Welcome to the University of Colorado Movement Disorders Center’s 5th Annual Parkinson Disease Symposium

Thank you to our sponsors for their continued support of our educational programs.

ADAMAS™  Allergan  ACADIA® Pharmaceuticals  Medtronic
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Good Vibrations: Music for a Healthy Voice, Body, and Brain

Thursdays, 1-2 PM
Rehabilitative Rhythms Music Therapy
2222 S Fraser St. #2, Aurora

Rebekah Stewart MA, MT-BC
Neurologic Music Therapist, Fellow
Rebekah@DenverMusicTherapy.com

303.817.1531
University of Colorado
Movement Disorders Center

5th Annual Parkinson Disease Symposium

October 27, 2018
University of Colorado Movement Disorders Center (MDC)

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

• “To foster an internationally recognized center for excellence in movement disorders related research, education, clinical care, and community outreach”
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
  – University of Colorado Hospital
  – Denver VA Medical Center
  – Children’s Hospital Colorado
  – Denver Health
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
• Gene therapy, 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
Movement Disorders Practice Locations

Please note that all providers may not be available at our satellite clinics.

**Anschutz Medical Campus**
1635 Aurora Court, Aurora, CO 80045  
P. 720-848-2080  F. 720-848-0117

**Boulder Family Medicine**
5495 Arapahoe Avenue, Boulder, CO 80303  
P. 720-848-9200

**Lone Tree**
9548 Park Meadows Drive, Lone Tree, CO 80124  
P. 720-848-2200  F. 720-553-0901

**Lowry Internal Medicine Clinic**
8111 E Lowry Boulevard, Suite 120, Denver, CO 80230  
P. 720-848-9500
Parkinson Disease
Etiology, Pathology & Treatment

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
# Types of Parkinsonism

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary PD</td>
<td>Most common</td>
</tr>
<tr>
<td>Multiple system atrophy (MSA)</td>
<td>Lightheaded, bowel &amp; bladder dysfunction</td>
</tr>
<tr>
<td>Progressive supranuclear palsy (PSP)</td>
<td>Early falls, vision complaints</td>
</tr>
<tr>
<td>Diffuse Lewy body disease (DLB)</td>
<td>Early dementia, hallucinations</td>
</tr>
<tr>
<td>others</td>
<td>From strokes, hydrocephalus, etc</td>
</tr>
</tbody>
</table>
Diagnosis of PD

- Clinical presentation
  - History
  - Examination
Pathology of PD
Etiology of PD

- Environment
- Genetics
- Aging brain
Environmental Risk Factors

- Farming
- Pesticides
- Well water
- Head trauma

Factors that ↓ PD Risk

- Smoking
- Caffeine
- NSAIDs

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

Common & rare gene variants

+ Environmental factors
## Single Gene Mutation -> PD

<table>
<thead>
<tr>
<th>Locus</th>
<th>Gene</th>
<th>Chromosome</th>
<th>Inheritance</th>
<th>Probable function</th>
</tr>
</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>
</tr>
<tr>
<td>PARK2</td>
<td>parkin</td>
<td>6q25.2-27</td>
<td>Recessive</td>
<td>Ubiquitin E3 ligase, mitophagy</td>
</tr>
<tr>
<td>PARK3</td>
<td>Unknown</td>
<td>2p13</td>
<td>Dominant</td>
<td>Unknown</td>
</tr>
<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>
</tr>
<tr>
<td>PARK7</td>
<td>Dj-1</td>
<td>1p36</td>
<td>Recessive</td>
<td>Oxidative stress</td>
</tr>
<tr>
<td>PARK8</td>
<td>LRRK2</td>
<td>12p11.2</td>
<td>Dominant</td>
<td>Kinase signaling, cytoskeletal dynamics, protein translation</td>
</tr>
<tr>
<td>PARK9</td>
<td>ATP13A2</td>
<td>1p36</td>
<td>Recessive</td>
<td>Unknown</td>
</tr>
<tr>
<td>PARK10</td>
<td>Unknown</td>
<td>1p32</td>
<td>Dominant</td>
<td>Unknown</td>
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<tr>
<td>PARK11</td>
<td>GIGYF2</td>
<td>2p37</td>
<td>Dominant</td>
<td>IGF-1 signaling</td>
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<td>PARK12</td>
<td>Unknown</td>
<td>Xq21-q25</td>
<td>X-linked</td>
<td>Unknown</td>
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<tr>
<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>FBXO7</td>
<td>22q11</td>
<td>Recessive</td>
<td>Ubiquitin E3 ligase</td>
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<tr>
<td>PARK16</td>
<td>Unknown</td>
<td>1q32</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

Genetic discoveries highlight biological pathways that are consistently abnormal in PD.

Gene abnormalities that cause PD in families

<table>
<thead>
<tr>
<th>Gene</th>
<th>Mode of Inheritance</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\alpha$-Synuclein</td>
<td>dominant</td>
</tr>
<tr>
<td>Parkin</td>
<td>recessive</td>
</tr>
<tr>
<td>DJ-1</td>
<td>recessive</td>
</tr>
<tr>
<td>GBA</td>
<td>recessive</td>
</tr>
<tr>
<td>LRRK2</td>
<td>dominant</td>
</tr>
</tbody>
</table>
Brain changes that cause PD

- \( \alpha \)-Synuclein \( \Rightarrow \) Lewy bodies
- Parkin \( \Rightarrow \) abnl protein recycling
- DJ-1 \( \Rightarrow \) free radical damage
- PINK-1 \( \Rightarrow \) ↓ mitochondrial function
- GBA \( \Rightarrow \) ↓ lysosome function
- LRRK2 \( \Rightarrow \) ↑ PO\(_4\)
α-synuclein clumping makes Lewy bodies
Start of PD: From the Nose or the Gut???

www.life.uiuc.edu/hing/research/introfig1.html
PD Pathophysiology Puzzle

Inflammation
HLA genes
(PARK18)

↓Protein Degradation
Parkin, PINK1, GBA

Mitochondrial Dysfunction
Parkin, PINK1

Oxidative Stress
Parkin, DJ1

↓Autophagy
GBA, others

Δ Kinase
PINK1, LRRK2

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

Neuronal Death
Rx

Interrupt α-synuclein pathology

Exercise

Interrupt pathology of single gene mutations
# Cost of Gene Testing: Invitae

<table>
<thead>
<tr>
<th>Get tested NOW &amp; every few years</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cash</strong></td>
</tr>
<tr>
<td><strong>Insurance co-pay</strong></td>
</tr>
<tr>
<td><strong>Medicare</strong></td>
</tr>
<tr>
<td><strong>Medicaid</strong></td>
</tr>
</tbody>
</table>
Treatment Principles

