



PARKINSON'S DISEASE

SPOTLIGHT ON YOUNG ONSET PARKINSON'S DISEASE: EXPLORING TREATMENT & MANAGEMENT OPTIONS

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WELCOME AND INTRODUCTIONS



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PRESENTATION



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FINANCIAL DISCLOSURES

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Speaker's Bureau: none

Equity & Consulting Agreements: none



YOUNG ONSET: DEFINITION

Onset at:

≤ 49 yrs

≤ 45 yrs

≤ 40 yrs

< 20 yrs = juvenile onset

CARDINAL FEATURES

- Resting Tremor: yo: → < tremor
- Bradykinesia/akinesia
- Rigidity
- Postural Instability
- Abnormal Gait



FREEZING: PRECIPITATING FACTORS

- Gait initiation
- Turning
- Narrow passages
- Dual tasking
- Stress

STRATEGIES TO IMPROVE GAIT

- Tango
- Waltz
- Foxtrot
- Tai Chi
- Big steps
- External cues



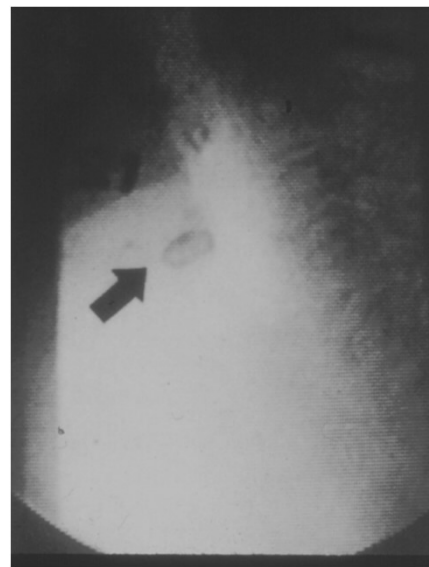
Earhart et al, 2009



OROPHARYNGEAL PROBLEMS

- Speech Abnormalities
 - Hypophonic, hyperkinetic
- Swallowing Problems

SWALLOWING PROBLEMS





AUTONOMIC PROBLEMS

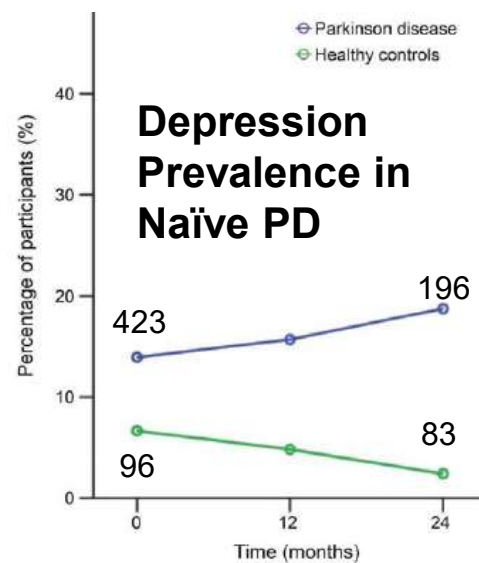
- Drooling
- Bowel/Bladder problems
- Orthostasis (lightheadedness)
- Sexual dysfunction
- Heat intolerance/sweating
- Convergence problems

PSYCHIATRIC PROBLEMS

- Apathy (20%)
- Mood Disorders
- Anxiety disorders
- Psychosis

yo: → > depression

de la Riva et Neurol 2014

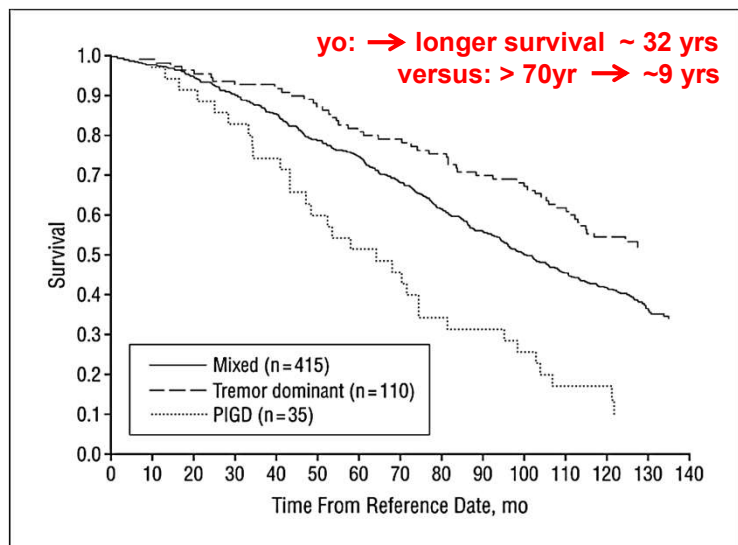




ASSOCIATED CONDITIONS

- REM Behavior Disorder
 - “acting out” dreams
- Restless Legs
- Reduced Olfaction

PROGRESSION





AGE OF ONSET

Community study:

Average onset: 60-70 yrs
< 45 yrs 3.6%

Tertiary care center:

Average onset: 61 yrs
< 40 yrs 8%

HOW COMMON IS PD?

