Welcome to the University of Colorado Movement Disorders Center’s 4th Annual Parkinson Disease Symposium

Thank you to our Gold Sponsors for their continued support of community educational programs through unrestricted funds.
University of Colorado
Movement Disorders Center

4th Annual Parkinson Disease Symposium

September 30, 2017
University of Colorado
Movement Disorders Center Team

Director: Lauren Seeberger, MD
University of Colorado Movement Disorders Center (MDC)

• History of excellence, growing talented faculty, unique geography, and amazing community of patients

• “To establish an internationally recognized center for excellence in movement disorders related research, education, clinical care, and community outreach”
History - Some Highlights

• Margaret “Peggy” Hoehn: co-creator of Hoehn and Yahr scale in 1967

• Lori Ramig: Creator of Lee Silverman Voice therapy in 1987

• Curt Freed, John Sladek and Bob Breeze: Pioneers in cell-based therapies for Parkinson’s

• Maureen Leehey: discovery & clinical description of Fragile X Tremor Ataxia Syndrome in 2001

• Benzi Kluger: Initiated one of the first supportive/palliative care clinics for movement disorders in 2013
A Regional Leader

• The largest (over 3000 patient annually) and most comprehensive movement disorders center in the Rocky Mountain Region

• Multi-hospital program that includes the University of Colorado Hospital, Denver VA Medical Center, Children’s Hospital Colorado, and the county hospital, Denver Health
University of Colorado Hospital

• Consistently ranks in top 10 US academic hospitals University HealthSystem Consortium rankings.

• Best hospital in the state past 6 years by *U.S. News & World Report*

• Ranked in nation’s top twenty hospitals by *U.S. News & World Report*
# Comprehensive, Multidisciplinary Specialized Care

## Team
- Neurologists
- Neurosurgeons
- Advanced Practice Providers & Nurses
- Physical, speech, occupational therapists
- Neuropsychologists
- Psychiatrists, Psychologists
- Social Workers, Chaplains
- Genetic Counselors

## Specialty Clinics
- Parkinson Annual
- Newly Dx’d PD Educational
- Supportive/Palliative Care
- Advanced Therapy
- Deep Brain Stimulation
- Neuro-ophthalmology Mvt
- Botulinum Toxin Rx
- Ataxia
- Huntington’s disease
MDC Research Advances

• Clinical Trials:
  – Medications, Surgery, Alternative Therapies
• Supportive & palliative care
• Neuroimaging
• Exercise
• Cell Transplantation
Education

• Movement Disorders Fellowship Program
  – 2 → 4 fellows per year.

• Teach Movement Disorders throughout campus and beyond to all levels and numerous types of students

• Provide research experiences for numerous students of various health professions – from here and internationally
Community Outreach

• Partnership with Michael J Fox Foundation
• Partnership with the Parkinson’s Association of the Rockies (PAR)
• Partnership with Parkinson Disease Foundation’s Parkinson’s Advocates In Research (PAIR) program
• Numerous lectures to support groups
## UCD Movement Disorders Center
### Pilot Grant Program
#### 2016 Winners

<table>
<thead>
<tr>
<th>PI/PIA</th>
<th>Mentor</th>
<th>Project Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kristin Mitrovich, MD</td>
<td>Benzi Kluger, MD, MS</td>
<td>Perceived palliative care needs for HD Patients</td>
</tr>
<tr>
<td>Stephanie Garcia, BS</td>
<td>Curt Freed, MD</td>
<td>Enhancing butyrate production by the microbiome may stop progression of Parkinson’s disease</td>
</tr>
</tbody>
</table>
Parkinson Disease
Etiology & Pathology

Maureen A. Leehey, MD
Professor of Neurology
Chief, Movement Disorders Division
University of Colorado Denver
“Primary PD”

Parkinsonian signs
- Tremor at rest
- Slow movement
- Stiffness
- Asymmetric
- Levodopa response

- Lewy body pathology
Parkinson Disease

blog.bioethics.net/2005/02/

www.fitsugar.com/249421
<table>
<thead>
<tr>
<th>Types of Parkinsonism</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary PD</strong></td>
</tr>
<tr>
<td>Multiple system atrophy (MSA)</td>
</tr>
<tr>
<td>Progressive supranuclear palsy (PSP)</td>
</tr>
<tr>
<td>Diffuse Lewy body disease (DLB)</td>
</tr>
<tr>
<td>others</td>
</tr>
</tbody>
</table>
Diagnosis of PD

- Clinical presentation
  - History
  - Examination
Etiology of PD

- Environment
- Genetics
- Aging brain
Environmental Risk Factors

- Farming
- Pesticides
- Well water
- Head trauma

Factors that ↓ PD Risk

- Smoking
- Caffeine
- NSAIDs
- ↑ Uric Acid

Normal gene variations can make you more or less likely to develop PD
Most persons get PD from:

Common & rare gene variants

+ Environmental factors

↓

Parkinson disease
## Single Gene Mutation -> PD

<table>
<thead>
<tr>
<th>Locus</th>
<th>Gene</th>
<th>Chromosome</th>
<th>Inheritance</th>
<th>Probable function</th>
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</thead>
<tbody>
<tr>
<td>PARK1 &amp; PARK4</td>
<td>α-synuclein</td>
<td>4q21</td>
<td>Dominant</td>
<td>Presynaptic protein, Lewy body, lipid and vesicle dynamics</td>
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<tr>
<td>PARK2</td>
<td>parkin</td>
<td>6q25.2-27</td>
<td>Recessive</td>
<td>Ubiquitin E3 ligase, mitophagy</td>
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<tr>
<td>PARK3</td>
<td>Unknown</td>
<td>2p13</td>
<td>Dominant</td>
<td>Unknown</td>
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<tr>
<td>PARK5</td>
<td>UCHL1</td>
<td>4p14</td>
<td>Dominant</td>
<td>Ubiquitin C-terminal hydrolase</td>
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<tr>
<td>PARK6</td>
<td>PINK1</td>
<td>1p35-36</td>
<td>Recessive</td>
<td>Mitochondrial kinase</td>
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<tr>
<td>PARK7</td>
<td>Dj-1</td>
<td>1p36</td>
<td>Recessive</td>
<td>Oxidative stress</td>
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<tr>
<td>PARK8</td>
<td>LRRK2</td>
<td>12p11.2</td>
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<td>Kinase signaling, cytoskeletal dynamics, protein translation</td>
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<tr>
<td>PARK9</td>
<td>ATP13A2</td>
<td>1p36</td>
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<td>PARK10</td>
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<td>PARK11</td>
<td>GIYF2</td>
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<td>PARK12</td>
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<td>Xq21-q25</td>
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<td>PARK13</td>
<td>Omi/HtrA2</td>
<td>2p13</td>
<td>Unknown</td>
<td>Mitochondrial serine protease</td>
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<tr>
<td>PARK14</td>
<td>PLA2G6</td>
<td>22q13</td>
<td>Recessive</td>
<td>Phospholipase enzyme</td>
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<tr>
<td>PARK15</td>
<td>FBX07</td>
<td>22q11</td>
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<td>Ubiquitin E3 ligase</td>
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</table>

- Up to PARK 20 now
- Genetic discoveries highlight biological processes and pathways that are consistently perturbed in idiopathic PD.

Gene abnormalities that cause PD in families

<table>
<thead>
<tr>
<th>Gene</th>
<th>Inheritance</th>
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<tbody>
<tr>
<td>α-Synuclein</td>
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</tr>
<tr>
<td>Parkin</td>
<td>recessive</td>
</tr>
<tr>
<td>DJ-1</td>
<td>recessive</td>
</tr>
<tr>
<td>PINK-1</td>
<td>recessive</td>
</tr>
<tr>
<td>LRRK2</td>
<td>dominant</td>
</tr>
</tbody>
</table>
Brain cell changes that cause PD

- **α-synuclein** $\Rightarrow$ Lewy bodies
- **Parkin** $\Rightarrow$ abnl protein recycling
- **DJ-1** $\Rightarrow$ free radical damage
- **PINK-1** $\Rightarrow$ mitochondrial dysfunction
- **LRRK2** $\Rightarrow$ $\uparrow$ PO$_4$
α-synuclein makes Lewy bodies
Start of PD: From the Nose???

www.life.uiuc.edu/hing/research/introfig1.html

Transmission of Lewy body (α-synuclein) pathology

PD Pathophysiology Puzzle

**Inflammation**
- HLA genes (PARK18)
  - ↓ Protein Degradation
    - Parkin, PINK1, GBA
  - Δ Kinase
    - PINK1, LRRK2

**Mitochondrial Dysfunction**
- Parkin, PINK1
  - Oxidative Stress
    - Parkin, DJ1
  - ↓ Autophagy
    - GBA, others

**SNCA accumulation & aggregation**
- SNCA, LRRK2, GBA, DJ1, others?

**Neuronal Death**
Cost of Gene Testing: Invitae

<table>
<thead>
<tr>
<th>Testing – 1 or more genes</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cash</td>
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<tr>
<td>Insurance co-pay</td>
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<tr>
<td>Medicare</td>
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<tr>
<td>Medicaid</td>
<td>$0</td>
</tr>
</tbody>
</table>
Maroon Bells, Aspen, Colorado

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colorado.naturephotographers.net
Medication Management of Parkinson Disease

Christopher Groth, MD
Fellow, Movement Disorders
University of Colorado Department of Neurology
Movement Disorder Center
Goals

• Review basic principles of pharmacological treatments specific to motor symptoms in Parkinson’s Disease

• Provide examples of treatment options
Dopaminergic Neurons

Cut section of the midbrain where a portion of the substantia nigra is visible

Substantia nigra

Diminished substantia nigra as seen in Parkinson's disease
Dopaminergic Pathways

- Prefrontal cortex
- Nucleus accumbens
- Striatum
- Meso-cortic pathway
- Meso-limbic pathway
- Nigrostriatal pathway
- SNc
- VTA

(Images and diagrams used with permission from the University of Colorado Anschutz Medical Campus.)
Theoretical treatment options

• Replace dopamine

• Prevent breakdown of dopamine

• Protect dopaminergic neurons from dying

• Regrow dopaminergic neurons

• Modify neuronal circuitry
Treatment Examples

• Replace dopamine
  • Levodopa
  • Dopamine agonists (Pramipexole, Ropinirole, Rotigotine, Apomorphine)

• Prevent breakdown of dopamine
  • AADC inhibitors (Carbidopa)
  • COMT inhibitors (Entacapone, Tolcapone)
  • MAO-B inhibitors (Rasagiline, Selegiline, Safinamide*)
Treatment Examples

- Protect dopaminergic neurons from dying?
  - Exercise
  - Selegiline and rasagiline?
  - Current studies:
    - inosine, isradipine, DBS

- Regrow dopaminergic neurons?