- Individualize therapy
- Prioritize protective therapy
- Promote activity
- Best Rx
  - Combination of meds
  - Lowest dose of each
Drug Classes in PD

- **Dopaminergic agents**
  - Levodopa (SINEMET, STALEVO, RYTARY, DUOPA)
  - Dopamine agonists (MIRAPEX, REQUIP, NEUPRO, APOKYN)
- **COMT inhibitors** (COMTAN)
- **MAO-B inhibitors** (selegiline, AZILECT)
- **Anticholinergics** (ARTANE)
- **Amantadine** (SYMMETREL)
sites of action of PD drugs

levodopa

Dopamine agonists
- pramipexole
- ropinirole
- rotigotine
- apomorphine

selegiline
rasagiline

amantadine

BBB
carbidopa
benserazide
entacapone

trihexiphenidyl
Levodopa - Cornerstone of Treatment

- Most effective med
- Combined with carbidopa
- Protein in diet interferes with delivery to brain
- Forms: regular (intermediate), long-acting & dissolvable
- ONLY MED THAT CAUSES DYSKINESIA
Dopamine Agonists

- Pramipexole (MIRAPEX)
- Ropinirole (REQUIP)
- Rotigotine (NEUPRO)
Treatment Strategy

- Initial therapy
  - DA agonist in young person
  - Levodopa in older person

- $\leq 400$ mg levodopa

- Use long acting levodopa preparations

- Use DA agonist & other meds
  - to Rx residual symptoms
  - Smooth out response
Genetic Testing

Get tested NOW & every few years
What to Expect When the Unexpected Happens

Christen Epstein NP-C
Jessica Barr PA-C
How Common Is Parkinson Disease

• The prevalence of PD rises with age:
  • 60,000 Americans diagnosed annually, 1 million in US
  • 1% over age 60
• Most cases are sporadic
• M > F: 60/40
Symptoms Prior to Diagnosis

- Non motor symptoms can predate diagnosis by years to decades
- Loss of smell
- Constipation
- REM Sleep Behavior Disorder
- Motor signs present when 50%-70% of dopamine neurons are lost
Motor Symptoms
TRAP

• T: Tremor at rest
• R: Rigidity (stiffness)
• A: Akinesia (slower, smaller movements)
• P: Postural instability (balance problems)
Do Symptoms Determine the Future?

- Studies suggest rate of progression varies for certain clinically defined subtypes.
- Major subtypes:
  - Tremor-dominant
  - Slowness/stiffness/gait impairment
- Several studies have found the tremor-dominant subtype is associated with slower progression.
No Two People with Parkinson Disease are the Same

- No one will get every symptom that is associated with Parkinson disease
- Unable to predict which symptoms you will or will not get
- Everyone has a different rate of progression
- Progression is slower in early onset
Stages of Parkinson Disease
The Hoehn and Yahr Scale

- Stage 0: no signs of disease
- Stage 1: unilateral disease
- Stage 2: bilateral disease, without impairment of balance
- Stage 3: mild to moderate bilateral disease; needs assistance to prevent falling on pull test, physically independent
- Stage 4: Severe disability, but still able to walk or stand unassisted
- Stage 5: Wheelchair-bound or bedridden unless aided
Non Motor Symptoms

- Decreased smell
- Sleep difficulties, REM Sleep Behavior Disorder
- Mood changes
- Low blood pressures
- Constipation
- Quiet speech
- Swallowing difficulties, drooling
- Cognitive changes
Cognitive Changes

• Changes with visuospatial, processing speed, attention/concentration, multitasking
• Incidence of dementia is 4-9% per year, more so with older patients
• After 20 years up to 80% may have dementia
• Risk may be lowered with physical and mental exercise as well as diet
Driving and Parkinson Disease

• Driving requires complex cognitive and motor function
• Many people with PD can drive without difficulty
• Changes in visuospatial skills, slowed reaction time, slower movement, impaired coordination
• Can try limiting driving
• Can get a formal driving assessment
• Use alternative sources of transportation
Role of Genetics

• Greater likelihood that genetics play a role when symptom onset is < 50 years
• Genetic testing has prognostic value
Mortality and Parkinson Disease

• Most studies suggest mortality is only modestly increased for patients with PD compared with age-matched controls.
• PD itself is not fatal, but disease complications can be.
• Per CDC complications from PD are the 14th leading cause of death in the US.
• Difficulty swallowing can lead to aspiration pneumonia or other pulmonary complications.
• Loss of balance can cause falls.
What’s the Overall Picture?

• While certain symptoms may guide to some degree, progression is variable
• No symptoms or signs to accurately predict an individual’s course
• Stable and slow progression
What Can Be Done to Make A Difference?

• Exercise!!
• Stress reduction
• Get involved in the community
• Get involved in research
SPARX Trial

• Spearheaded at UCH by Dr. Margaret Schenkman PT
• 4 different sites nationally, 128 patients
• 6 month long collaborative study
• High-intensity group did not have worsening of motor scores compared to moderate-intensity (1.5 points) or control (3 points) groups
MAO-I May Slow Progression

- Significant association between longer duration of MAO-B inhibitor exposure and less clinical decline
- Supports the possibility that MAO-B inhibitors may slow clinical disease progression
- There have been 2 other studies that did not show disease modifications
- A definitive long term trial is needed
Research to Slow Progression

- Phase III Clinical trials:
  - Isradipine (a blood pressure medication)
  - Inosine (a supplement that raises urate)
- Early phases of clinical trials:
  - Nilotinib (a cancer drug to modify a-synuclein)
  - Exenatide (a diabetes drug, binds to GLP-1 Receptors)
  - Alpha-synuclein modifiers
Parkinson Disease Self-Efficacy

- Spearheaded by Diane Cook
- Provide tools, empowerment, and knowledge in order to improve quality of life
- With better quality of life, more likely to change trajectory of disease!
- Multiple groups in Colorado and nation-wide
“No one chooses Parkinson’s, but everyone has a choice when deciding how they will live with it.”
References


References

- Nutt JG. Motor subtype in Parkinson’s disease: Different disorders or different stages of disease? Mov Disord 2016; 31:957.
References


Not All Is As It Seems

Hallucinations and Delusions in Parkinson’s Disease

Samantha Holden, MD, MS
Assistant Professor of Neurology
Sections of Behavioral Neurology and Movement Disorders
“Romeo and Juliet” by Octavio Ocampo
Parkinson’s Disease Psychosis

• Can occur in up to 60% of people with PD
• Range of severity of symptoms
• More common if cognitive impairment also present
• Can be caused or worsened by medications
Hallucinations

• Seeing, hearing, feeling, and/or smelling things that aren’t really there

• Most commonly presence or passage hallucinations
  • Feeling someone standing behind you
  • Catching movement in the corner of your eye

