, medications, etc.)

### Assessing functional ability in PSP

- Performance-based and caregiver-based reports
- Overall, over 80% of sample had significant decline in functional mobility, mostly in medical decision making and financial decision making (highly susceptible to financial fraud/scams) and inability to call 911
- Caregiver report was not significantly correlated with any IADL measure or with cognitive performance
- Found that caregivers were not good at quantifying level of daily functioning in patients
  - Caregivers need education



## What we Know and Don't Know About PSP & CBD Genetics

*Gerard Schellenberg, PhD, Penn Neurodegeneration Genomics Center*

### Human disease genetics

- Study human disease mechanisms directly in humans
- Prediction – Because there's no treatment, we can use this when we have preventative therapies
- Mechanism
- Drug targets – Going from a gene to a drug target (finding a cure)

### Does this work?

- PCSK9 drug for CAD → protective loss-of-function mutations
- If we reduce PCSK9, we reduce risk
- Approved drug came from this trial
- Can also help with preventative drugs in the future

### MAPTau mutations

- If you biochemically change tau, you make tangles

### PSP GWAS –

- Effects 4 genes including MAPT, MOBP, EIF2AK3, and STX6
- MAPT encodes tau – protein in neurofibrillary tangles

### PSP genetics

- GWAS array data
- Whole exome sequence data
- Whole genome sequence data
- Imputed genotypes

Genetic testing is extremely expensive

## **Panel of Previous Four Speakers**

***Moderated by Alex Klein, PhD, CurePSP***

### **For Dr. Haung (Ho) Yu:**

**Q:** Is there actually a natural way of boosting your defense mechanism/tau count?

**A:** A type of sugar has been tested to help, but you have to take it in very high amounts. Creating more tau may not help in the long run, so it may actually be more harmful.

**Q:** Are you trying to discover some sort of pill you take once a day for the long run in parallel to other therapy? (to remove “garbage”)

**A:** The ultimate goal is to create a drug that an individual can take to help remove the “garbage”. Some of the early stages in drug discovery are being done now.

### **For Dr. Gerard Schellenberg:**

**Q:** Can you comment again on the risk of passing PSP on to the next generation?

**A:** There are mutations that are 50% chance of passing it on in tau, but those are extraordinarily rare unless you have a very dense family history. They are so rare there is no percent on how often they occur. Does not get passed on generation to generation.

**Q:** You mentioned 2,000 genomes are being analyzed, can people participate in this?

**A:** Most of the 2,000 are autopsy proven cases. PSP is a pretty solid diagnosis, but for now (and when there's more \$), it is mostly autopsy. Always taking more volunteers for genetic testing. Very important to contact experts and genetic counselors. I strongly recommend you do not go with any full-profit providers. It is very important to get face-to-face genetic counseling. Many big centers offer it. If you go to genetic counseling counselors association, they provide a founder where you can type in your zip code and get an analysis. For research it is so important.

### **For Dr. Stewart Clark:**

**Q:** When you develop these animal models, have you already tested the drugs being used in them?

**A:** The ultimate goal is to test drugs. We've done some tentative work with the animal model. Actively in the process of selecting other drug candidates, but no news currently.

**Q:** Can you speak on using animal models vs. humans?

**A:** It is so important to have actual brains to do research on, instead of cultures in a tray. However I do have a deep appreciation for animals that are being used, because it is so important for research.

## **Resilience and Coping Strategies in the Face of PSP & CBD**

***Donna Schempp, LCSW***

### Resilience

- Learning to cope with stress and adversity and sustain well-being
- The act of rebounding or springing back after being stretched or pressed or recovering strength, spirit, and good humor
  - Not just surviving

### What works

- You can modify the negative effects of adverse life situations
- Relationships that provide care, support, love trust, and encouragement
- Capacity to make realistic plans, having self confidence and a positive self image, developing communication skills, and the capacity to manage strong feelings and impulses
- Making realistic plans – you can't do this 24/7, you need time away so you can comeback refreshed and energetic

Caregivers – you cant get through this alone.