- Modify neuronal circuitry
  - DBS
Sites of Action of Parkinson’s Disease Medications

- **Dopamine agonists**
  - Pramipexole
  - Ropinirole
  - Rotigotine
  - Apomorphine

- **Selegiline**
- **Rasagiline**
- **Safinamide**

- **Levodopa**

- **BBB**
- **Carbidopa**
- **Entacapone**
- **Tolcapone**

- **DA**
- **GABA**
- **ACh**
Why can’t I just take dopamine?
Levodopa Formulations

• Immediate release (IR) – Sinemet

• Controlled release (CR) – Sinemet CR

• Stalevo (Combined with entacapone)

• Rytary
1. Patient questions?

• Why do I need to make medication adjustments?
2. Patient questions?

• If I miss a dose, I don’t even realize it. So do I really have Parkinson’s disease?
3. Patient questions?

• Can levodopa cause dyskinesias?
Dopamine Agonists

- Ropinirole, Pramipexole and Rotigotine
- Can be used at any time in the course
- Side effects
  - Low blood pressure, sleepiness, leg swelling,
  - Impulse control disorder
Long Acting Dopamine Agonists

- ReQuip XL 2, 4, 6, 8, and 12 mg
- Mirapex ER 0.375 mg, 0.75 mg, 1.5 mg, 3 mg, 4.5 mg.
Apomorphine (Apokyn)

- D1/D2 agonist
- Subcutaneous, pen system
- Rapid “off” period rescue
- Treatment of unpredictable, frequent motor fluctuations
- Adverse effects: nausea, vomiting, hypotension
  —Trimethobenzamide
Inhibitors of Dopamine Breakdown

**Periphery**
- COMT
- 3-OMD inhibitors
- L-DOPA
- Carbidopa

**Blood-brain barrier**
- L-DOPA

**Neuron**
- AADC
- DA

**Brain**
- MAO-B inhibitors
- DOPAC
- DA
- Dopamine receptors

**Inhibitors**
- DA
- DOPAC
- DA
Sites of Action of Parkinson’s Disease Medications

- Selegiline
- Rasagiline
- Safinamide
- Dopamine agonists:
  - Pramipexole
  - Ropinirole
  - Rotigotine
  - Apomorphine

- Levodopa
- Carbidopa
- Entacapone
- Tolcapone
- BBB

- DA
- GABA
- ACh
Other treatments for motor symptoms

- Dyskinesias
  - Amantadine
  - Clozapine

- Tremor
  - Anticholinergics (Artane)

- Dystonia
  - Botulinum Toxin injections
## Treatments for other symptoms

<table>
<thead>
<tr>
<th>Drug class</th>
<th>Drug name</th>
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<tbody>
<tr>
<td><strong>Cognitive impairment</strong></td>
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<tr>
<td>Dementia</td>
<td>Acetylcholinesterase inhibitor</td>
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<tr>
<td></td>
<td>Rivastigmine</td>
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<tr>
<td><strong>Psychiatric symptoms</strong></td>
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<tr>
<td>Depression</td>
<td>Dopamine agonist</td>
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<tr>
<td></td>
<td>Serotonin reuptake inhibitor</td>
</tr>
<tr>
<td></td>
<td>Serotonin and norepinephrine reuptake inhibitor</td>
</tr>
<tr>
<td></td>
<td>Tricyclic antidepressant</td>
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<tr>
<td>Psychosis</td>
<td>Atypical antipsychotic</td>
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<tr>
<td></td>
<td>Clozapine, quetiapine</td>
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<tr>
<td></td>
<td>Acetylcholinesterase inhibitor</td>
</tr>
<tr>
<td></td>
<td>Rivastigmine</td>
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<tr>
<td><strong>Sleep disorders</strong></td>
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<tr>
<td>REM sleep behaviour disorder</td>
<td>Benzodiazepine</td>
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<tr>
<td></td>
<td>Hormone</td>
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<tr>
<td></td>
<td>Clonazepam</td>
</tr>
<tr>
<td></td>
<td>Melatonin</td>
</tr>
<tr>
<td><strong>Autonomic dysfunction</strong></td>
<td></td>
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<tr>
<td>Constipation</td>
<td>Osmotic laxative</td>
</tr>
<tr>
<td></td>
<td>Chloride channel activator</td>
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<tr>
<td></td>
<td>Polyethylene glycol</td>
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<td></td>
<td>Lubiprostone</td>
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<tr>
<td>Gastrointestinal motility</td>
<td>Peripheral dopamine antagonist</td>
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<tr>
<td></td>
<td>Domperidone</td>
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<tr>
<td>Orthostatic hypotension</td>
<td>Peripheral dopamine antagonist</td>
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<tr>
<td></td>
<td>Domperidone</td>
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<tr>
<td></td>
<td>Fludrocortisone</td>
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<tr>
<td></td>
<td>Midodrine</td>
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<tr>
<td></td>
<td>Pyridostigmine</td>
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<td>Droxidopa</td>
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<td>Sialorrhoea</td>
<td>Anticholinergic</td>
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<td></td>
<td>Atropine drops, glycopyrrolate</td>
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<tr>
<td>Other</td>
<td>Neurotoxin</td>
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<tr>
<td></td>
<td>Botulinum toxin A, botulinum toxin B</td>
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<tr>
<td>Fatigue</td>
<td>Stimulant</td>
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<tr>
<td></td>
<td>Methylphenidate, modafinil</td>
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</tbody>
</table>

REM-REM rapid eye movement.

*Table 3: Pharmacological treatments for non-motor symptoms*  
Kalia & Lang, 2015
How to select which treatment?

Connolly & Lang, 2014
A potential disaster
Work with your doctor
dance FOR every BODY

RECONNECT WITH YOUR BODY
Reconnect with Your Body

Dance for people with and without Parkinson’s Disease

Mondays, 12:00-1:00pm in Broomfield
Wednesdays, 2:30-3:45pm in Arvada
artasaction.org
Self-Image and Coping with Parkinson’s Disease

Christina L. Vaughan, MD, MHS
Assistant Professor
Department of Neurology, Section of Neuro-palliative Care

September 30, 2017
Disclosures

- Private contractor with University of Rochester through the Huntington Study Group.
Overview

1. Parkinson’s disease (PD) brief epidemiology
2. PD symptoms (non-motor)
3. PD and self image
   • How to improve self image
4. PD and coping
   • Adaptive and maladaptive
5. Grieving styles
   • Intuitive and instrumental
6. Coping strategies
PD: brief epidemiology

- 2\textsuperscript{nd} most common progressive neurodegenerative disorder affecting older American adults
  - 7 - 10 million people worldwide
  - ~1 million people in U.S.

- Age = biggest risk factor

- Described as one of the most complex syndromes in clinical medicine

PD symptoms

- Depression is common (~40%) – due to changes in neurochemistry but also as a reaction to disease
- Loss of interest and initiative, fatigue, indecisiveness and inability to feel pleasure
- Anxiety ~1/3 of patients
  - medical, neurochemical and psychosocial phenomena

Poewe W, 2008; Chen JJ & Marsh L, 2014

PD and self-image

- Self image = “how you see yourself”
- Self esteem = “how you feel about yourself”
- Body image = perception that you have of your physical self and the thoughts and feelings that result from that perception
- Role = a set of expected behaviors that are determined by familial, cultural, and social norms
- Identity = what sets you apart from others

Affected by:
- presence of illness
- age
- inappropriate social relationships
- disease of the nervous system which influences processing of mental images

Gamarral AHE, Molski CS, et al 2009
PD and self-image

• Research shows that people with PD have worse perception of body image and self concept compared to controls
  • no correlation between body image and disease severity
  • self concept worse with more depressive symptoms

http://www.rehabcenternearme.com/tips-improve-self-esteem/

Gamarral AHE, Molski CS, et al 2009
How to improve self-image

• Ignore all “Positivity” advice
• Focus elsewhere
  • pursuit of a goal that makes you happy
  • spending some quality time with loved ones
• 3 compliments Journal
  • encourage self-love, self-respect and have a better mental picture about your own worth
• Plan challenges you can achieve
• Have a routine
• Make a contribution
• Self-compassion

http://self-compassion.org/category/exercises/
PD and coping

“The worst day of this disease was the day I was diagnosed. The best day was when I understood that I could do something about it. It gave me back a sense of control in my life, and some power.” --Phyllis, 63, five years after diagnosis

• We can all respond to stressful experiences in both adaptive and maladaptive ways
  • Helpful or harmful

• Grief
  • = a reaction to a major loss
  • also experienced with an illness for which there is no cure,
  • or a chronic condition that affects quality of life

http://www.pdf.org/newly_diagnosed_pd
PD and coping

ADAPTIVE

• Positive reinterpretation and growth
  • Search for the positive

• Seeking instrumental social support
  • Advice from others with similar experiences