• Can be well-formed, visual hallucinations
  • People, children, animals
Illusions

• Misinterpretation of a sensory stimulus, usually visual
  • Mistaking a lamp for a person
  • Seeing faces in patterns in the rug, or in the leaves on a tree
Delusions

• Falsely held, fixed belief
• Cannot be persuaded to the contrary, despite ample evidence
• Paranoid, persecutory, infidelity
Causes

• Can be due to the brain changes in Parkinson’s disease itself

• Can also be due to medication side effects
  • Parkinson’s medications
    • MAO-B inhibitors (rasagiline, selegiline)
    • Amantadine
    • Dopamine agonists (ropinirole, pramipexole, rotigotine)
    • Trihexyphenidyl (Artane)

• Other medications
  • Sleeping medications (Ambien, Lunesta, Benadryl)
  • Antibiotics
  • Pain medications
  • Some anti-depressants (tricyclics)
  • Benzodiazepines (alprazolam, midazolam, lorazepam)
Treatment Options

• Only needs to be treated if it is bothersome or distressing

• Hallucinations are often non-threatening and insight is retained

• Keep rooms well-lit while awake, avoid clutter in rooms

• Reduce or remove potential causative medications
Treatment Options

• Vast majority of anti-psychotic medications will make motor symptoms of PD worse by blocking dopamine

• People with PD should **never** receive the following medications:
  • Haloperidol (*Haldol*)
  • Risperidone (*Risperdal*)
  • Olanzapine (*Zyprexa*)
  • Ziprasidone (*Geodon*)
  • Aripiprazole (*Latuda*)
Treatment Options

• If symptoms are bothersome, can treat with a few safer medications
  • Quetiapine, or Seroquel
  • Clozapine, or Clozaril
  • Pimavanserin, or Nuplazid – new as of April 2016
Delirium

• Acute confusional state

• Temporary symptoms of cognitive impairment and psychosis, with waxing and waning course

• Often occurs during hospitalization
  • New medications
  • Unfamiliar environment
  • Infections
Delirium

• Temporary state, but if it occurs, there is an increased risk of dementia in the future

• **Aware in Care** kit from National Parkinson Foundation
  
  • 1-800-4PD-INFO (473-4636)
  
  • [http://www.awareincare.org](http://www.awareincare.org)
  
  • Order it for free!
Summary

• Hallucinations and delusions are common in Parkinson’s disease
  • However, they are often mild and non-distressing

• Treatment should only occur if symptoms are serious, threatening
  • Need to be careful about which medication is chosen

• Hallucinations and delusions can also indicate a delirium – which may be a sign of an infection, constipation, dehydration, etc.
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 a 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
Technology in Parkinson’s Disease

MICHELLE FULLARD, MD, MS
UNIVERSITY OF COLORADO
OCTOBER 27, 2018
Wearable Devices

- Track symptoms
- Track response to medications
- Help tailor treatments
- Provide feedback to improve knowledge about disease
- Improve access to care
- Collect data in more natural setting
- Research
- Early diagnosis
Symptom tracking

**Clinic visits** – Unified Parkinson’s Disease Rating Scale (UPDRS)
- Subjective – user dependent
- Snapshot of symptoms

**Patient recall**
- Difficult to accurately recall fluctuating events (falls, freezing of gait, etc)

**Motor diaries**
- Cumbersome to complete
Parkinson’s KinetiGraph

FDA cleared

Measures bradykinesia (slowness) and dyskinesia (extra movements)

Medication reminder

Worn for 7 days then returned to clinician to download data

Part of Parkinson’s Foundation’s Outcomes Project

Other validation studies ongoing
MC10 Biostamp nPoint recently received FDA clearance.

Commercially available for research

Collects information on heart rate, respirations, activity, posture, and sleep
Fox Insight Wearables

- Wearable device and smartphone application
- Measures activity level, tremor, nighttime tracking and gait detection
- Electronic diary
- Pebble smartwatch large-scale deployment in Netherlands (Parkinson@Home study)
Verily Study Watch

Partnered with Michael J. Fox Foundation Parkinson’s Progression Markers Initiative (PPMI)

Monitors movement, heart rate, EKG

Battery life and storage up to 1 week
Great Lakes NeuroTechnologies

**Kinesia 360™**
- Wrist and ankle sensors
- Smartphone app
- Measures tremor, dyskinesia and mobility
- Electronic diary
Provides information to caregivers through remote monitoring

**Theora Connect** – wrist watch wearable

**Theora Link** – smart phone application with GPS tracking

**Theora Sense** – wall mounted home monitoring sensors, show activity within the home, alert to falls

**Theora Rest** – bed area monitoring

Alert to falls or wandering

---

The smartphone app that connects all Theora Care devices.

A smart wearable to connect with your loved one anywhere.

Wall-mounted situational awareness sensors for the home.

Intelligent, predictive bed-area specific monitoring.
Laser Technology for Freezing of Gait
Freezing of gait

Sudden inability to continue moving

Common triggers: walking through doorways, tight spaces and turning

Risk for falls

Break a freeze with cues:
- Visual
- Auditory
- Tactile

TheLancetTV
Freezing of gait

Sudden inability to continue moving

Common triggers: walking through doorways, tight spaces and turning

Risk for falls

Break a freeze with cues:
- Visual
- Auditory
- Tactile

TheLancetTV
Laser Cane

Provides visual input of laser to help break freeze

Press button or put weight on cane

https://www.youtube.com/watch?v=GN2Yzymuu4
U Step Walker

Reverse braking system
Laser light
Auditory cue
Covered in part by many insurance plans

https://www.youtube.com/watch?v=mirtZhHJSB4
Laser Shoes

Laser activates when foot is resting on the ground

Provides visual cue

**Clinical Study:** reduced freezing by nearly 50% and decreased duration of freezes

Barthel et. Al. *Neurology* 2018
Path Finder

Straps on to any shoe

Laser can be adjusted to each individual’s stride length

**Clinical studies:** 55% reduction in FOG

https://www.walkwithpath.com/science
Wearable motion sensing and visual cuing device

Automatically detects when user starts to freeze, then projects a red dot onto the ground

Visual cue helps break the freeze
Gyenno Gait Aid

Devices attach to the torso, legs and/or cane

Sensors detect freezing

Devices work together to generate visual, aural and tactile signals
Gait Aid

Augmented Reality

Earphones for auditory cues and glasses for visual cues

Practice 20-30 minutes per session to improve stride length and reduce freezing without the glasses

https://link.springer.com/chapter/10.1007/978-3-319-46062-8_10
Smartphone Apps in PD