### Success comes from

- Feeling competent when feeling under stress, using problem solving skills
- Support from family, friends, faith, community, neighbors, and professionals
- Using community resources and professional counselors
- The ability to cope with stress without hurting yourself
- Believe that there is something one can do to manage your feelings and cope
- Not keeping secrets
- Take care of yourself so you can take good care of someone else

### Ways to build resilience

- Avoid seeing illness or stressful events as unbearable problems
- Accept circumstances that cant be changed
- Develop realistic goals and move towards them
- Take decisive actions in adverse situations
- Look for opportunities on self discovery after struggling with loss
- Develop self confidence, even though you are not perfect
- Keep a long term perspective and consider stressful events in a broader context, particularly day to day stuff
- Maintain a hopefully outlook, optimism helps
- Take care of your mind and body exercise, eat right, sleep, laugh
- Pay attention to your own needs and feelings

- Have a sense of purpose/meaning
- Accept your own strengths and weaknesses
- Sense of control and power/ability to affect change

#### Grief and Loss

- Accept brief episodes of the blues
- Grieving is necessary and important
- Ambiguous loss
  - Loss of future, who you or someone else was, relationship as it was, roles, and independence

#### Challenges: Common stressors

- Resistant, angry caregiver, difficult feelings
- Physical care needs
- Change and uncertainty
- Poor/ineffective medical care and money issues
- Legal matters
- A need for a move to more supportive housing
- Care supervision needs
- Life, health, safety concerns

#### Depression

- 50% higher for caregivers than non-caregivers
- Acknowledging that you're depressed is very important

#### Anger

- Frustration is normal, how you express the anger is the biggest issue/point
- Have to learn forgiveness

#### Feelings

- Self monitor your emotions, write about them
- Change negative self talk
  - No one can help me, I can't do it all, it's not fair, etc.

#### Developing a help network: Never pass up an opportunity

- Always accept offers of assistance from family, friends, neighbors, etc.
- Have a mental list of jobs ready
- Ask for help, and receive help when its offered

#### Find out your stress relievers

#### Importance of touch and laughter

## **Holding Steady on Shaky Ground**

***Leslie Wolf, person with CBD (Diagnosed 4 years ago)***

### Timeline

- 2012 – loss of use of left side
- Rotator cuff surgery
- First brain MRI – showing brain shrinkage
- 2013 – at the worst, started seeing every doctor possible
- 2014 – first diagnosis of CBD/CBDS
- Phase 1 trial to treat CBS and PSP
- 2017 – Living on Carbidopa and Levodopa with Entacapone  
5 years and holding steady

### Symptoms

- Clumsiness
- Cant type with left hand
- Holding arm
- Jerkiness
- Slowness of movements
- Stiffness

### Professional Clinical trial volunteer – part of what helps

- Volunteering for every single possible trial
- Done 2 sleep studies

### What's working?

- Studies
- Meds every 3-4 hours
- Working out & water aerobics
- Having my own business
- Supportive husband
- Kids

### What's next?

- Communication is great
- Online program

## **Eight Things we Learned From Jackie's PSP Journey**

***Phil Myers, (former) caregiver to wife with PSP***

8 items we learned from Jackie's PSP journey

1. Get second or third opinions early, especially for unexplained symptoms
2. Don't accept an unconfirmed or non-specific diagnosis. Push to get to a top neurologist preferably a movement disorder specialist
3. Make the significant care decisions early
  - Feeding tubes, DNR, hospitalization or die at home, brain donation
  - Use an advanced health care directive and physicians orders for life sustaining treatment (POLST)
4. Start exercise early and continue exercise as long and as much as possible
5. Make life as normal as possible
6. Check out available clinical trials. [Clinicaltrials.gov](http://Clinicaltrials.gov)
7. As the caregiver or patient, be proactive. Participate in support groups, go to presentations, and do your research online. A big success of the disease is attitude and fighting it.
8. Keep a "binder" of cross doctor communications and researchers, keep things filed safely

## Being (A) Patient With PSP

**Jeanette Brown, MD (retired), person with PSP**

Diagnosed in March 2016

- At UCSF since 1987
- Chair of multiple NIH review committees
  - Director of UCSF women's health clinical research center, Director, specialized center of research, Director of urogynecology, UCSF mentor of the year award 2011

Retirement (shortly after PSP diagnosis)

- No multi-tasking
- Opt for social security benefits
- Move to SF a condo with an elevator near family
- Installed grab bars, had to re-do bathroom to have a walk-in shower

UCSF Memory & Aging

- 3 car accidents in 3 months
- Primary doc sent to neurologist, neurologist sent her to UCSF memory and aging center. Dr. boxer made the diagnosis
- Offered a phase 2 clinical trial which she is involved in now