• Active coping
  • Take action to deal with the problem

• Restraint
  • Hold off from doing anything too quickly

• Acceptance
  • Learning how to live with it

• Planning
  • Plan of action; strategy of what to do

MALADAPTIVE

• Mental avoidance
  • Turning to others to take mind off things; sleeping more

• Disengagement
  • Give up trying

• Focusing on and venting emotions
  • Expressing emotional distress

• Alcohol/drug use
  • Self-medicating

• Denial
  • Saying “this isn’t real”
PD and grief

- Instrumental
  - More thinking than feeling
    (an inward, quiet process, less expression of emotions)
  - Being physical, expressing grief through doing something

- Intuitive
  - Strong, affective reactions
    (waves of powerful emotions)
  - Expressions that mirror feelings (more like an open book)

- Push aside feelings to cope with the present
- Choose active or physical ways of coping
- Use humor or anger to express feelings
- Seek solitude to reflect and adapt
- May not benefit from traditional support group

- Openly express feelings
- Allow time to experience inner pain
- Discuss the grief
- Identify others as sources of support
- Choose ways to express feelings
  (journal, art)
- Support group

Dyer KA, 2009
PD and grief

• Know your grieving style
  • How do you process the world?
  • Extrovert/introvert
  • “Doer” – vs- “thinker”

• What can you do to be more balanced?
  • Ex: instrumental→ workaholic… (go to gym, gardening, etc)
  • Ex: intuitive→ staying at home ruminating… (start a support group, journaling, etc)
PD and coping

- Best served by a multi-disciplinary approach
  - health care professionals aware of each other and communicate regularly
- Build a Health Care Team
- Find the Right Doctor
- Manage Your Medications
- Cope with Symptoms and Side Effects
- Exercise
- Nutrition
- Complementary Therapies
- Find Support
- Advance Directive

http://www.pdf.org/managing_pd
Final Points

- PD is becoming more prevalent, currently ~1 million people in U.S.
- Non-motor symptoms are common, and include depression (40%) and anxiety (30%) which can affect self image
- People with PD have low self image, and this can be addressed by managing mood, and lifestyle modifications
- Coping with illness can be adaptive or maladaptive
- It is normal to feel some degree of grief with a chronic illness
  - Important to identify your grieving style and then work to balance this to help with coping
- You can take charge by building a health care team, educating yourself, and being proactive
“No one chooses Parkinson’s, but everyone has a choice when deciding how they will live with it.”
Thank you
Exercise is Medicine!

Renee Peter PT, DPT, ATC, NCS
Cellular Benefits of Exercise

Promotes brain health, repair, adaptation
Functional Benefits of Exercise

• Improved cognitive function: “think better”
• Prevention of depression: “feel better”
• Improved sleep: “sleep better”
• Decreased constipation: “better digestion”
• Improved functional motor performance: “move better”
• Improved drug efficacy: “medication works better”
Barriers to Exercise Participation

• Not sure what type of exercise to do?
• Can’t afford it
• Pain!
• How can I find a class?
What Type of Exercise Should I do?

Aerobic conditioning
- Walking, cycling, swimming, dancing, group class

Strength training
- Functional strengthening (stair climbing, sit to stand), strength training class

Flexibility training
- Yoga, group class

Balance training
- Yoga, Tai Chi, dance, group class
What Type of Exercise Should I do?

Principles of Neuroplasticity

- Specificity
  - Sit to stand, step up, step back, turn step
- Intensity
  - Higher than you think! Increase challenge with resistance or move faster
- Frequency
  - Do something everyday!
- Duration
  - 30-60 minutes
- Challenging
  - “new” activities, do two things at once
- Salience
  - meaningful, fun, enjoyable, something that requires attention
- Repetition
  - Do more than you think you should, over 1,000 repetitions
Overcoming barriers: Can’t afford it

Ways to lower cost
• Exercise at home with a DVD
• Wellness program through medical insurance
• Look for free group classes on PDF or PAR
• Bundle classes
Overcoming barriers: Pain

Physical therapy
• Perform an individualized assessment and treatment of your pain
• Educate you on movements to avoid
• Instruct you in best type of exercise for your pain condition
• Teach you restorative exercises to correct muscle imbalances contributing to your pain
Overcoming barriers: group classes

Benefits of group exercise
• Increased motivation to stick with it
• Push harder than you normally would
• Active support group
Finding a Group Exercise Class
Parkinson’s Association of the Rockies

- Go to website: https://www.parkinsonrockies.org/
- Click on Community
- Click on Exercise and Activity Classes
Exercise Classes in Denver Metro Area

Click on
• Exercise Classes
or
• Community Exercise Classes

EXERCISE AND ACTIVITY

Exercise is one of the most important keys to success when living with Parkinson's disease (PD). Exercise has been proven to help alleviate the symptoms of Parkinson's. There are a variety of exercises that are beneficial for individuals with Parkinson's. No matter what you like to do, the most important key to exercising - keep moving! The Parkinson Association of the Rockies offers a variety of exercise and activity classes to help you stay physically and mentally healthy. View our Suggested Exercise page for tips on exercises you can do at home and the most common exercises individuals with PD participate in.

To find all available classes, first select a class type from the list below:

• Exercise Classes
  • Yoga Classes
  • Art Classes
  • Community Exercise Classes
Anschutz Health and Wellness Center
Parkinson’s Exercise Program

- **When:** Monday, Wednesday and Friday at 1:15 pm – 2:15 pm
- **Where:** Anschutz Health and Wellness Center. Check in at front desk.
- **Address:** 12348 E. Montview Blvd., Aurora, CO 80045
- **What:**
  - Monday – Pool class
  - Wednesday – Group exercise in studio 3
  - Friday – Group exercise in studio 3
- **Who:** Instructor – Alyssa Joel
- **Cost:** Each session is $10 or purchase a bundle from the front desk: $90 for 10 classes
Interactive Break: Physical Therapy

Lee Bernhardt, PT, DPT
University of Colorado Outpatient Rehabilitation Medicine
SMARTPHONE APPS IN PD

TREVOR HAWKINS, MD
Background

• Apps continue to expand in capability and access
• Possible uses include:
  • Tracking medications
  • Tracking symptoms
  • Diary
  • Searching for best deals on medications
  • Collecting patient’s data for studies
  • Therapeutic
  • Knowledge about disease
Practical considerations

• Read the fine print!
  • Beware if asking for info especially if free
• Limitations of practice
Disclaimer

• No financial ties to any of the following apps
• Some may work for apple, android or both
• Most of the screenshots are the apple version
Pharmacy Apps

GoodRx
- Use Coupons
- Not insurance
CareZone

CareZone Pharmacy Services are available in your state!

Order refills easily from the comfort of your smartphone.

We'll analyze insurance to minimize copays.

Free home delivery.

Try CareZone Pharmacy Services
Medication Reminder

• Medisafe
Frequency: Every Day

HOW MANY TIMES A DAY?
5 times a day

WHAT TIME?
7:00 AM
Take 1

11:45 AM
Take 1

3:30 PM
Take 1

7:15 PM
Take 1

11:00 PM
Take 1

Starts Sep 28, 2017
Tap to set end date

Rx Number: 2

Pills Left: 25

Refill Reminder: On

Reminder: 5 pills before I run out

Reminder Time: 11:00 AM

Enter Times

Track Refills

Med Pics
Medisafe

Manage your meds

Blood Glucose

Medication Adherence

Stay organized

Weekly Adherence

May 11, Thursday

May 10, Wednesday

Taked (3)

Zyrtec, 10:42

Vitamin C, 10:42

Prilosec, 10:42

Missed (0)
Point of Care
Available on Apple devices
It can be hard to tell if you have Parkinson's disease.

Here are the 10 signs you might have the disease. No single one of these signs means that you should worry. But if you have more than one symptom you should make an appointment to talk to your doctor.

Tremor or Shaking

Have you noticed a slight shaking or tremor in your finger, thumb, hand, chin or lip? Does your
Parkinson’s Diary
• Wearable device study through the Michael J Fox Foundation
• Can go to foxinsight.org to determine if you are eligible and sign up
## mPower

**A Parkinson Disease Research Study**

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</table>
National Parkinson’s Foundation
Speech Aids

- May be best under guidance of speech therapist
- Could design home exercises
- May require additional equipment, i.e. bluetooth mic
Exercise Apps

Parkinson Home Exercises
- Youtube video available
EasyCall- Help with dialing for those with tremor
Welcome to the University of Colorado Movement Disorders Center’s 4th Annual Parkinson Disease Symposium

Thank you to our Gold Sponsors for their continued support of community educational programs through unrestricted funds.

Medtronic  abbvie  ACADIA Pharmaceuticals
PRESENTING: Nutrition and Complementary Therapies for Parkinson’s Disease: What the Health?

BY: Lisa W. Corbin, MD, FACP
Medical Director, Center for Integrative Medicine
University of Colorado Hospital
Professor of Clinical Practice, Internal Medicine
University of Colorado School of Medicine
Questions

• What are complementary therapies and how might these and nutrition impact Parkinsons?
• What’s the Integrative Medicine program at the University of Colorado Hospital?
• Where can I find more information?
Definitions

**CAM**
- Complementary / Alternative Medicine
- Therapies not historically part of conventional medicine
  - Chiropractic, acupuncture, massage, herbs…

**Lifestyle medicine**
- Use of stress reduction, exercise, nutrition for health benefits

**Integrative medicine**
- CAM therapies and lifestyle approaches *coordinated with* conventional medical treatments
Using an Integrative Approach

1. Avoid harmful practices
2. Focus on lifestyle / self-care
   - Sleep (Dr. Kluger)
   - Exercise (Dr. Peter)
   - Mind / body techniques (Dr. Vaughan)
   - Nutrition
3. Discuss safe, plausible CAM therapies
   - Herbs / supplements
   - Acupuncture
   - Massage
   - Chiropractic
4. Coordinate care with other providers
5. Return care of the patient to the patient!!
Nutrition in 7 Words
This might be different for PD patients. I'll check with Benzi on this...
Kristina, 9/24/2012
HEALTHY EATING PLATE

Use healthy oils (like olive and canola oil) for cooking, on salad, and at the table. Limit butter. Avoid trans fat.

The more veggies—and the greater the variety—the better. Potatoes and french fries don't count.