Trevor Hawkins, MD
The Scope

• Estimated over 300,000 health apps
• 78,000 added in past year
• 3.6 billion downloads in the last year
• Recent study found over 100 related to PD

Linares-del Rey et al 2017
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
Possible uses include:

- Searching for best deals on medications
- Tracking medications
- Tracking symptoms/Diary
- Therapeutic
- Collecting patient’s data for studies
- Knowledge about disease
Pros and Cons of Smart Phone Apps

**Pros**
- Cheap, often free
- Easily accessible
- Wide variety

**Cons**
- No such thing as a free lunch
- May be lost on updates
- Not universal to all smart phones
Practical considerations

• Read the fine print!
  • Beware if asking for info especially if free
  • Recent study in 2017:
    • Of 72 apps for dementia only 46% had a privacy policy
Tour of the Apps
<table>
<thead>
<tr>
<th>Name</th>
<th>Distance</th>
<th>Coupon</th>
</tr>
</thead>
<tbody>
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<td>3.2 miles</td>
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<tr>
<td>Albertsons</td>
<td>2.0 miles</td>
<td>$18.54</td>
</tr>
<tr>
<td>Safeway</td>
<td>1.2 miles</td>
<td>$18.54</td>
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<td>King Soopers</td>
<td>1.2 miles</td>
<td>$18.79</td>
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<tr>
<td>Target (CVS)</td>
<td>1.5 miles</td>
<td>$20.55</td>
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<tr>
<td>CVS Pharmacy</td>
<td>1.7 miles</td>
<td>$29.68</td>
</tr>
<tr>
<td>Walgreens</td>
<td>0.2 miles</td>
<td>$34.11</td>
</tr>
</tbody>
</table>

$18.54 at Albertsons
Carbidopa / Levodopa 25mg/100mg 90 tablets

Member ID: HL1965682
RxGroup: 06340003
RxBIN: 600428
RxPCN: 05100000

Customer Help: (866) 921-7286
Pharmacist Help: (866) 921-7286

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Medication Reminder - Medisafe

- Medisafe
Medisafe

Manage your meds

Blood Glucose

Medication Adherence

92 mmol/L 11 May 2017 10:43
100 mmol/L 10 May 2017 10:44
110 mmol/L 9 May 2017 10:44

Weekly Adherence
May 05, 2017 – May 11, 2017

100% 100%

Taylor

Send

May 11, Thursday
• MISSED (0)

May 10, Wednesday
• MISSED (0)
Speech Aids

- Can help with volume, rate
- 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
iPhone Settings

Accessibility Touch Accommodations

Touch Accommodations

If you have trouble using the touchscreen, adjust the following settings to change how the screen will respond to touches.

You can triple-click the Home button at any time to turn Touch Accommodations on or off.

HOLD DURATION

Hold Duration

0.10 Seconds

The duration you must touch the screen before a touch is recognised.

IGNORE REPEAT

Ignore Repeat
Android- Touch Guard

Figure 1. Enhanced area touch working on existing Android application interface: (a) Touch area over single target. (b) Touch area intersecting with multiple targets. (c) Disambiguation in a magnified area of interest. (d) Disambiguation in a full screen list of captured target descriptions.
EasyCall- Help with dialing for those with tremor
Coming Soon! - Freezing of gait

- Stairway to Stability
Community Partner Award

Presented by Dr. Brian Berman
Lunch & Learn: Nutrition and Parkinson’s Disease  
Megan Frisk, MS, RD  
(in the lunch room)
Advanced Treatments for Parkinson Disease

Drew S. Kern, MD, MS
Assistant Professor
Departments of Neurology and Neurosurgery
October 27, 2018
Disclosures

- **Dr. Kern:** Served as an advisor for Colorado Clinical and Translational Sciences Institute (CCTSI) Data Safety Monitoring Board, Knoebel Institute for Healthy Aging, Michael J. Fox Foundation and AbbVie Pharmaceutics; received honorarium from Merz Pharma, AbbVie Pharmaceutics, and SAI-Med Partners, LLC; received grants from the Parkinson’s Society of Canada, University of Colorado Skin Disease Research Center and National Institutes of Health.
Treatments: Potentially disease modifying
Treatments: Potentially disease modifying

Olanow & Kordower, 2017
Antibodies

First-in-Human Assessment of PRX002, an Anti–α-Synuclein Monoclonal Antibody, in Healthy Volunteers

Dale B. Schenk, PhD,1† Martin Koller, MD, MPH,1 Daniel K. Ness, DVM, PhD,1 Sue G. Griffith, MD, PhD, MRCP,2 Michael Grundman, MD, MPH,3,4 Wagner Zago, PhD,1 Jay Soto, BS,1 George Atiee, MD,5 Susanne Ostrowitzki, MD, PhD,6 and Gene G. Kinney, PhD1∗

Schenk et al., 2016
Nilotinib Effects in Parkinson’s Disease and Dementia with Lewy Bodies


Pagan et al., 2016
Treatment of motor symptoms

1. Patient with Parkinson disease
   - Identify source of greatest disability
     - Tremor
     - Bradykinesia with slowness and impaired dexterity
     - Postural instability and/or gait impairment

2. See Figure 3
   - Age ≤60y
      - Initial treatment: Anticholinergic drug or β-blocker
         - Benefit? Yes: Monitor*
         - Benefit? No: Add or change to dopamine agonist*
         - If excellent tremor control, discontinue anticholinergic drug or β-blocker
         - Benefit? Yes: Monitor*
         - Benefit? No: Add to levodopa

3. If excellent tremor control, discontinue anticholinergic drug or β-blocker

4. Add clozapine

5. Consider surgery to treat refractory tremor

6. Consider surgery to treat refractory tremor

7. See Figure 4
   - Age >60y
      - Initial treatment: Dopamine agonist
         - Benefit? Yes: Monitor*
         - Benefit? No: Add or change to levodopa, anticholinergic drug, or β-blocker

8. Add or change to levodopa

9. Add dopamine agonist or COMT or MOABI

10. Good but motor fluctuations

11. None or suboptimal benefit

12. Benefit? Yes: Monitor*


14. Consider surgery to treat refractory tremor

Connolly & Lang, 2014
### Non-motor features

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

REM=rapid eye movement.