Current symptoms

- No driving since 2015
- Slow speech, inability to write, down to typing with one finger and lots of mistakes
- Wobbly and must be careful, always tired
- Feels sad, worried, fearful, anxious, powerless, disillusioned, indecisive, incapable

Travel

- Went to Macchu Picchu with brother in January, just returned from Viking river cruise
- Now is the time to go – always travel with assistance at the airport

Lessons Learned

- Travel now or do whatever you want to do
- Enjoy the moment, try not to live your diagnosis, live one day at a time
- Get your finances in order
- Start PT and OT before you really need it
- Prepare your family and yourself for the inevitable decline

Questions?

- Feel free to contact at [brownmdj556@gmail.com](mailto:brownmdj556@gmail.com)
- Started a support group in SF – join us!

- Meet once a month at Café Roma 526 Columbus in North Beach the third Tuesday of the month at 11:30

## **Panel of Previous Four Speakers**

***Moderated by Robin Ketelle, RN, UCSF MAC***

### **For Leslie Wolf:**

**Q:** How do you stay positive?

**A:** You just have to, have a great support network, keep going.

**Q:** Do you have any daily practices?

**A:** No, but I hide it well too, you just keep going. Grit.

**Q:** Leslie what kind of meds do you take?

**A:** I take Nodoz, antidepressant, heartburn, and Cinnamet/Carbidoba. Didn't work for her at first, but now it does and she needs it. She now goes to see someone just to regulate her meds.

**Q:** What is your best hack/tip to function daily?

**A:** Best tip is to "do it now" and ask for help

### **For Phil Myers:**

**Q:** What kinds of things would you record in the binder that you mentioned?

**A:** different reports that you'd get from your doctor, symptoms, what they said, how you should treat them. Get copies of tests. You don't know what might be a factor. You get a lot of information; keep taking it to each doctor.

**A (Leslie):** I take notes on excel or word – when was the last time you got tests, dates, shots, etc. Saves you a lot of time if you can just hand your doctors a piece of paper.

**Q:** Did your children agree with advance care decisions made by your wife?

**A:** Yes, we had a good faith. We were a catholic family, brought all of our four kids together.

**Q:** Did you talk about it just the two of your first?

**A:** Yes, reached the decisions what she wanted, and then got the family together and told them.

### **For Dr. Jeanette Brown:**

**Q:** Do you have swallowing problems?

**A:** I don't, yet. I'm sure I will at some point.

### **For Everyone:**

**Q:** Exercise – what forms are best and how intense

**(Jeanette Brown):** I exercise every day. I joined a senior center in which I do a class. Combination of aerobics and non-aerobics for about an hour a day.

**(Donna Schempp):** For caregivers, anything that moves your body works

**(Phil Myers):** as intense as you can make it (break a sweat for your heart) it's the moving of all the different parts that's important. Whatever you think you might not want to use in the future.

**Q:** When do you decide to tell family members/other people about what's going on?

**Phil Myers:** It's an individual thing, it's very important. And the main thing is to think about it, and remember that when you tell people, it's going to be emotional.

**Jeanette Brown:** I've told everybody and they're fully aware, and it is very individual

**Donna Schempp:** The longer you're a caregiver, the more people disappear. You're not available, diagnosis scares people, you really have to cultivate staying connected. You may have to be the one that does the initial outreach.

**Leslie Wolf:** Only one of my coworkers knows fully. It's very hard not to tell. Tries to push it off as a back problem.

**Q:** Does anyone want to say anything about his or her groups?

**Jeanette Brown:** We've had a couple of meetings and I really enjoy them. Anyone who wants to join in, please do. I was surprised there wasn't one in San Francisco. One person brings her caregiver; otherwise I don't think its necessary to bring caregiver.

**Donna Schempp:** It's good to separate groups, so everyone can feel like they are speaking their minds and wont hurt anyone's feelings

**Leslie Wolf:** Coming to these meetings just helps me see where I'm going to be at and lets me know what to expect and when, and it is so important.

**Q for the mothers:** How do you talk to your children, what's your approach?

**Jeanette Brown:** I don't discuss it very much with my son. He's definitely aware of it, and I think that this will make me talk with him more.