Eat plenty of fruits of all colors.

STAY ACTIVE!

Harvard School of Public Health
The Nutrition Source
www.hsph.harvard.edu/nutritionsource

Harvard Medical School
Harvard Health Publications
www.health.harvard.edu
What diet slows progression?

Do I have to eat organic?

Is protein bad?

Should I take supplements?

How about gluten free?
CAM Therapies

- Supplements
- Massage therapy
- Acupuncture
- Chiropractic
What herb should I drink to help me sleep?

That depends on whether you want to wake up again.
Herbs and Supplements

• Three types of medicines:
  – Prescription (Rx)
  – Over-the-counter (OTC)
  – Dietary Supplements

• Unlike Rx and OTC, supplements:
  – Are not required to prove safety or efficacy
    • Burden of proof on FDA to show unsafe
  – Are not required to enforce quality control
    • GMP required but burden on FDA
  – Can vary in concentration of ingredients
Supplements

• Natural ≠ safe
• Watch for drug / herb interactions
• Use good resources for information
• If you choose to recommend supplements:
  – Look for well-labeled brands
  – Avoid combination products, MLM
• Tell your doctors and pharmacists
• Having an elective surgery?
  – General recommendation – stop all supplements 2 weeks before
“Snap out of it.”
Manufacturers More Likely to Produce Quality Products

- Costco
- Equiline / Equate
- Nature’s Way
- Nature’s Made
- Nature’s Bounty
- Phytopharmica
- Puritan’s Pride
Coenzyme Q10

• Antioxidant; heart protection
• Patients with PD are low in CoQ10 vs people without PD (and are not in other antioxidants)
• Two large randomized trials contradictory
  – 80 people: placebo, 300 mg / d, 300 mg 2x / d, 300 mg 4x / d for 16 months or until needed l-dopa; benefits found at highest dose
  – 600 people on stable l-dopa: placebo + 1200 IU vitamin E, 1200 mg CoQ10 + vitamin E, 2400 mg CoQ10 + vitamin E – no differences
• Recent meta-analysis (8 studies): not helpful
• Safe

Zhu et al. Neuro Sciences 2017
Mischley et al. J Neuro Sciences 2012
Shults CW et al. Arch Neurol 2002
NCT00740714 clinicaltrials.gov 2011
Creatine

• Early studies suggested possible role for this muscle building protein

• RCT underway in 1741 early (< 5 years of L-dopa) PD patients
  – 10 gm creatine 3 x / day, at least 5 years (enrolled 2007 – 2010)

• Safe unless kidney disease or heavy caffeine
  – 2016 study of caffeine / creatine noted if people took creatine and drank a lot of caffeine that PD progressed more rapidly. No effect of creatine on progression if no caffeine intake.

Elm JJ. Mvmt disord 2012
Caffeine

- Coffee, green tea, black tea
  - Epidemiologic studies associate increased caffeine intake with decreased risk of PD
  - Observational study did not associate caffeine intake with progression
  - No interventional studies

Vitamin E

- 800 patients
- Selegiline, vitamin E (2000 IU), placebo, or selegiline + vitamin E
- Time until need for L-dopa
- Selegiline was effective; vitamin E did not work
- Other studies with safety concerns for vitamin E

NEJM 1993
Ann Int Med 2005
Background
Safety
Cost
"On the plus side, you’ve cured my back pain."
Acupuncture for PD

• Systematic review: 4 RCT of scalp acupuncture for PD motor symptoms
  – 2 showed benefit, 2 did not; quality of trials low

• Consider for associated symptoms
  – Fatigue
  – Balance
  – Constipation
  – Pain
  – Anxiety / depression

Lee, SH. Medicine 2017
Hun-Soo L. Chin J Integ Med 2013
Background
Safety
Cost
Massage Therapy for PD

- Relaxation, improved QOL
- Pain management
- Improved shoulder mobility and increased walk speed
  - Few studies; case series in 2012 showed benefit after one 30 min session
- Improved sleep

Donovama N. J Alt Comp Med 2012
Finding a Good Practitioner

• Training and licensure
• Experience with condition
• Expected benefits
• Risks
  – Direct risks or side effects, interactions?
• Costs / reimbursement
• Time frame / progress assessment
• Ability to work with conventional providers
Integrative Medicine Services

General Assessment / Overview
Lisa Corbin, MD  Lauren Grossman, MD
Tish Bolshoun, PA  Jen Carroll, MD

Traditional Chinese Medicine
Daisy Dong, LAc  Nancy Nguyen, LAc
Ban Wong, LAc

Massage therapy
Ann Mathews, CMT  Debra Szuster, CMT

Nutritional Counseling
Holly Prehn, RD

Pharmaceutical / Herbal Consults
Monika Nuffer, Pharm D

Chiropractic
Brian Enebo, DC  Craig Kozak, DC

Mind-body / Biofeedback
Carrie Landin, PsyD  Meredith Shefferman, PsyD
Justin Ross, PsyD  Joanne Whalen, PsyD
Felicia Greher, PhD

Physical therapy
Marcus Kurek, PT

Yoga Therapy
Carolyn Valdez, CYT
The Center for Integrative Medicine

- **Stapleton**
  3055 Roslyn Street
  suite 250
  Denver, CO 80238

- Anschutz Health and Wellness
- Lowry
- CeDAR
- Inpatient at UCH
What the Health!

• Integrative medicine coordinates lifestyle approaches and CAM with conventional care
  – Don’t use harmful CAM therapies
  – Use beneficial, safe therapies
  – Consider plausible, safe therapies
  – Don’t forget about lifestyle!

• Find good practitioners
• Use reliable information sources
Summary

• Nutrition
  – Increase fiber and water to help constipation
  – Avoid large, high fat meals (better medication absorption)
  – Restrict protein if advanced disease with motor fluctuations

• Supplements:
  – CoQ10 still possibly helpful; safe

• Acupuncture
  – Data not great for PD; trial of 8-10 weekly visits can determine if you feel it is helpful for you
  – May help other symptoms

• Massage: you can be your own trial!
“Be open minded, but not so open minded that your brains fall out”

Widely attributed
Research Resources

• Fox Trial Finder:  
  https://foxtrialfinder.michaeljfox.org/register/

• National Parkinson’s Foundation:  
  http://www.parkinson.org/

• www.clinicaltrials.gov
Internet resources

General CAM resources:

• National Center for Complementary and Integrative Health: nccih.nih.gov
• UCD Health Science Library’s Strauss-Wisneski Complementary and Indigenous Medicine Collection – the website has links to other resources and journals and books held in the collection: http://hslibrary.ucdenver.edu/strauss
• Mayo Clinic: http://www.mayoclinic.com/health/parkinsons-disease/DS00295
Herbal / Supplement resources:
  • USP Dietary Supplement Verification Program [www.usp.org/USPVerified/dietarySupplements](http://www.usp.org/USPVerified/dietarySupplements)
  • NIH information on supplements: [http://ods.od.nih.gov](http://ods.od.nih.gov)

Acupuncture
  • National Certification Commission for Acupuncture and Oriental Medicine: [http://www.nccaom.org](http://www.nccaom.org)

Massage
  • American Massage Therapy Association: [www.amtamassage.org](http://www.amtamassage.org)

Mind / body
  • [www.psychologytoday.com](http://www.psychologytoday.com) “Find a therapist”
Sleep and Fatigue

Benzi Kluger, MD, MS
Associate Professor of Neurology
Director, Neurology Palliative Care Section
University of Colorado
Goals

• Sleep
  – Why is sleep important in PD?
  – What are the most common sleep disorders?
  – Why are these important to recognize?
  – Why do they happen?
  – What can I do about it?
Goals 2

• Fatigue
  – What is fatigue?
  – Why is it important to recognize?
  – Why are people with PD affected by fatigue?
  – What can I do about it?
SLEEP

FOOD FOR THOUGHT 24

WHY IS IT THAT PEOPLE SAY ‘SLEPT LIKE A BABY’ WHEN BABIES WAKE UP EVERY TWO HOURS???
Effects of Sleep deprivation

- Irritability
- Cognitive impairment
- Memory lapses or loss
- Impaired moral judgement
- Severe yawning
- Hallucinations
- Symptoms similar to ADHD
- Impaired immune system
- Risk of diabetes Type 2

- Increased heart rate variability
- Risk of heart disease
- Increased reaction time
- Decreased accuracy
- Tremors
- Aches

Other:
- Growth suppression
- Risk of obesity
- Decreased temperature
Sleep and PD

- Motor symptoms
- Mood
- Memory
- Energy
The evolution of PD

This figure shows how PD progresses from the earliest symptoms (often non-motor symptoms) to diagnosis and start of treatment through to the early and advanced stages of the condition.