Table 3: Pharmacological treatments for non-motor symptoms

Kalia & Lang, 2015
**Pharmacological treatment**

**Carbidopa/Levodopa**
- Short-acting CD/LD (Sinemet)
- Sustained release CD/LD (Sinemet)
- ODT CD/LD (Parcopa)
- Extended CD/LD (Rytary)
- LD intestinal gel (Duopa)

**Dopamine agonists:**
- Pergolide (Permax)
- Ropinirole (Requip)
- Pramipexole (Mirapex)
- Rotigotine patch (Neupro)
- Apomorphine (Apokyn)

**COMT-inhibitors**
- Tolcapone (Tasmar)
- Entacapone (Comtan)

**NMDA receptor antagonist**
- Amantadine

**Anticholinergics**
- Trihexyphenidyl (Artane)
- Benztropine (Cogentin)

**MAO-B inhibitors**
- Selegiline
- Rasagiline (Azilect)
- Salfinamide
Narrowing therapeutic window
Timing of DBS

Chronic levodopa response is a narrowing of the therapeutic window

Alternate drug delivery systems
Carbidopa/levodopa enteral suspension (intestinal gel)
Subcutaneous carbidopa/levodopa
Collagen injections in vocal folds

- More then 90% of PD patients have voice impairments
- The current treatment
  - Speech therapy, Lee Silverman Voice treatment (LSVT)
- Investigational treatment
  - Vocal fold augmentation with collagen injections is being used safely for many disorders of vocal folds
Stereotactic neurosurgery for movement disorders
Lesions

- Radiofrequency
- Gamma Knife Radiosurgery
- Focused Ultrasound (FUS)
Radiofrequency
Gamma knife radiosurgery
Outcomes of gamma knife radiosurgery

Mean and SEM of each subscore. ***p < 0.001. All subscores improved after radiosurgery as compared with before radiosurgery for the blinded rater. GK = Gamma Knife.
Risks of gamma knife radiofrequency
MRI guided focused ultrasound
MRI guided focused ultrasound
FUS outcomes

1. No significant change in ipsilateral tremor, axial or vocal tremor
   - 79%
   - 75%

2. 2 patients appear to have worsened scores at 1 year compared with at 3 months
   - 55%

Elias et al., 2013
Lesions pros and cons

- **Pros**
  - Single procedure
  - No hardware
  - Cost?
  - Fewer appointments

- **Cons**
  - Permanent
  - Cannot be adjusted
  - Concern of bilateral procedures worsening cognition and speech
Deep brain stimulation

- First DBS surgery – early 1990s
- FDA approved in USA
  - Essential tremor – 1997
  - Parkinson disease – 2002
  - Dystonia – 2003
  - Obsessive Compulsive Disorder – 2009
DBS 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 electrodes

Programmers
DBS for Parkinson’s disease

Kern & Kumar, 2007

TABLE 2. Effects of Unilateral and Bilateral Deep Brain Stimulation (DBS) of Ventralis Intermeius Nucleus (Vim), Globus Pallidus Pars Interna (GPI), and Subthalamic Nucleus (STN), in Patients With Parkinson’s Disease

<table>
<thead>
<tr>
<th></th>
<th>Unilateral</th>
<th></th>
<th>Bilateral</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Vim</td>
<td>GPI</td>
<td>STN</td>
</tr>
<tr>
<td>Motor UPDRS “off”</td>
<td>10%-30%</td>
<td>~30%</td>
<td>25-50%</td>
</tr>
<tr>
<td>Motor UPDRS “on”</td>
<td>0%-10%</td>
<td>No change</td>
<td>0-39%</td>
</tr>
<tr>
<td>ADL UPDRS “off”</td>
<td>No change</td>
<td>-30%</td>
<td>-30%</td>
</tr>
<tr>
<td>ADL UPDRS “on”</td>
<td>No change</td>
<td>-30%</td>
<td>-30%</td>
</tr>
<tr>
<td>Dyskinesias</td>
<td>No change</td>
<td>-75%</td>
<td></td>
</tr>
<tr>
<td>Medication dosage</td>
<td>No change</td>
<td>No change</td>
<td>No change</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Vim</th>
<th></th>
<th>GPI</th>
<th>STN</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>30-50%</td>
<td>~50%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>~25%</td>
<td>~25%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>30-40%</td>
<td>30-50%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>30-40%</td>
<td>20-30%</td>
</tr>
<tr>
<td></td>
<td>No change</td>
<td>80-100%</td>
<td>60-100%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No change</td>
<td>No change</td>
<td>No change</td>
<td></td>
</tr>
</tbody>
</table>

Percentages represent average reduction in standardized rating scale scores, symptoms, and drug dosage compared with preoperative measurements for unilateral or bilateral DBS. Dashed lines indicate no reported data. All percentages represent average reductions at 6-12 mo postoperatively. “Off” represents assessments scored after overnight drug withdrawal and “on” indicates scores with drug treatment. Data compiled from references detailed in manuscript as well as our own experiences.
### Gpi & STN DBS: PD

<table>
<thead>
<tr>
<th>Off phase (n=125)</th>
<th>Baseline</th>
<th>12 months*</th>
<th>Mean change at 12 months from baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>GPI DBS</td>
<td>STN DBS</td>
<td>GPI DBS</td>
</tr>
<tr>
<td>UPDRS motor examination (range 0-108)</td>
<td>43.8 (13.5)</td>
<td>44.4 (15.5)</td>
<td><strong>32.4 (12.6)</strong></td>
</tr>
<tr>
<td>Clinical dyskinesia rating scale (range 0-28)</td>
<td>6.6 (1.2)</td>
<td>16 (2.0)</td>
<td>0.5 (1.6)</td>
</tr>
<tr>
<td>ALDS (range 0-100)</td>
<td>53.1 (11.8)</td>
<td>48.8 (23.8)</td>
<td>64.9 (22.0)</td>
</tr>
<tr>
<td>UPDRS activities of daily living (range 0-52)</td>
<td>17.9 (6.2)</td>
<td>18.2 (6.5)</td>
<td>14.0 (6.6)</td>
</tr>
<tr>
<td>Schwab and England scale (range 0-100, median [range])</td>
<td>50 (10 to 90)</td>
<td>40 (10 to 90)</td>
<td>60 (10 to 100)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>On phase (n=125)</th>
<th>Baseline</th>
<th>12 months*</th>
<th>Mean change at 12 months from baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>GPI DBS</td>
<td>STN DBS</td>
<td>GPI DBS</td>
</tr>
<tr>
<td>UPDRS motor examination (range 0-108)</td>
<td>16.0 (8.0)</td>
<td>17.0 (9.3)</td>
<td>16.0 (3.4)</td>
</tr>
<tr>
<td>Clinical dyskinesia rating scale (range 0-28)</td>
<td>5.3 (1.8)</td>
<td>4.8 (3.7)</td>
<td>2.3 (3.2)</td>
</tr>
<tr>
<td>Parkinson’s disease sleep scale (range 0-150)</td>
<td>8.1 (6.8)</td>
<td>8.1 (7.1)</td>
<td>90.8 (18.3)</td>
</tr>
<tr>
<td>ALDS (range 0-100)</td>
<td>84.2 (9.3)</td>
<td>81.1 (33.0)</td>
<td>83.4 (8.9)</td>
</tr>
<tr>
<td>UPDRS activities of daily living (range 0-52)</td>
<td>6.0 (4.9)</td>
<td>7.5 (5.1)</td>
<td>7.5 (4.4)</td>
</tr>
<tr>
<td>Schwab and England scale (range 0-100, median [range])</td>
<td>80 (40 to 100)</td>
<td>80 (30 to 100)</td>
<td>80 (30 to 100)</td>
</tr>
<tr>
<td>Quality of life questionnaire (range 0-185)</td>
<td>86.3 (7.8)</td>
<td>85.4 (23.2)</td>
<td>96.9 (19.1)</td>
</tr>
</tbody>
</table>

