Brief Review of Advances in Diagnostic and Treatment Options for Parkinson’s Disease

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• This presentation does not, and is not intended to, provide medical advice
• This presentation reviews current concepts in diagnostic and treatment options for Parkinson’s Disease for general educational purposes on this website only
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What is Parkinson’s Disease (PD)?

- **Difficulty with *syndromic* diagnosis**
  - It’s a TRAP: Tremor, Rigidity, Akinesia, Posture
  - These symptoms can be seen in individuals without PD
  - Improved ability to diagnose PD beyond clinical symptoms is critical
  - Significant impact of incorrect diagnosis given expected doubling of PD to at least 10-15million patients in next 20yrs

- **Difficulty with *early* diagnosis**
  - Will become important to enable appropriate application of disease-modifying/slowing therapies when these emerge
Cellular Pathology of PD

- **Lewy Bodies (LBs)**
  - Intra-cytoplastic neuronal inclusions
  - LB density and distribution correlate with disease symptoms/severity

- **LB Core of Alpha-Synuclein (AS)**
  - Fibrillar AS aggregation in LBs

Emerging concept that AS-based diseases act as prion-like diseases

Cells grafted into LB brains develop LB pathology

*Lancet Neurol* 2010; 9: 1128–38
Pathologic Progression of PD
AS/LBs seem to spread from gut/olfactory system to inferior and then superior brain structures

Lancet Neurol 2010; 9: 1128–38
What is Parkinson’s Disease (PD)?

Summary

• Abnormal AS results in LB pathology
• AS/LB pathology contributes to damage in neurons and other nervous system cells
  - Multiple cellular mechanisms involved
• Nervous system damage results in the hallmark motor symptoms of PD, as well as more recently recognized non-motor symptoms
• Emerging evidence suggests these pathologic processes spread in a prion-like fashion from cell to cell in the nervous system
PD Diagnostic Tools
Past

- Structural MRI
  - Helpful in ruling out atypical or secondary causes
  - Normal in PD using standard structural MRI scans

Example of atypical parkinsonism (PSP) on structural MRI

*BMJ.* 2011; 342:d638
PD Diagnostic Tools Present

- Dopamine Transporter (DaT) Imaging (DaT-SPECT)
  - DaT level assay
  - Correlates with some PD symptoms
  - FDA-approved as an adjunctive diagnostic tool in certain circumstances

*J Nuc Med. 2010; 51:596-609*
PD Diagnostic Tools
Future?

• Potential imaging biomarkers (presently for research only and not appropriate for clinical use)
  - Positron Emission Tomography (PET)
    • Potential for automated, unbiased aid in diagnosis and tracking response to treatment
  - Transcranial Ultrasound (TUS)
    • Potential for inexpensive, non-invasive diagnostic aid
  - AS imaging
    • Potential for direct visualization of PD pathology
• Potential fluid biomarkers
  - CSF α-synuclein
  - Serum urate
Pharmacologic Treatment in PD Presently Available

• Motor therapies (most common)
  - MAO-B-Inhibitor: rasagiline
  - Dopamine agonist: pramipexole and ropinirole immediate- and extended-release preparations
  - Levodopa: immediate and continuous-release preparations, addition of entacapone
  - Most address brain dopamine-based deficiencies which are important for the hallmark motor features of PD
  - Others are available which do not primarily impact brain dopamine

• Non-motor therapies (most common)
  - Depression/Anxiety: bupropion, SSRI’s
  - Cognitive impairment: rivastigmine
  - Hallucinations: quetiapine
  - Restless legs and REM disorder: benzodiazepines, dopamine agonists
  - Address dopamine and non-dopamine-based deficiencies which are important for the non-motor features of PD
Pharmacologic Treatment in PD Future?

• >100 clinical trials ongoing for PD, including:
  - Levodopa intestinal gel for steady release
  - New neurotransmitter targets for symptom relief
  - New surgical options for symptom relief
    • Deep Brain Stimulator (DBS) enhancements
    • Non-DBS ablation options
  - Ultimate target of disease-slowing/stopping therapeutics remains the unmet goal
Deep Brain Stimulation (DBS) in PD

• Patient selection is important, and key criteria for consideration include:
  - Levodopa responsiveness and side effects
  - Symptom profile
  - Cognitive/behavioral profile
  - Brain structure profile

• Anatomic target selection is important, and includes:
  - Unilateral v. Bilateral implantation
  - GPi v. STN v. Thalamus v. clinical trial

• Future?
  - Combined anatomic targets
  - Novel anatomic targets (e.g. PPN)
  - Possibility for implantation early in PD

• Emerging consensus: one size does not fit all
PD Diagnostic and Treatment Options Summary

- Structural and DaT imaging can help inform diagnosis
- Emerging brain imaging and non-brain-imaging biomarkers hold promise to aid diagnosis
- Numerous dopaminergic and non-dopaminergic medications are available to address motor and non-motor PD symptoms
- DBS is an option for some carefully selected PD patients
- Emerging pharmacologic and surgical therapeutics hold promise to aid in PD symptomatic treatment
- The goal of disease-slowing/stopping therapy remains unmet, but >100 clinical trials are ongoing in PD so stay tuned...
Thank You

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