Preclinical PD
- Olfactory loss
- RBD
- Constipation
- Anxiety
- Depression
- Impaired colour vision

Onset motor symptoms

Early treated PD (stable)
- Bradykinesia
- Rigidity
- Rest-tremor
- (+/- non-motor symptoms)

Advanced PD
- Motor complications
  - Wearing off / Dyskinesias
  - Gait & balance problems
  - Axial deformities
  - Dysarthria / Dysphagia
- Non-motor complications
  - Cognitive decline / Dementia
  - Depression
  - Psychosis
  - Autonomic dysfunction
  - Sleep-awake dysregulation
Sleep Problems
PD is a 24/7 Disease
PD and Sleep 2

- Affects internal clock (melatonin)
- Sleep comfort
- Dreams
- Insomnia
Insomnia

• Problems with Sleep Initiation
  – Medication side effect
• Problems with Sleep Maintenance
  – Medication wearing off
• Early Morning Awakening
  – depression
PD and Sleep 3

- Motor symptoms
- Medications wearing off
- Tough start in the morning
- Nocturnal Dyskinesias
- Dystonia
- Neuropathy
Medications and Sleep

- Stimulants
- Amantadine
- Selegeline and Rasagiline
- “Sleeping Pills”
Mood and Sleep

- Depression
- Anxiety
- Grief
- Worry
Other Common Problems

• Nocturia
• Pain
SLEEP HYGIENE - THE GOOD AND THE BAD

**Helps you sleep**
- Go to bed and get up at the same time every day
- Don't watch TV before bed
- Don't do the things below!
- Stay hydrated
- Doing relaxation exercises before bed
- Spend time in the daylight
- Read a book in bed
- Have a light dinner, and not too late

**Keeps you awake**
- Coffe and chocolates after dinner
- Hot bedroom with no air circulation
- Poor quality bedding
- Stay indoors all day and do no exercise
- Worrying about things happening in the future
- Using a computer just before bedtime
- Go to bed too early when you're not tired
- Lie in bed for hours getting annoyed that you can't sleep
- Lie in bed for hours getting annoyed that you can't sleep

[www.nosleeplessnights.com](http://www.nosleeplessnights.com)
Sleep Hygiene

- Exercise and sunlight
- Avoiding caffeine and alcohol
- Limiting food and beverages
- Avoid late afternoon naps
- Establish bedtime routine
- Make the bedroom comfortable
- Use the bed only for sleep (and sex)
Natural Sleep Aids

• Teas (chamomile, valerian root, kava)
• Melatonin (3-12 mg)
• Self-hypnosis/relaxation
• Music and sounds
• Acupuncture
Am I going crazy?
Am I going crazy?

- Illusions
- Nightmares
- Hallucinations
- Sundowning
Sleep Disorders
REM Behavior Disorder (RBD)

- REM = rapid eye movement sleep
- Acting out vivid dreams
- Causes problems for sleeper and bedmate
- Treatable
  - Melatonin
  - clonazepam
Restless Legs Syndrome (RLS)

- Uncomfortable sensations in the legs
- Typically occurs when still and at bedtime
- Somewhat relieved by moving
- Can be associated with iron deficiency or worsened by some medications
- Treatment may include dopamine agonists, levodopa, clonazepam or opioids
- Can get worse with treatment (augmentation)
Periodic Leg Movements of Sleep

- Intermittent leg movements (kicking) at night
- Often not remembered by sleeper
- Disrupts sleep quality
- Treatments are similar to RLS
Sleep Apnea

• Periods of shallow, infrequent or pauses in breathing during sleep
• Can be associated with snoring, morning headaches and large neck
• Disrupts sleep quality and increases blood pressure
• Can be treated with oxygen, mouth guards, positive pressure ventilation (CPAP, BiPAP)
What can I do?

Doctor, can you prescribe something to stop me from sleepwalking?

No, you need the exercise!
Sleep Study
Medications

• Avoid habit-forming medications when possible
• Treat specific conditions
• Start with natural remedies
• Antidepressants (mirtazepine, trazodone)
• Antipsychotics (quetiapine)
• Benzodiazepines (zolpidem, clonazepam, temazepam)
• Antihistamines (diphenhydramine)
time for questions
FATIGUE
Fatigue is not...

- Sleepiness
- Apathy
- Depression
Excessive Daytime Somnolence
Excessive Daytime Somnolence

- Medications
  - Dopamine agonists
  - Antidepressants
  - Pain medications
- Sleep Disorders
- Insomnia
- Depression
Apathy

I was trying to figure out which is worse, ignorance or apathy...

Then I realized I don't know and I don't care.
Apathy

- A flatness of emotion, often accompanied by loss of motivation (abulia)
- Can affect 30-40% of PD patients
- Distinct from depression
- Often difficult to treat, may respond to routine/habits, exercise and stimulants
- Lower expectations
Depression and Fatigue

• Fatigue may be a symptom of depression
• Fatigue can be depressing
• Treatment of depression often helps fatigue
Fatigue Defined

• Subjective perceptions of increased effort, exhaustion and lethargy

• Objective decrements in physical or mental performance as a result of continued performance
Pathological Fatigue

- Present with minimal or no exertion
- Unpredictable
- Prolonged recovery
- Interferes with daily function
Secondary Fatigue

- Anemia
- Sleep Disorders
- Medications
- Orthostatic hypotension
- Thyroid Disease
- Low testosterone
- Low vitamin D
- Chronic Pain
- Depression or anxiety
Primary Fatigue

- Cognitive and attentional processes
- Changes in perceived effort
- Thermostat/homeostasis
- Changes in brain neurotransmitters (e.g. low dopamine)
Management
Energy Management

• Learn to budget your energy over the day
• Take advantage of your best times
• Don’t over do it
• Power naps
  – 20-45 minutes
  – Early afternoon
Exercise

• Find the right time for your habit
• Slow and gradual
• Aerobic
• Strength training
• Tai Chi and Yoga
Natural Remedies

• Hydration
• L-carnitine
• Caffeine
• Stress/relaxation
• Acupuncture
Medications

• Dopaminergic medications
• Amantadine
• Stimulants
  – Methylphenidate (ritalin)
  – Metamphetamine (adderall)
  – Provigil/nuvigil
Emily Nauman, MA, CCC-SLP
Speech Language Pathologist - National Jewish Health
LSVT LOUD Faculty
LSVT Global Consultant
First speech treatment with level 1 evidence and established efficacy for treating voice and speech disorders in people with Parkinson disease (PD).

Developed and scientifically researched over the past 25 years with funding from the National Institutes of Health. LSVT LOUD outcome data have been published in a series of refereed articles in speech, otolaryngology and neurology journals.

Research on LSVT LOUD has documented improved impact on multiple levels of functioning in people with PD following treatment including:

- Increased vocal loudness
- Improved articulation and speech intelligibility
- Improved intonation
- Improvements in facial expression
- Changes in neural functioning related to voice and speech

LSVT LOUD is being delivered by over 16,000 certified LSVT Speech Therapists in 69 countries.

“My voice is alive again”
“Communicate”

“I am confident I can communicate”
LSVT BIG is an intensive, amplitude focused physical and occupational therapy approach developed from principles of the effective Parkinson’s specific speech treatment LSVT LOUD.

Research on LSVT BIG has documented improved ratings on tests of motor functioning in people with Parkinson disease following treatment including:
- Faster walking with bigger steps
- Improved balance
- Increased trunk rotation
- Improvements in activities of daily living such as bed mobility
- Improved UPDRS Motor Score

LSVT BIG is being delivered by over 10,000 certified LSVT PTs and OTs in 38 countries.
“It is possible to take charge of your life, even with Parkinson’s.

It is possible for your will to override your brain.

It is possible to have Power Over Parkinson’s”

~Sharon Kha
LSVT BIG and LSVT LOUD Graduate
Visit the LSVT Global table for

More Information
How to find certified therapists
View pre/post LSVT LOUD and LSVT BIG videos

LET’S EXERCISE!!!!

Phone: 1-888-438-5788
Email: info@LSVTGlobal.com
Website: www.LSVTGlobal.com
Deep Brain Stimulation and other surgical treatments for Parkinson disease

Olga Klepitskaya, MD, FAAN
Associate Professor of Neurology
University of Colorado Denver

Deep Brain Stimulation Program
Movement Disorders Center
Deep Brain Stimulation

Implanted electrode delivers continuous high frequency electrical stimulation to structures involved in the control of movements.

- Reversible
- Adjustable
DBS system components

The lead delivers mild, electrical stimulation to the thalamus.

The extension connects the pulse generator to the lead.

The implantable pulse generator is generally implanted near the collarbone.

DBS electrode

© Mayfield Clinic
Targets for DBS in PD

- **STN**
  - Subthalamic Nucleus

- **Gpi**
  - Globus Pallidus

- **Thalamus**
DBS is proven and effective treatment

- First DBS surgery – early 1990s
- FDA approved in USA
  - Essential tremor - 1997
- Parkinson disease - 2002
- Dystonia - 2003
- Obsessive Compulsive Disorder – 2009
- More than 120 thousand patients implanted
DBS is not a cure Parkinson disease

DBS is a powerful symptomatic treatment

- Improves motor problems caused by PD
- Is not expected to improve non-motor problems
  - Cognition (memory, attention etc.)
  - Mood and behavior
  - Blood pressure control, etc..
- Exception:
  - if these problems are caused by medications, decrease of medications can help with non-motor problems
Indications for DBS in PD

Diagnosis of advanced levodopa responsive idiopathic PD
Not everything that looks like PD is PD

- Vascular Parkinsonism
- Drug-induced Parkinsonism
- Post traumatic Parkinsonism
- Post infectious Parkinsonism
- **LBD** – Lewy Bodies Dementia
- **FTDP** – Frontotemporal dementia-parkinsonism
- **PSP** – Progressive Supranuclear Palsy
- **CBD** – Corticobasal degeneration
- **MSA** – Multiple Systems Atrophy

Watch for look-alikes!!!
Indications for DBS in PD

Diagnosis of **advanced** levodopa responsive idiopathic PD
Indications for DBS in PD

Diagnosis of advanced levodopa responsive idiopathic PD

All currently available pharmacological treatment should be optimized: combination of medication from different groups
Indications for DBS in PD

Diagnosis of advanced levodopa responsive idiopathic PD
Indications for DBS in PD

Diagnosis of advanced levodopa responsive idiopathic PD

The best predictor of improvement after DBS is improvement from medications

At least 30% improvement in UPDRS motor scores between On and Off medications
Indications for DBS in PD

Diagnosis of advanced levodopa responsive idiopathic PD

AND

Presence of *motor fluctuations*

despite optimal medication management

- Dyskinesia
- Wearing off before next dose
- Unpredictable wearing off
- Sudden wearing off
- Dose failure
Indications for DBS in PD

Diagnosis of advanced levodopa responsive idiopathic PD

**Exception:**

*TREMOR* can be resistant to medications, but improves with DBS
Indications for DBS in PD

Diagnosis of advanced levodopa responsive idiopathic PD AND Parkinsonian tremor that causes disability despite optimal medication management
Indications for DBS in PD