### Medication and DBS settings (n=125)

<table>
<thead>
<tr>
<th>Levodopa equivalent dose5</th>
<th>Baseline</th>
<th>12 months*</th>
<th>Mean change at 12 months from baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>GPI DBS</td>
<td>STN DBS</td>
<td>GPI DBS</td>
</tr>
<tr>
<td></td>
<td>1321 (637)</td>
<td>1254 (473)</td>
<td><strong>1127 (60.4)</strong></td>
</tr>
<tr>
<td>Voltage (V)</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Frequency (Hz)</td>
<td>--</td>
<td>--</td>
<td>127.5 (20.0)</td>
</tr>
<tr>
<td>Pulse width (µs)</td>
<td>--</td>
<td>--</td>
<td>72.0 (23.3)</td>
</tr>
<tr>
<td>Post-hoc analyses</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>

### 3-day diaries (n=90)

<table>
<thead>
<tr>
<th>Time in off phase (hours a day)</th>
<th>Baseline</th>
<th>12 months*</th>
<th>Mean change at 12 months from baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time in off phase</td>
<td>6.0 (3.2)</td>
<td>6.2 (3.5)</td>
<td>4.8 (3.6)</td>
</tr>
<tr>
<td>Time in on phase without dyskinesias (hours a day)</td>
<td>6.5 (3.6)</td>
<td>6.3 (4.4)</td>
<td>9.5 (3.7)</td>
</tr>
<tr>
<td>Time in on phase with dyskinesias (hours a day)</td>
<td>2.5 (2.5)</td>
<td>2.9 (2.8)</td>
<td>0.5 (1.2)</td>
</tr>
</tbody>
</table>

### Posture and gait (n=125)

<table>
<thead>
<tr>
<th>UPDRS motor examination items 27, 28, 29, 30 (range 0-16; off phase)</th>
<th>Baseline</th>
<th>12 months*</th>
<th>Mean change at 12 months from baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>GPI DBS</td>
<td>STN DBS</td>
<td>GPI DBS</td>
</tr>
<tr>
<td></td>
<td>6.1 (2.8)</td>
<td>7.3 (3.7)</td>
<td>5.4 (2.6)</td>
</tr>
<tr>
<td>UPDRS motor examination items 27, 28, 29, 30 (range 0-16; on phase)</td>
<td>Baseline</td>
<td>12 months*</td>
<td>Mean change at 12 months from baseline</td>
</tr>
<tr>
<td></td>
<td>GPI DBS</td>
<td>STN DBS</td>
<td>GPI DBS</td>
</tr>
<tr>
<td></td>
<td>2.9 (1.5)</td>
<td>33 (2.6)</td>
<td>3.5 (2.1)</td>
</tr>
</tbody>
</table>

Odekerken et al, 2013
### TABLE 1. Outcome parameters at baseline and 5- and 24-month follow-up

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>5-Month follow-up</th>
<th>24-Month follow-up</th>
<th>P&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Post hoc tests&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>mean</td>
<td>SD</td>
<td>mean</td>
<td>SD</td>
</tr>
<tr>
<td>NMSS total score&lt;sup&gt;d&lt;/sup&gt;</td>
<td>67</td>
<td>63.2</td>
<td>34.3</td>
<td>44.7</td>
<td>24.4</td>
</tr>
<tr>
<td>NMSS domains</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular&lt;sup&gt;c&lt;/sup&gt;</td>
<td>67</td>
<td>1.9</td>
<td>3.4</td>
<td>1.3</td>
<td>2.3</td>
</tr>
<tr>
<td>Sleep/fatigue&lt;sup&gt;d&lt;/sup&gt;</td>
<td>67</td>
<td>16.1</td>
<td>9.5</td>
<td>9.6</td>
<td>8.9</td>
</tr>
<tr>
<td>Mood/apathy</td>
<td>67</td>
<td>6.1</td>
<td>10.1</td>
<td>4.8</td>
<td>10.0</td>
</tr>
<tr>
<td>Perceptual</td>
<td>67</td>
<td>1.4</td>
<td>3.2</td>
<td>0.4</td>
<td>1.1</td>
</tr>
<tr>
<td>Problems/hallucinations&lt;sup&gt;c&lt;/sup&gt;</td>
<td>67</td>
<td>5.5</td>
<td>6.5</td>
<td>4.0</td>
<td>5.6</td>
</tr>
<tr>
<td>Attention/memory</td>
<td>67</td>
<td>12.0</td>
<td>9.9</td>
<td>8.4</td>
<td>7.2</td>
</tr>
<tr>
<td>Gastrointestinal&lt;sup&gt;d&lt;/sup&gt;</td>
<td>67</td>
<td>6.1</td>
<td>7.2</td>
<td>5.6</td>
<td>6.4</td>
</tr>
<tr>
<td>Urinary&lt;sup&gt;y&lt;/sup&gt;</td>
<td>67</td>
<td>11.1</td>
<td>9.0</td>
<td>8.3</td>
<td>7.2</td>
</tr>
<tr>
<td>Sexual function</td>
<td>67</td>
<td>11.4</td>
<td>9.0</td>
<td>8.3</td>
<td>7.2</td>
</tr>
<tr>
<td>Miscellaneous&lt;sup&gt;d&lt;/sup&gt;</td>
<td>67</td>
<td>11.4</td>
<td>9.0</td>
<td>8.3</td>
<td>7.2</td>
</tr>
<tr>
<td>PDQ-8 SF&lt;sup&gt;f&lt;/sup&gt;</td>
<td>65</td>
<td>33.3</td>
<td>17.4</td>
<td>23.3</td>
<td>14.4</td>
</tr>
<tr>
<td>SCOPA-A&lt;sup&gt;d&lt;/sup&gt;</td>
<td>61</td>
<td>12.8</td>
<td>6.0</td>
<td>8.7</td>
<td>4.9</td>
</tr>
<tr>
<td>SCOPA-B&lt;sup&gt;d&lt;/sup&gt;</td>
<td>61</td>
<td>7.4</td>
<td>3.4</td>
<td>5.4</td>
<td>2.8</td>
</tr>
<tr>
<td>SCOPA-C&lt;sup&gt;d&lt;/sup&gt;</td>
<td>67</td>
<td>5.0</td>
<td>3.0</td>
<td>2.4</td>
<td>2.4</td>
</tr>
<tr>
<td>LEDD (mg)&lt;sup&gt;d&lt;/sup&gt;</td>
<td>63</td>
<td>1121.6</td>
<td>515.2</td>
<td>632.6</td>
<td>358.4</td>
</tr>
</tbody>
</table>

LED, levodopa-equivalent daily dose; NMSS, Non-Motor Symptom Scale; NMSQ, Non-Motor Symptoms Questionnaire; PDQ-8, 8-Item Parkinson’s Disease Questionnaire; SCOPA-A, -B, and -C, Scales for Outcomes in Parkinson’s Disease-motor examination, -activities of daily living, and -motor complications, respectively.