**Leslie Wolf:** Try to explain it, but for mine its not as obvious. Until things get really bad, I don't think it's going to come to reality for them.

**Q:** PSP, first word is progressive. Saw it on one of the slides and part of the progression. How do you deal with the isolation that can come to you with this and how do you still bring meaning to your life?

**Jeanette Brown:** I deal with it with my friends. I continue to go out to dinner and lunch and all of that, and that's' very helpful. But my guess is that they'll tire up eventually.

**Leslie Wolf:** They tell you to reduce the stress, and that's a joke. I've tried to give up a little. Giving in to having help and divvy up responsibilities. You figure out how to divide up, ask for help, and use all the resources you have available.

**Jeanette Brown:** Asking for help is very important, and that's what I do with my friends. I ask them to take me to dinner/lunch and all of that.

**Donna Schempp:** You have to grieve. Just allow yourself to be aware of yourself and your grief.

## Understanding CBS, CBD, and PSP: What Are Tauopathies?

*Sharon Sha, MD, Stanford*

Tau – called tauopathy because there's an abnormal buildup

CBD, FTLD, & PSP – Many diseases are tauopathies

PSP

- Behavior – apathy obsessive/compulsive behaviors, utilization
- Cognitive – executive dysfunction
- Motor – parkinsonism, axial rigidity, postural, instability, bradykinesia, reduced blink
- Language disorders
- Supranuclear gaze palsy

PSP criteria was updated this year

- Sporadic occurrence, age 40 or older at onset, gradual progression of PSP related symptoms
- Core features
  - Oculomotor dysfunction, postural instability, loss of movement, and cognitive dysfunction
- Many symptoms can have underlying PSP pathology

PSP Richardson's syndrome

- Classic symptoms – unexplained falls, unsteady gait, slowness in movements
- Personality changes – apathy or disinhibition
- Cognitive slowing, executive dysfunction (multitasking)
- Slow speech, slurred speech, spastic speech, swallowing problems
- Eye movement problems – slow vertical, difficulty opening eyelids
- Vertical supranuclear gaze palsy – onset variable, decreased velocity

PSP-Corticobasal Syndrome

- Variable combo of
  - Progressive limb rigidity, apraxia, cortical sensory loss (not a primary sensory problem), alien limb (floating limb), bradykinesia (slowness), and unresponsive to levodopa

PSP Speech Language Component

- nfvPPA (nonfluent variant)
- Agrammatism (mainly lacking of function words)
- Effortful, halting speech with inconsistent speech sound errors and distortions (AOS)

PSP Pathology

- Neuronal loss and gliosis
- Hyperphosphorylated MAPT

Corticobasal Syndrome: Patient 1 (58 year old right handed male, 1 year left sided clumsiness)

- Difficulty walking down stairs, now has to hold railing
- 6 months later difficulty with sequence of starting a car
- Handwriting became worse, tremor
- Anxiety

Exam

- Praxis worse on left side, tone increased, cogwheel, coordination worse on left, slow
- Cognitive testing – pretty good overall with minor problems in calculations and copying, but impaired phonemic fluency.

Classic for CBD/CBS

Typical FDG PET and MRI Patterns

- Asymmetric, metabolism is diminished in the same area as atrophy

CBS/CBD can have multiple pathologies

CBS/CBD Degeneration

- Different presenting syndromes can have CBD pathology
  - Behavioral syndrome (FTD), Non-fluent aphasia syndrome, PSP, CBS
- Macroscopic Pathology

Clinical phenotypes of CBD

- Probably CBS
  - Asymmetric limb rigidity or akinesia, limb dystonia, limb myoclonus plus 2 of orobuccal or limb apraxia, cortical sensory deficit, alien limb phenomena
- Possible CBS - may be symmetric
- FBSS
- nfvPPA
- PSPS (PSP Richardson's syndrome)

Patient 2 (70 year old male, 1.5 years progressive motor/cognitive changes)

- Skiing accident with concussion
- Right hand coordination problems, cant write or type
- Speech is slow and slurred
- Memory problems, difficulty with details, planning

Exam

- Memory loss recall 1/5, names 4 F words, eye movements with overshoot, saccadic, slurred speech and slow speech, right hand dystonic with increased tone RUE, RLE

Amyloid PET is suggestive of AD pathology

Looked at ways to predict underlying pathology

End notes

- PSP & CBD can have different clinical presentations

- PSP-RS is the most common and most predicts
- CBS usually indicates CBD but can have alternate pathologies

## Speech, Language, and Swallowing Treatment for PSP & CBD

*Megan DePuy, SLP, private practice, San Mateo*

Why speech therapy?