Diagnosis of advanced levodopa responsive idiopathic PD
AND
Presence of motor fluctuations despite optimal medication management
OR
Parkinsonian tremor that causes disability despite optimal medication management
Tremor is an exception to the medication responsiveness rule!!
## B-STN DBS vs Medications

### A

<table>
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<tr>
<th>Metric</th>
<th>Neurostimulation</th>
<th>Medication</th>
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<td>Mobility</td>
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<td>P&lt;0.001</td>
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<tr>
<td>Activities of Daily Living</td>
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<td>P&lt;0.001</td>
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<tr>
<td>Emotional Well-Being</td>
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<td>Stigma</td>
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<td>Bodily Discomfort</td>
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<td>Social Support</td>
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</tr>
<tr>
<td>Cognition</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Communication</td>
<td></td>
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</tr>
</tbody>
</table>

### B

<table>
<thead>
<tr>
<th>Hours in Day (%)</th>
<th>Neurostimulation</th>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline (N=63)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.0</td>
<td>3.2</td>
<td>7.6</td>
</tr>
<tr>
<td>3.2</td>
<td>4.8</td>
<td>4.3</td>
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<tr>
<td>4.8</td>
<td>6.2</td>
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<tr>
<td>6.2</td>
<td>7.7</td>
<td>8.4</td>
</tr>
<tr>
<td>7.7</td>
<td></td>
<td></td>
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<tr>
<td>6 Mo (N=53)</td>
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</tr>
<tr>
<td>1.0</td>
<td>7.6</td>
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<td>7.6</td>
<td>5.5</td>
<td>5.5</td>
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<tr>
<td>5.5</td>
<td>7.2</td>
<td>7.4</td>
</tr>
<tr>
<td>7.2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Legend:**
- Mobile with troublesome dyskinesias
- Mobile without troublesome dyskinesias
- Neither fully mobile nor fully immobile
- Immobile
- Sleeping
Therapeutic effects of DBS in PD

- Decrease dyskinesia
- Longer periods and better quality of mobility
- Improvement of quality of life
- Decrease medication intake
Deep Brain Stimulation
Potential complications and risks

- **Surgery-related** – very rare <1%
  - Stroke
  - Bleeding in the brain
  - Seizure
  - Transient confusion
  - *Infection* (typically occurs at the site of generator)
    - up to 10%

- **Stimulation-related**
  - Usually can be minimized or eliminated by adjusting stimulation
  - Tingling,
  - Slurry speech
  - Balance problems
  - Behavioral and mood problems
Expert consensus on DBS

• DBS is the best performed by an experienced neurosurgeon with expertise in stereotactic surgery

• working as a part of multidisciplinary team of experts

• Good relationship between referring neurologist and DBS team are very important for continuity of care

• DBS programming can take 3 to 6 months to obtain optimal results
  • Optimize stimulation
  • Minimize stimulation related side effects, if any
  • Decrease medication

• DBS programming is best accomplished by a highly trained clinician

Deep brain stimulation for Parkinson disease: an expert consensus and review of key issues, DeLong MR at all, Arch Neurol. 2011
Multidisciplinary DBS team at UCH MDC

- **Neurosurgeons:**
  - Steven Ojemann, Aviva Abosch
- **Neurologists:**
  - Olga Klepitskaya, Lauren Seeberger, Drew Kern
- **Pediatric neurologist:** Abigail Collins
- **Neuropsychologists:** Brian Hoyt and others
- **Rehabilitation:** Heather Baer
  - **Physical therapists:** Jane Ott, Renee Peters
  - **Speech therapist:** Jill Newcombe
- **Psychiatrists:** Alison Heru, Rachel Davis
- **Programming:** Christen Epstein, NP, Jessica Barr, PA
- **Neuroradiology:** Jody Tanabe
- **Neurophysiologist:** John Thompson
- **DBS coordinator**
Multidisciplinary DBS team

**Referral to a DBS center**

**Initial evaluation by a movement disorders neurologist**

**DBS Evaluation Pathway**
- Video “On-Off” Evaluation
- Cognitive Evaluation by neuropsychological testing
- Speech Pathology
- Rehabilitation Evaluation
- Brain MRI
- Neurosurgery Evaluation
- If required additionally: Psychiatric evaluation
- Social Worker

**DBS Team Meeting**

- **DBS surgery**
- **Medication management/ Clinical trials**

**DBS programming and medication management**

**Physical therapy**
- Speech therapy
Deep Brain Stimulation Programming parameters

- **Electrode configuration**
  - Choice of active electrode
  - Monopolar vs bipolar

- **Pulse Width**
- **Frequency**
- **Amplitude**
DBS Programming Parameters

Interleaving

Monopolar vs bipolar

Up to 4 different groups of stimulation
Directional stimulation

Novel electrodes

Shaping electrical field
- Directional
- Segmented
- Steerable
St. Jude Medical Infinity™ DBS System

The only FDA-approved directional lead

Modern, mobile app experience

Uses familiar personal electronic devices for ease of use

Upgradeable technology allows for non-invasive software

Real-time battery estimation

Secure Bluetooth® wireless technology for wireless communication with IPG

Patient programmer

Clinician programmer
Chronic levodopa response is a narrowing of the therapeutic window

Chronic levodopa response is a narrowing of the therapeutic window

Review and meta-analysis of published literature, reporting long-term outcomes of STN DBS on motor function in PD patients

- Analyze the long-term effects of STN DBS on the progression of motor disability, measured by UPDRS.
- Compare the rate of progression with estimated expected natural progression.

Results:
- 38 articles were included.
- The total number of subjects: 1,341.
- The maximum follow-up time: 11.7 years.
The optimal time for DBS in PD

• Time from the symptoms onset to DBS
  • 2006 – 10.7 years
  • 2014 – 6.4 years

  **DBS is not a last resort!**

• **Studies on DBS for earlier stages of PD**
  • *Controlled Clinical trial of DBS for Early Patients with Parkinson disease.* German Parkinson Study Group
    • changed FDA indications as far as timing of DBS for earlier stages

  • *Prospective study to compare results of STN DBS between early-treated and late-treated PD patients.* Italian Parkinson Association

  • *DBS for Early Stage Parkinson disease: prospective clinical trial.* Vanderbilt University, USA
New DBS surgical techniques

• MRI guided “asleep” DBS surgery
  – UCH Neurosurgeon Steven Ojemann
• The only in the region real-life MRI-guided DBS
ClearPoint System

**MRI-guided asleep DBS**

- MR visualization of target
- MR-guided placement of electrode
Future of DBS
Novel Targets for DBS
Zona Incerta (ZI) – Dr. Kern’s research

• ZI has been shown to be as efficacious compared with the traditional targets

• It is now possible to implant and compare
  • ZI independently to STN
  • ZI and STN concomitantly to STN alone through interleaving stimulation
Future technological advances: “On-demand” stimulation
Other types of functional neurosurgery for PD
Stereotactic neurosurgery for movement disorders

- **1890s** - Lesions in basal ganglia: an invasive procedure, where a selected portion of the nucleus (Thalamus or Gpi) is surgically destroyed (ablated) to create a lesion.

- **1990s** - Deep Brain Stimulation

- Re-emergence of ablation (lesion) surgeries:
  - Gamma knife
  - Focused Ultrasound
Re-emergence of ablative surgery

Gamma knife

- Radiation surgery where specialized equipment focuses beams of radiation on a target in the brain
- **Indications:**
  - brain tumors,
  - abnormal blood vessels,
  - trigeminal neuralgia
Re-emergence of ablative surgery
High intensity Focused Ultrasound

HIFU or FUS is a medical procedure that applies HIFU energy to locally heat and destroy diseased or damaged tissue through ablation.

*Indications*: tumors, ex: prostate cancer
Incision–free invasive stereotactic surgery

= Thalamotomy

- Effective treatment for tremor
- Surgical risks are similar to traditional thalamotomy and DBS
- Absence of MER eliminates functional targeting
- Bilateral lesions are not recommended
- Can be a viable option in selected cases of disabling tremor when DBS is too risky or not feasible
Emerging treatments

- Fetal dopamine transplant
- Trophic factor infusions
- Spheramine
- Gene therapy
  - GAD
  - Neurturin
- Stem cells
- Antibody infusions
The promise of cell-based therapies

To be useful for transplant purposes, stem cells must be reproducibly made to:

• Proliferate extensively
• Generate sufficient quantities of cells
• Differentiate into the desired cell type(s).
• Survive in the recipient after transplant.
• Integrate into the surrounding tissue after transplant.
• Function appropriately for the duration of the recipient's life.
• Avoid harming the recipient in any way (ex. tumors)
• Avoid the problem of immune rejection

Stem cells offer exciting promise for future therapies, but significant technical hurdles remain that will only be overcome through years of intensive research.
Thank You
Other Advanced Treatments

Drew S. Kern, MD, MS
University of Colorado
Department of Neurology
Movement Disorders Center
Challenges in Advanced PD

- 58% of patients with PD do NOT have a neurologists
- Care by neurologists leads to:
  - Greater utilization of cost effective therapies
  - Fewer hospitalizations
  - Less fractures
  - Improved patient mood
  - Reduced nursing home placement

As the Disease Progresses, the Therapeutic Window Narrows

Symptoms and side effects occur as the levodopa therapeutic window diminishes*

Plasma Levodopa Concentrations

Smooth, extended response  Diminished duration  Shorter, unpredictable response
Absent or infrequent dyskinesia  Increased incidence  “On” time with increased dyskinesia of dyskinesia

Treatments of Motor Symptoms

Connolly & Lang, 2014
Sublingual apomorphine
Inhaled CD/LD CVT-301
Intec Accordion CL formulation gastroretentive platform
Alternate drug delivery systems
Carbidopa/levodopa enteral suspension
Carbidopa/levodopa enteral suspension
Carbidopa/levodopa enteral suspension

Olanow et al., 2014
Apomorphine
Subcutaneous carbidopa/levodopa
Other treatments for motor symptoms