<sup>a</sup>Friedman test or repeated-measures ANOVA when parametric test criteria were fulfilled.

<sup>b</sup>Wilcoxon signed rank or t-test when parametric test criteria were fulfilled.

*Significant difference between visits (P < 0.05, Friedman test or repeated-measures ANOVA).

Highly significant difference between visits (P < 0.001, Friedman test or repeated-measures ANOVA).

Post hoc comparisons (Wilcoxon signed rank or t-test):
- Baseline vs 5 months of follow-up: a, significant (P < 0.05); a<sup>f</sup>, highly significant (P < 0.001).
- Baseline vs 24 months of follow-up: b, significant (P < 0.05); b<sup>f</sup>, highly significant (P < 0.001).
- 5 vs 24 months of follow-up: c, significant (P < 0.05); c<sup>f</sup>, highly significant (P < 0.001).
STN DBS QoL

Deuschl et al, NEJM, 2006:
- Randomized, unblinded, controlled trial of STN DBS vs. best medical management
- 1° endpoints = change in QOL & mUPDRS
- Follow up of 6 months; 156 patients (78 DBS + 78 med)
- 25% QOL improvement in DBS vs. ~0% in best medical
- 41% mUPDRS improvement in DBS vs. none in best medical
- Conclusion: Significant & meaningful improvement in QOL for STN DBS vs. best med tx
Selection of surgical candidates
Movement disorders neurologists

- Multidisciplinary team
  - Neurology
  - Neurosurgery
  - Neuropsychology
  - Rehabilitation
  - Neuroradiology
- Cognitive function
- Optimized non-surgical treatments
- Social Support
- Realistic expectations
- Co-morbidities
Symptoms that do not respond to DBS

- Dementia
- Bulbar symptoms
  - speech & swallowing
- Pure balance
  - gait improves
- Autonomic dysfunction
# Parkinson’s DBS variables

<table>
<thead>
<tr>
<th>Awake versus asleep</th>
<th>Frame versus frameless</th>
<th>Microelectrode recording versus direct targeting</th>
<th>Traditional versus directional electrodes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Awake: Allows for direct testing</td>
<td>Frame: traditional, time-tested, highly accurate</td>
<td>Microelectrode recording: allows for direct testing and to check for side effects</td>
<td>Traditional: FDA approved since 1997; more familiar programming for most neurologists</td>
</tr>
<tr>
<td>Asleep: Good for patients with severe tremor, anxiety, PTSD</td>
<td>Frameless: more comfortable for patients, accuracy is comparable to frame</td>
<td>Direct targeting: image guidance used to place electrode (only for STN and Gpi)</td>
<td>Directional: minimize side effects by changing shape of electrical fields; conditional MRI approval in past month</td>
</tr>
</tbody>
</table>
Surgical procedure
Asleep DBS
Postoperative imaging
Programming

Contacts | Monopolar | Bipolar | Multipolar
--- | --- | --- | ---
Case (off or +) | 1-, Case (+) | 0-, 3+ | 0+, 1-, 2-, 3+

C1 d: -1V | C0/C2 d, C1 a/c: 1V, C1 d: -1V | C0 a-d: -1V

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UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS

University of Colorado Movement Disorders Center
Department of Neurology | School of Medicine

uchealth
Programming parameters

Pulse width (µs)  
[duration of each stimulus]

Amplitude (V)  
[intensity of stimulation]

Frequency (Hz)  
[number of pulses per second]
Selection of therapy
Thank you!

“Billy and I are playing doctor. So far, I’ve kept him waiting three hours.”
dance FOR every BODY

RECONNECT WITH YOUR BODY
Reconnect with Your Body

DANCE FOR PEOPLE WITH AND WITHOUT PARKINSON’S DISEASE

Mondays, 12:00-1:15pm in Broomfield
Wednesdays, 2:30-3:45pm in Arvada

artasaction.org
Parkinson’s Disease and Sleep

Stephen P Duntley, MD
The “Pillars” of Good Health

• Health Diet
• Regular Exercise
• Adequate Sleep
What is Sleep?

• Behavioral definition of sleep:
  • Quiescent state
  • Species specific stereotypic posture
  • Reduced response to stimulation
  • Rapid reversibility

• Other features:
  • Nonrandom circadian distribution
  • Homeostatic regulation
What is Sleep?

• Exceptions:
  • Arousability: unihemispheric sleep
  • Species specific posture: severe sleep deprivation
  • Quiescent state
    • Aquatic animals
    • REM sleep behavior disorder
  • Homeostasis: migratory birds?
Why Do We Sleep?
Drosophila

Graphic by www.nature.com
What is Required for Good Sleep?

• Appropriate timing
• Adequate duration
• Adequate continuity
• Other factors
Circadian Rhythm of Sleep Propensity
<table>
<thead>
<tr>
<th></th>
<th>1998</th>
<th>1999</th>
<th>2000</th>
<th>2001</th>
<th>2002</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 6 hours</td>
<td>12%</td>
<td>12%</td>
<td>13%</td>
<td>13%</td>
<td>15%</td>
</tr>
<tr>
<td>6 to 6.9 hours</td>
<td>23</td>
<td>22</td>
<td>24</td>
<td>18</td>
<td>24</td>
</tr>
<tr>
<td>7 to 7.9 hours</td>
<td>28</td>
<td>31</td>
<td>30</td>
<td>31</td>
<td>29</td>
</tr>
<tr>
<td>8 or more hours</td>
<td>35</td>
<td>35</td>
<td>33</td>
<td>38</td>
<td>30</td>
</tr>
<tr>
<td>Mean (# of hours)</td>
<td>na</td>
<td>7.0</td>
<td>6.9</td>
<td>7.0</td>
<td>6.9</td>
</tr>
<tr>
<td>Median (# of hours)</td>
<td>na</td>
<td>na</td>
<td>na</td>
<td>7.0</td>
<td>7.0</td>
</tr>
</tbody>
</table>
Percent Reporting Daytime Sleepiness Interfering with Daily Activities (at least a few days a month) by Age