- Swallowing (dysphagia) speech (dysarthria, dysphonia) language (aphasia)

If you are going to go see a speech therapist...

- Do some research and make sure they have a background in neurological disorders

Swallowing

- Symptoms and challenges
  - Head and neck stiffness can make looking down at a plate challenging
  - Portion control – eating and drinking too quickly, tremor or stiffness interfere with self-feeding
  - Restricted head and neck posture
  - Delayed pharyngeal swallow onset
  - Poor cough
  - Occasional difficulty opening the mouth
  - Swallowing management
  - Evaluation should include both subjective and objective measures
  - Observation of client during a meal
  - Caregiver input about feeding habits and challenges
  - Evaluation techniques
    - Modified barium swallow
    - Fiber optic endoscopic evaluation of swallowing (FEES)

Many people have poor function, and don't know if food or drink are stuck in the wrong place

- Prevention is the easiest treatment – go and see a speech therapist before you even consider you may have difficulty swallowing.

Some slight differences with PSP/CBD

- CBD is unilateral, so sometimes there are strategies a speech therapist can give. If food or liquid is swallowed and there's a unilateral weakness, sometimes say turn head or tuck head to the weak side

Management

- Medical management
  - Medications to control motor symptoms
- Modified Barium swallow/FEES
  - MBE – one is an x-ray of your swallow
  - FEES – looking with a small camera into your vocal chord/throat
  - Both can tell if someone aspirates or penetrates

- Not always able to prevent

Aspiration is not always obvious; the most severe aspiration is often silent.

Speech Challenges – PSP affects muscle strength and coordination

Decreased muscle strength and coordination of the face mouth, tongue and throat can result in:

- Speech deficits – hypokinetic dysarthria – quiet voice and quick pace. Stutter can result from quick pace of speech. Voice quality can become breathy.
- Spastic dysarthria – quiet and strained voice quality with bursts of loud voice caused by stiff muscles.

Motor speech symptoms

- Characterized by hypokinetic and spastic dysarthria, as well as progressive apraxia of speech and oral apraxia
- Progressive non-fluent aphasia
- MSA-A: often ataxic or hypokinetic dysarthria, but may be mixed with spastic
- MSA-C ataxic dysarthria is most often expected, or in combination with spastic

Exercises for swallowing voice and speech

- Tongue
  - Stick tongue out as far as you can. 10 repetitions
  - Move tongue from one corner of your mouth to the other, slowly and in a controlled manner. 10 repetitions
  - Move tongue up and down, touching your top teeth and then bottom teeth. 10 repetitions
  - Touch the roof of your mouth with the tip of your tongue without moving your lower jaw
  - Close your mouth and push your tongue out against the inside of your cheek. Provide resistance with your hand if it is easy. 5 repetitions on each side
  - Move tongue in clockwise motion around upper and then lower teeth keeping your mouth closed. 10 times around. Switch directions.

## **Move It or Lose It: Strategies to Stay Mobile and Stay Safe**

***Erica Pitsch, DPT, UCSF***

### Do's and Don'ts

- Don't lose ground from deconditioning
- Do keep moving and stay safe
- Don't fall
- Do get help
- Exercise!

### Consequences of a sedentary lifestyle

- Decreased endurance, strength, and bone density
- Increased stiffness and risk of medical complications

### Do people with PSP/CBD improve with rehab?

- A four week intensive inpatient program showed improvements in disease severity and gait
- One case study of a person with mixed PSP/CBD reduced falls and preserved ambulation with a walker for 10 years of participation in a group balance class
- Long term rehab is key

### Recovery/Preservation

- Balance programs are effective in improving balance performance, but not incidence of falls in people with Parkinson's
- Any physical therapy is better than nothing

### Exercise Challenges

- The earlier stages of the disease, the more you can do safely
- The uncomfortable truth
  - Balance deficits - worries about the instant fall
  - Cognitive deficits - impaired memory (reminder to take a walk or do exercises)
- BUT people with dementia DO respond to intense exercise