• Dyskinesias
  — Amantadine
  — Clozapine

• Tremor
  — Anticholinergics

• Dystonia
  — Botulinum Toxin injections
Collagen injections in vocal folds

- More than 90% of PD patients have voice and speech impairments.
- The current treatment:
  - Speech therapy, Lee Silverman Voice treatment (LSVT)
  - Vocal fold augmentation with collagen injections is being used safely for many disorders of vocal folds.
- Few reports in PD demonstrate improvement in voice loudness.
Gamma Knife

Stereotactic Radiosurgery - Gamma Knife Concept

Multiple radiation beams converge on target tumor, delivering high-dose radiation to the tumor, but little to surrounding tissues. It is a single treatment and to ensure proper patient positioning and immobility, a positioning frame is secured to the patient’s skull, then attached to the radiation source. Treatment lasts 45 to 60 minutes.
## Non-Motor Features

<table>
<thead>
<tr>
<th></th>
<th>Drug class</th>
<th>Drug name</th>
</tr>
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<tbody>
<tr>
<td><strong>Cognitive impairment</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dementia</td>
<td>Acetylcholinesterase inhibitor</td>
<td>Rivastigmine</td>
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<tr>
<td><strong>Psychiatric symptoms</strong></td>
<td></td>
<td></td>
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<tr>
<td>Depression</td>
<td>Dopamine agonist</td>
<td>Pramipexole</td>
</tr>
<tr>
<td></td>
<td>Serotonin reuptake inhibitor</td>
<td>Citalopram, escitalopram, fluoxetine, paroxetine, sertraline</td>
</tr>
<tr>
<td></td>
<td>Serotonin and norepinephrine reuptake inhibitor</td>
<td>Venlafaxine extended release</td>
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<td></td>
<td>Tricyclic antidepressant</td>
<td>Desipramine, nortriptyline</td>
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<td>Psychosis</td>
<td>Atypical antipsychotic</td>
<td>Clozapine, quetiapine</td>
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<tr>
<td></td>
<td>Acetylcholinesterase inhibitor</td>
<td>Rivastigmine</td>
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<tr>
<td><strong>Sleep disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>REM sleep behaviour disorder</td>
<td>Benzodiazepine</td>
<td>Clonazepam</td>
</tr>
<tr>
<td></td>
<td>Hormone</td>
<td>Melatonin</td>
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<tr>
<td><strong>Autonomic dysfunction</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constipation</td>
<td>Osmotic laxative</td>
<td>Polyethylene glycol</td>
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<tr>
<td></td>
<td>Chloride channel activator</td>
<td>Lubiprostone</td>
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<tr>
<td>Gastrointestinal motility</td>
<td>Peripheral dopamine antagonist</td>
<td>Domperidone</td>
</tr>
<tr>
<td>Orthostatic hypotension</td>
<td>Peripheral dopamine antagonist</td>
<td>Domperidone</td>
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<tr>
<td></td>
<td>Mineralocorticoid</td>
<td>Fludrocortisone</td>
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<tr>
<td></td>
<td>Vaspressor</td>
<td>Midodrine</td>
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<tr>
<td></td>
<td>Acetylcholinesterase inhibitor</td>
<td>Pyridostigmine</td>
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<td>Norepinephrine prodrug</td>
<td>Droxidopa</td>
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<td>Sialorhoea</td>
<td>Anticholinergic</td>
<td>Atropine drops, glycopyrrolate</td>
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<tr>
<td></td>
<td>Neurotoxin</td>
<td>Botulinum toxin A, botulinum toxin B</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>Stimulant</td>
<td>Methylenedate, modafinil</td>
</tr>
</tbody>
</table>

REM = rapid eye movement.

Table 3: Pharmacological treatments for non-motor symptoms

Kalia & Lang, 2015
Dementia

• An estimated 80% of patients with disease greater than 20 years of disease will become demented.
Depression

• A common feature of PD (30-45% of patients) and greater than age-matched controls with chronic disease

• Tricyclic antidepressants (nortriptyline and desipramine) are effective for depression
  - Rarely used due to anticholinergic side effects – orthostatic hypotension & cognitive impairment

• SSRI and SNRI: although not demonstrating efficacy in a number of studies, commonly used

Connolly & Lang, 2014
Psychosis

- A feature of later stage of PD or due to medications

- Antipsychotics that do not worsen parkinsonism
  - Quetiapine
  - Clozaril
  - Pimavanserin
  - Cholinesterase inhibitors (rivastigmine)
Pimavanserin

Cummings et al., 2014
Orthostatic Hypotension

- Non-pharmacological treatments
- Fludrocortisone
- Midodrine
- Pyridostigmine
- Droxidopa
Droxidopa (L-threo-3,4-dihydroxyphenylserine) is a prodrug converted peripherally and centrally by aromatic amino acid decarboxylase (AADC) into norepinephrine. The conversion pathway involves tyrosine hydroxylase, aromatic-L-amino acid decarboxylase, dopamine-beta-hydroxylase, phenylethanolamine-N-methyltransferase.
• Standing SBP at week 1 increased +6.4 mmHg in droxidopa compared with 0.7 in placebo, no significant differences at other time points

Hauser et al., 2015
Thank you
Good Vibrations:
Music for a Healthy Voice, Body, and Brain

Rebekah Stewart, MA, MT-BC

Thursdays, 1PM at Rehabilitative Rhythms Music Therapy
2222 S Fraser St. #2, Aurora
New and upcoming Treatments for Parkinson disease

Brian D. Berman, MD, MS

University of Colorado Movement Disorders Center
• **Basic science** – pure/fundamental scientific research that is typically conducted “benchtop” or in a lab and aims to improve understanding of disease.

• **Clinical research** – the study of health and illness in people.

• **Clinical trials** – clinical research that aims to determine the safety and effectiveness (efficacy) of medications, devices, diagnostic products and treatment regimens intended for human use.
Terminology

Phases of a Clinical Trial

- **Lab Studies**: Several Years
- **Human Safety**: Days - Weeks
- **Expand Safety**: Weeks - Months
- **Efficacy & Safety**: Several Years

Pre-Clinical → Phase I → Phase II → Phase III

**Double-Blind Clinical Trials**

Doctor

Patient
Clinical Research at the University of Colorado

• We have pharmacological and surgical clinical trials that aim to find novel ways to slow, stop or reverse the progression of PD, as well as find better treatments for motor and non-motor symptoms.

• We also conduct clinical research into non-pharmacological and complementary approaches to treatment as well as have a research focus on caregivers in addition to patients.
Neuroprotection
SURE – PD3
Study of URate Elevation in PD

• Gout (elevated uric acid) is associated with a lower risk of PD
• Urate is a strong antioxidant - comparable to Vitamin C
  – accounts for most of the antioxidant capacity in the blood
• Inosine increases urate levels
• Does increased urate slow progression?
• Inosine (active drug) or lactose (placebo) capsules three times per day for 24 months.
• Inclusion criteria:
  – + PD on DaTscan
  – early stage
  – On no PD meds or only rasagiline (Azilect)
Phenylbutyrate in PD

- PD gene PARK7 encodes the protein DJ-1
- Increasing DJ-1 expression may clear α-synuclein and block its toxic effects
- Phenylbutyrate shown to increase DJ-1 expression
- Study now to see if phenylbutyrate can clear α-synuclein from the brain and slow PD (enrolling soon).
Nilotinib in PD

The c-Abl inhibitor, Nilotinib, protects dopaminergic neurons in a preclinical animal model of Parkinson’s disease

Senthilkumar S. Karuppagounder1,2,6, Saurav Brahmachari1,2,6, Yunjong Lee1,2,3,6, Valina L. Dawson1,2,3,5,6, Ted M. Dawson1,2,4,5,6* & Han Seok Ko1,2,7*
A Randomized, Double-Blind, Placebo-Controlled, Phase IIa, multicenter study of Nilotinib in PD

- MJFF and PSG study
- Two-Cohort Study:
  - Moderate to advanced PD (N=75, 6 months)
  - Early/de novo PD (N=60, 12 months)
- Two doses (150mg and 300mg) vs placebo
- Goal to determine safety, tolerability, clinical and biological activity of Nilotinib in PD
Motor symptom treatment

Adapted from information presented in Rodriguez-Oroz et al., 2009.4
Dopaminergic Therapy in PD
Treatment of the **voice impairment** with collagen injections in vocal folds *(VoCAL-PD)*

- More than 90% of PD patients have voice and speech impairments
- Current treatment options only speech therapy, Lee Silverman Voice treatment (LSVT), etc.
- Vocal fold augmentation with collagen injections is being used safely for many disorders of vocal folds
- The goal of this study is to objectively analyze effect of injections in PD
Effect of Cannabidiol on Parkinson Disease

• Cannabidiol (CBD) is a component of cannabis (marijuana)
  – Does not cause “high”
  – May be help symptoms in PD and be neuroprotective
• Persons with PD have been trying all different kinds of cannabis, but there have been no good studies done
• This study evaluates the effect of CBD on all aspects of PD
• Is blinded crossover study, lasts ~3 months
• I/E criteria: must have frequent tremor
Motor fluctuation treatment
Recently FDA Approved

- Extended-Release Amantadine (Gocovri)
  - Treatment of dyskinesia in those taking levodopa
  - May be better tolerated than short-acting form
- Safinamide (Xadago)
  - Reversible inhibitor of MAO-B (reduces dopamine uptake) and inhibitor of excessive release of glutamate (anti-dyskinesia?)
  - Similar to selegiline (Eldepryl) and rasagiline (Azilect) but is more selective and reversible
  - Adjunct therapy (not shown effective as monotherapy)
Selective Partial D1-like Agonist

• Selective partial D1-like receptor agonist has similar proprieties to levodopa but may result in less dyskinesias.

• A 15 week Phase 2, double blind randomized placebo controlled study with an optional 1 year open label extension.