18-29 year olds: 44%
30-64 year olds: 38%
65 or older: 23%
Percent Reporting Their Experiences While Driving During the Past Year (% Yes)

- Driven a vehicle while feeling drowsy
  - 1998: 51%
  - 1999: 53%
  - 2000: 51%
  - 2001: 62%
  - 2002: 57%

- Dozed off while at the wheel of a vehicle
  - 1998: 23%
  - 1999: 17%
  - 2000: 19%
  - 2001: 27%

- Had an accident because they dozed off or were too tired
  - 1998: 1%
  - 1999: 2%
  - 2000: 1%
  - 2001: 1%
  - 2002: 1%
Consequences of Inadequate Sleep

- Sleepiness
- Impaired judgment/cognition
- Impaired learning
- Impaired quality of life
- Impaired metabolism, increased inflammatory markers
- Increased mortality and morbidity
- Specific sleep disorders may add additional disorder specific consequences
Consequences of Inadequate Sleep: The Glymphatic System

• Sleep appears to assist in clearance of waste products from the brain
AB and Sleep in Mice

• In vivo microdialysis performed in wild type and human APP transgenic mice
• Diurnal variation in interstitial AB found
  • AB levels increased during dark period
  • AB levels significantly correlated with time spent awake
  • AB levels negatively correlated with time spent asleep
  • AB level negative correlation stronger with NREM than REM sleep
AB in Mice

- APP transgenic mice subjected to chronic sleep restriction for 20 hours daily for 21 days
- Sleep-restricted animals exhibited markedly greater AB plaque deposition compared to controls
- Almorexant treatment for 8 weeks decreased plaque formation
AB in Mice

- Reduction in Interstitial AB levels of 20% blocks plaque formation in gamma secretase inhibitor model
- Behavioral and pharmacological manipulations above resulted in 20-25% reduction in AB levels and could be clinically significant
AB in Humans

- CSF AB levels assessed in 10 healthy normal individuals
  - Lumber catheter for 33 hours
  - CSF AB vs interstitial AB delayed by about 6 hours
- Diurnal fluctuation in AB levels
  - AB levels increased throughout first day
  - AB levels decreased during night
  - AB levels increased again throughout second day
Consequences of Sleep Deficit: Severity of Deficits

- Meta-analysis of sleep deprivation studies suggests that sleep deprivation results in overall impairment of cognitive and motor performance, and mood comparable to that of 9th percentile of non-sleep-deprived subjects
  - Pilcher and Huffcutt 1996;19:318
Consequences of Sleep Deficit: Severity of Deficits

- Extended wakefulness compared to ethanol consumption at 30 minute intervals on performance of hand-eye coordination task
  - Performance declined in a near-linear fashion in both sustained wakefulness group after 10 hours and ethanol group at all levels
  - Each hour of wakefulness after 10 hours was equivalent to 0.004% rise in blood alcohol
    - 17 hours wakefulness = 0.05 BAC
    - 24 hours wakefulness = 0.1 BAC
      - Dawson and Reid Nature 1997;388:235
Classification of Sleep Disorders

• Dyssomnia
  • Disorders where complaint is about quality of sleep itself
    • Hypersomnia
    • Insomnia

• Parasomnia
  • Disorders where complaint is about unusual behavior arising from sleep
Excessive Sleepiness: Definition

• Drowsiness or sleep onset that occurs during inappropriate or undesirable times

• Must be differentiated from
  • Fatigue or tiredness
  • Decreased level of arousal secondary to generalized cerebral dysfunction
Excessive Sleepiness: Etiologies

• Dysfunction of Neurological sleep or wakefulness generating networks
• Sleep fragmentation
• Inadequate sleep time
• Circadian mechanisms
Insomnia: Definition

• Complaint of unsatisfactory sleep
  • Difficulty initiating sleep
  • Difficulty maintaining sleep
  • Early morning awakening

• Complaint of daytime consequences
  • Sleepiness or fatigue
  • Impaired concentration
  • Impaired social or occupational functioning

• Symptoms must occur in setting of sufficient opportunity for sleep
Insomnia: Epidemiology

• More common in women
• Severity and frequency of insomnia increases with age
• Increases with co-morbid medical conditions
Insomnia: etiologies

• When patients report sleeping problems, consider:
  • Medical disorders
  • Psychiatric disorders
  • Drug effects
  • Circadian rhythm disorders
  • Primary sleep disorders
  • Primary Insomnia
Parasomnias

• Arousal disorders
  • Confusional arousals
  • Sleep walking
  • Sleep terrors

• Sleep-wake transition disorders
  • Rhythmic movement disorder
  • Sleep starts
  • Sleep talking
  • Nocturnal leg cramps
Parasomnias

• Parasomnias associated with REM sleep
  • Nightmares
  • Sleep paralysis
  • REM sleep behavior disorder

• Other Parasomnias
  • Sleep bruxism, sleep enuresis, sleep related abnormal swallowing syndrome, nocturnal paroxysmal dystonia, sudden unexplained nocturnal death syndrome, primary snoring
Sleep and Parkinson’s Disease

• Prevalence of sleep problems in PD estimated 50-81%,
• Polysomnography reveals decreased total sleep time and decreased sleep efficiency, reduced REM latency, alpha intrusion
Sleep and Parkinson’s Disease: Causes of Sleep Disruption

- Inadequate control of motor symptoms
- Restless Legs and Periodic Limb Movements
- Nocturia
- Depression (up to 50% of PD patients)
- Chronic pain (up to 46% of PD patients)
Causes of Sleep Disturbance in PD

- Increased incidence of central and obstructive sleep apnea
- REM sleep behavior disorder (25-50% of PD patients)
- Nocturnal limb dystonia
- Sweating
- Nightmares
- Medications
Hypersomnia and PD

• About a third of PD patients complain of excessive daytime sleepiness
• PD and narcolepsy
• Dopamine agonists and sleep attacks
Polysomnography

- Procedures performed in sleep lab
  - All-night polysomnogram (ANPSG)
  - Multiple sleep latency test (MSLT)

- Indications for sleep lab evaluation
  - Symptoms of sleep apnea
  - Excessive sleepiness that does not respond to simple hygiene measures such as obtaining adequate time in bed
  - Symptoms specific for narcolepsy
  - Parasomnia of unclear etiology or potentially injurious
  - Insomnia and RLS are diagnosed clinically and polysomnography indicated only for specific questions or atypical or treatment resistant cases
Questions?