### Activity continuum

- Most safe (& least balance challenging) – sitting exercises, bed exercises
- Least safe (& most balance challenging) – standing exercises, walking, multitasking
- Most important is working on balance or endurance while being safe

### What is the best exercise?

- The one that is safe and challenging for you
- In general, goal directed, FUNctional activities are more motivating
- Music based interventions are showing more potential
  - (Hint: Aretha Franklin and "Uptown Funk" are great for this)

- Movement based video gaming systems like Xbox Kinect may improve function

External focus (outside your body) is better for performance

- If you do the movements without relating them to steps (i.e. the movement you make to shake out a towel) you are more likely to do them correctly.
- Your disease may want you to move slowly. Anytime you can do something that can help you move fast, you're holding on to that movement.

Overcoming Barriers to exercise

- "But I'm not an athlete"
  - You don't have to be an athlete to work out, if you want to keep your muscles, you use them
- "I can't find the time"
  - Put it on your calendar, set an alarm.
- "I have a hard time getting motivated"
  - Try group classes, a personal trainer, get moving with a friend, etc..
- Drive and Dementia

Environmental

- Hazard elimination – how many fall hazards can you think of?
  - Grab bars, raised toilet sets, shower chair, etc..

Physical

- Assistive devices, physical assistance, exercise

Do get help

- Physician clearance, physical therapy, occupational therapy, personal trainer

## Vision Symptoms in PSP & CBD: What Causes Them and What Can be Done?

*Heather Moss, MD, Stanford*

Eye movements are critical to vision

- Coordinated by the brain – how vision gets from the eye back into the brain, and gets interpreted in the brain

Although there can be problems with perception, eye movements are the biggest problem

Vertical gaze palsy in PSP

- The eyes have a problem looking down more so than up
- Not a problem with the eye muscles or nerves, it's a control problem (determined by reflex movements)

Inability to move the eyes can interfere with navigation

- With PSP, your eyes do not look down, but straight ahead
- No ways to make eyes move better, but if you are aware of it, there are tips
- Using head position to compensate for eye movements

Inability to move the eyes can interfere with using glasses

- Bifocal glasses don't work well if you have a vertical gaze problem
- Distance in top, near on bottom
- Need to move your eyes to use them, but moving your head isn't going to be helpful for this, because your glasses will move with you
- Solution: have single distance glasses for near and distance (2 pairs)
  - Then you can position your eye gaze with head movement

Misalignment of eyes causes double vision

- Inability to move the eyes together or apart can lead to double vision
- Normally when you look straight ahead your eyes come together a bit to focus
- If you can't bring eyes together, it creates double vision at near

Divergence insufficiency

- When your eyes are not going apart at distance, then you see double as well

Strategies for treatment of double vision

- Optically align the images by using prisms (prism insert in glasses lens)
- Block one of the images

Trouble moving the eyes affects dynamic eye movements as well

- Saccades – eye movements used to look around at things (looking at 2 things on opposite ends)
- Smooth pursuit – tracking a movement moving across your visual field

Rapid eye movements in PSP and CBD have delayed initiation and fall short of target

- CBS – longer delay time and then quick jump up

- PSP – longer delay and slower movement to get up to target
- Smooth pursuits
  - CBS – slow speed of following target, never reaches, behind
  - PSP – slow speed of following target, never reaches, behind

How does it apply?

- Looking at an object
- Reading
  - Need to move eyes through lines of text

Left to right reading task in person with Parkinson's disease

- With no disease (12 seconds)
- With Parkinson's disease (21 seconds) (another patient took 119 seconds)

Strategies – Trial and Error

- Line guide (isolates lines when reading)
- Font size, spacing (accessibility features)
- Color, contrast
- Audio

Visual perception is also critical to vision

- Glaucoma
- Cataract
- Macular Degeneration

Take home points

- Can't look down?
  - Move head
  - Single vision glasses (not bifocals)
- Double vision?
  - Patch/cover one eye
  - Prism glasses
- Trouble reading?
  - Adjust display
  - Reading guide
- Keep your eyes healthy
- Have the right prescription

**Panel of Previous Four Speakers**

***Moderated by Robin Riddle, CEO, Brain Support Network***

**For Dr. Sharon Sha:**

**Q:** Why do we call PSP & CBD atypical Parkinsonism diseases if they have so many similarities to Alzheimer's diseases?