• Primary outcome is reduction of OFF time.
Cynapsus CTH-301 Trial

Investigating the safety and effectiveness of an oral, sublingual therapy of Apomorphine for patients with Parkinson’s disease who are experiencing motor fluctuations (known as OFF episodes)

Major Inclusion Criteria:
- Response and stable dosing to L-Dopa
- At least 2 hours or more of OFF times

Major Exclusion Criteria:
- Atypical or secondary parkinsonism
- Prior neurosurgical procedure for PD
- Cankers or mouth sores within 30 days prior to the first visit
Accordion pill for fluctuating PD patients

- Study of Intec Accordion CL formulation gastroretentive platform.
- Active control (immediate release carbidopa/levodopa)
Open-Label Study of Apomorphine by Continuous Subcutaneous Infusion in Advanced PD

- Put on in AM, take off in PM
- Small needle just into the skin under the white patch

- Dopamine agonist
  - Not related to morphine
- Approved & used in UK and other European countries
- Only available in US through research study
  - 1 year open label study, then can continue
- Major I/E criteria
  - At least 3 hours OFF time/day
Sub-cutaneous infusion of carbidopa/levodopa for patients with PD

- Patients with advanced PD and irregular, not reliable effect of medications with early wearing off.
- Constant infusion of liquid CD/LD under the skin
  - Very small (insulin-like) needle and small pump
  - Constant infusion provides smooth, steady effect
Surgical treatment
Infinity Deep Brain Stimulation System

PROGRESS

• Long – term follow up of the performance of newest implanted DBS system.

• Demonstrate superiority of directional (steerable) DBS lead

• Patients, who need DBS are implanted with this system and followed long term
Novel Targets for DBS

- Adverse effects can occur with STN DBS:
  - Dyskinesias, ataxia, behavioral & mood problems
- Stimulation of zona incerta (ZI) may be more effective than traditional targets.
- Clinical study of the effects of combined ZI and STN compared to standard STN.
- *Does not require any change to standard STN DBS procedure with exception that one contact will be placed in the ZI.
Non-motor symptom treatment
Recently FDA Approved

- Pimavanserin (Nuplazid) is a first-in-class atypical antipsychotic with recent FDA approval for the treatment of hallucinations and delusions in PD.
- Pimavanserin acts as a serotonin receptor with negligible effects at dopamine and histamine receptors, and thus tends to not worsen motor symptoms or cause excess sedation in patients with PD.
Dementia treatment

- Cognitive impairment in PD is common and there are only limited treatment options.
- Some of the cognitive symptoms are likely related to the dopamine insufficiency.
- There is a brand new type of medication that can improve the effect of dopamine in the brain and may improve memory and cognition.
- Phase II 12-week trial of LY3154207 in Mild-to-Moderate Parkinson Disease Dementia
Why Participate?

THE BIOPHARMACEUTICAL RESEARCH AND DEVELOPMENT PROCESS

From drug discovery through FDA approval, developing a new medicine takes at least 10 years on average and costs an average of $2.6 billion.* Less than 12% of the candidate medicines that make it into Phase I clinical trials will be approved by the FDA.

**Potential New Medicines**

- **Basic Research**: 10,000-15,000
- **Drug Discovery**: 250
- **Pre-Clinical**: 5
- **Clinical Trials**: 6-7 years
- **FDA Review**: 1-2 years
- **Post-Approval Research & Monitoring**: 3-6 years

*Source: Biotechnology Industry Organization (BIO)
Why Participate?

• All of your current treatments came through clinical trials
  – ↓male death rate from CAD 50%
  – Now 75% survival from childhood leukemia

• 90% of clinical trials do not finish on time
  – This means delays in advances, more expensive research, more expensive treatments

• People in clinical trials have better outcomes
  – Close observation by expert clinicians
  – Placebo effect
  – Gives an ill person hope

• It is a unique gift that you can give to the PD community
Your Research About Research

• Sponsor?
• Inclusion/Exclusion criteria?
• Time and commitment?
• Will the treatment harm me? What are the risks?
  – Closely monitored by IRB, FDA
• What are the potential benefits?
• Privacy protected?
• Chances of being in “control” or “placebo” group?
Research Resources
“Trust Your Gut!”
Bowel Dysfunction in PD: Constipation

Lauren Seeberger, MD
Associate Professor Neurology
University of Colorado
Anatomy of the Lower GI Tract
Normal Function of the Lower GI Tract

• Final part of the digestive system
• Functions to take up fluids, process waste and eliminate waste
• An important part of the process is peristalsis
Nervous System Control of Bowel

The Brain in Your Gut
The gut’s brain, known as the enteric nervous system, is located in sheaths of tissue lining the esophagus, stomach, small intestine and colon.

Small Intestine Cross Section
Mesentery
Attaches the bowel to the body wall and contains major arteries, veins, lymphatics and external nerves.

Submucosal plexus
Layer contains sensory cells that communicate with the myenteric plexus and motor fibers that stimulate the secretion of fluids into the lumen.

Myenteric plexus
Layer contains the neurons responsible for regulating the enzyme output of adjacent organs.

Lumen
No nerves actually enter this area where digestion occurs. The brains in the head and gut have to monitor conditions in the lumen across the lining of the bowel.

Source: Dr. Michael D. Gershon, Columbia University

BRAIN and GUTS
Microbiome

• Microbiota - An community of microbes (microscopic organisms) living inside us, mostly in digestive system

• Microbiome - can mean all the microbes in a person or the genes of the microbes

People with PD may have less of the bacteria that protect from toxins and inflammation
What is Constipation?

- Decreased frequency of BMs
- Fewer than 3 BMs per week
- May be seen in up to 80-90% PWPD
- Slowness of transit present early in course

- Constipation may precede motor PD
- Average colon transit time is twice that of controls
Causes of Constipation

- In PD, dysfunction of the autonomic nervous system regulates the smooth muscles
- Not drinking enough water
- Diet low in fiber
- Lack of exercise
- Large amounts of dairy
- Certain medications
Treatment of Constipation

• Conservative Measures
  • Increased fluids 1.5 l
  • Fiber 15-25 grams
  • Exercise
  • Diet
  • Probiotic supplements
  • Digestive yogurts

• Pharmacologic Therapies
  • Osmotic agents-polyethylene glycol 17 gm/day has been shown effective
  • Recently, lubiprostone, enhances colon secretions tested in PD
  • Treat like chronic constipation
Can We Alter Diet to Affect Microbiome?

- Too early to know
- Unknown which probiotics or how much is needed to impact PD-associated gut bacteria
- Healthy diet is always a good idea (high fiber, low sugar, low saturated fats)
- Combination of probiotic with prebiotic helps constipation
From The Kitchen of

NPF-Prune Juice Cocktail: ½ cup applesauce, 2 tbsp wheat bran (miller’s bran) and 4-6 oz prune juice, store in fridge and take a tablespoon per day then increase to amount that works best
Natural Fruit Paste for PD: 1 lb. pitted prunes, 1 cup lemon juice, 1 cup brown sugar, 1 lb. raisins, 1 lb. dried figs, 1 3oz. Package Senna Tea (loose leaf). Steep tea for 5 minutes in 3.5 cups boiling water, then strain out tea leaves, reserve two cups of tea. Add finely chopped fruit to 2 cups of tea and boil 5 minutes. Then, add sugar and lemon juice, cool. Process til smooth in food processor. Divide in 1-2 Tablespoon portions to freeze.

Janet’s Molasses Bran Muffins—it is a secret!
Thank You!

Honor the Urge!
Sex & Parkinson disease
Sexual problems in PD

- General population - Kinsey Institute’s 2010 National Survey of Sexual Health and Behavior
  - 63% of partnered men >70 yo had sex ≥2 x month
  - 25% of partnered women >70 had sex ≥4 x month

- Problems in PD may be overestimated
  - Men 68%
  - Women 36%

- Sexual dissatisfaction
  - Highest in young men
  - Highest in men with ↑ motor symptoms
  - Highest in women with anxiety
  - Highest in couples in which man has PD

- Sexual dysfunction is commonly assoc with depression
Important aspects of sexual relationship

• Physical
• Emotional
• Intimacy
Sexual dysfunction in PD

Men
• Erectile dysfunction
• Premature ejaculation
• ↓ orgasm
• ↓ desire

Women
• ↓ orgasm
• ↓ desire
Compulsive sexual behavior

- Impulse control disorders - 13% in PD
- 5% of persons on dopamine agonists
- Aberrant, excessive, time/money consuming sexual activity:
  - ↑ sexual desire, masterbation, requests,
  - Pornography
  - Cybersex
  - Sexual activity with multiple partners
  - Use of prostitutes
  - Paraphilias
  - Sexual harassment
Drugs that cause sexual dysfunction

• SSRIs (esp ↓ orgasm)
• Valium type meds
• Blood pressure lowering meds:
  • Beta-blokers (atenolol, propranolol)
  • Diuretics
• Others
Treatment

• Dopamine?
• Treat depression & anxiety
  • Bupropion (Wellbutrin)
  • Mirtazapine (Remeron)
  • Duloxetine (Cymbalta)
  • Desvenlafaxine (Pristiq)
• Testosterone replacement
• PDE5 -I
Treatment: PDE5 inhibitor meds

- Sildenafil (Viagra)
- Vardenafil (Levitra)
- Tadalafil (Cialis)

- Treats ↓ erection & ↓ orgasm (both genders)
- Watch for lightheadedness, drug interactions
- Reasons for failure
  - Not absorbed due to constipation
Treatment: Referrals

- Counseling
  - Sex therapy
  - Psychological counseling
  - Couples therapy
- Urology
- Gynecology
Treatment: Sex Therapy

• “Pleasure oriented” rather than “goal oriented”

• Timing
  • When have ↓ fatigue
  • When in ON state
  • Take pain medication before

• Choose position that demands ↓ effort

• Effective stimulation

• Dryness: lubricants, hormonal Rx
FEMALE LISTENING SKILLS

TONE, INFLECTION, POINT OF VIEW, INUENDO, HIDDEN MESSAGES...

MALE LISTENING SKILLS

MMM... PEPPERONI.