**A:** Usually Parkinson diseases have certain pathology causing the disease and that a certain type of medication helps improve those motor symptoms. People might say Parkinsonism to imply symptoms that you see. PD & LB diseases have a different pathology because they have a similar one as well.

**Q:** What does it matter what the patient was diagnosed with?

**A:** Can better expect what is going to happen in the future, enroll in clinical trials, etc.. Can be helpful in treatments and medicines and help to provide answers for others.

**Q:** You mentioned new diagnostic criteria for PSP&CBD, how do these types help laypeople?

**A:** They help researchers mostly. Clinicians understand that there are different variants and patterns of symptoms. Then we can help counsel you when you come to the clinic and understand that better. Gives everyone greater certainty.

**Q:** Can a concussion trigger PSP/CBD?

**A:** If there were memory or movement problems from a concussion, things would be static and not get worse. Usually it doesn't cause it, but the disease was already brewing, and the concussion brought it to light.

**For Dr. Megan DePuy:**

**Q:** LSVT loud – speech therapy for Parkinson's, can it be helpful with PSP or CBD?

**A:** Yes, it's absolutely shown to be helpful across neurodegenerative disease patients. I've sent many patients to be reevaluated after doing it, because I see many symptoms a neurologist hadn't picked up on the first time around.

**Q:** If someone is not coughing, what are the signs of aphasia pneumonia?

**A:** watery eyes, irritated, etc. Usually there is nothing that is causing a red light.

**Q:** You mentioned the epiglottis, how can you strengthen or exercise that? Can you?

**A:** The muscles that are attached go all the way around your larynx/pharynx area, so you can try and strengthen the muscles that hold the epiglottis, (indirectly.) So you can move your larynx up and down. If you can strengthen the vocal chords, that helps too.

**Q:** Why can a PSP/CBD patient sing but not speak?

**A:** Right hemisphere = music, left = speech, by using music, you can use the strengths of both hemispheres. Using your musical center to help with speech and language fluency. Where your ability to sing comes from is in your right hemisphere.

**For Dr. Erica Pitsch:**

**Q:** Struggle between autonomous vs. safety and security. If someone does not have dementia and someone wants to go horseback riding or be walking on their own, what do you suggest to the family/caregiver?

**A:** Informed consent – weigh the benefits and risks first. Classic example is patients wanting to use a walker or not. In evaluation, walking speed is x vs. y, without the walker I could you x times, with the walker you maintained your balance. Showing the risks and benefits. Consequences of failure. Outweighing those consequences of failure. If you are OK with those, then go ahead.

**Q:** Why do people with PSP fall backwards? What are the options for walkers/mobility?

**A:** The axial rigidity (stiffness), makes us more likely to tip over. Postural instability and stiffness make the combination for people more likely to tip. Not much to catch you when you fall backwards.

**Q:** Medicare/Insurance – how can you get them to pay?

**A:** It is required to educate providers about the standard (progressing over time). Have to objectively prove that someone will get worse without it. Can't be at a frequency that you can do by yourself. If you can track your progress, and find problems to solve, and give people a "tune-up" when you need it. But to get it paid for, there needs to be a new problem to solve or learn.

**For Dr. Heather Moss:**

**Q:** What about convergence/divergence video games? Is there such a thing for that?

**A:** There probably are. There are simple things that can help those. Pencil push-ups. Start with target in front of you. Look at eraser and slowly pull it in until it splits, and then repeat.

**Q:** I have amblyopia that is corrected so I cant have double vision. However I notice I close one eye and it does not give me the same image as the other eye. Can you comment on this?

**A:** In childhood due to eyes not being straight or one eye having different prescription, pathway between eye and brain doesn't work as well. Sometimes eyes can never have double vision at all. One eye suppresses and gets ignored.

**Q:** Because of convergence, our neurologist said to raise reading material onto music stand, this was an easy fix.

**A:** Yes, with vertical eye movements. If you can't look down, it is good to like upwards or up straight ahead to help neck posture.

**Q:** Eyelid apraxia – can you talk about that?

**A:** Controlling our eyelids is like controlling other muscles. One problem can be decreased blink. Surface of eye can get dry if not enough blinks. Can purchase eye drops to help. Eyelid apraxia is the motor control missing and can't close. Which means you can't open them very well.

Sometimes have to use fingers to open the eyes manually. Problem isn't that they're weak; it's the control to make that action.