AGES	PREVELANCE*
65-69	.55%
70-74	1.1%
75-79	1.9%
80-84	2.8%
85+	2.9%

(Males:Females = 1.6)



PREVALENCE: ETHNICITY

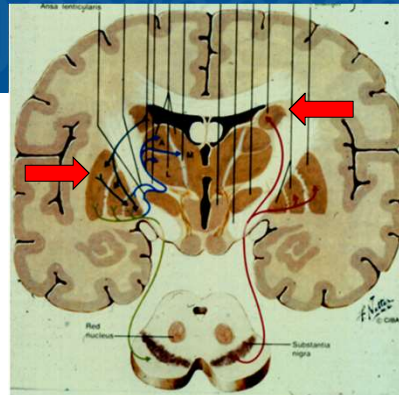
GROUP	PREVALENCE*	RATIO (CI)
White	1.67%	(ref)
Black	1.04%	.58 (.575-.581)
Hispanic	1.54%	.89 (.881-.896)
Asian	1.14%	.62 (.657-.631)

*U.S. Medicare Beneficiaries

* Wright-Willis et al,
Neuroepidemiology, 2010

PATHOLOGY

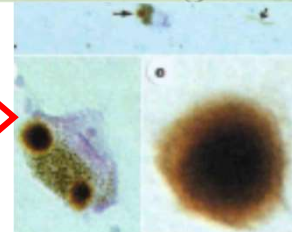
1. α -synuclein deposition
2. dopamine neuron loss
3. Striatal DA loss



Normal

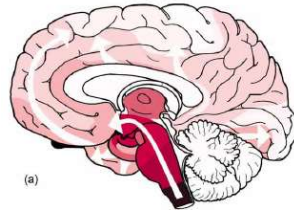


PD





DEMENTIA: CORTICAL PATHOLOGY



α -synuclein spread

Braak, Neurobiol Aging 2004

yo: \rightarrow < dementia

α -synuclein only	α -synuclein & A β	α -synuclein & A β & Tau
12	20	1
Lewy pathology	Lewy & A β pathology	Lewy & Alzheimer's

Kotzbauer P et al, JAMA Neurol 2012

GENETICS

Alpha-synuclein: autosomal dominant chromosome 4 (duplications, triplications & missense mutations)

GBA mutations (Gaucher mutations)

Lewy bodies

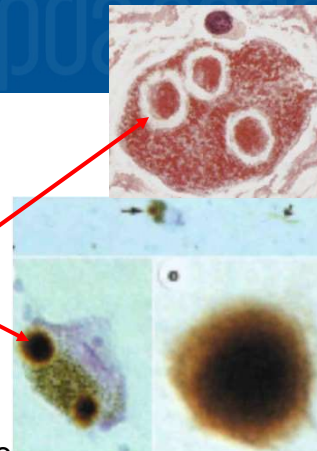
(yo: \rightarrow > + family history)

parkin: autosomal recessive, juvenile onset, chromosome 6

LRRK2 – auto domin; most common gene defect – up to 30 -40% (North African Arabs) & 19% (Ashkenazi Jews)

DJ-1: chromosome 1, auto recess, rare young onset PD

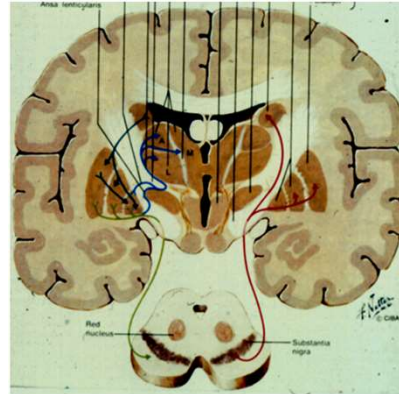
Pink1: auto recessive, rare early onset, chromosome 1p36



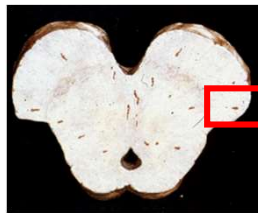
Nalls MA et al, Nat Genetics 2014



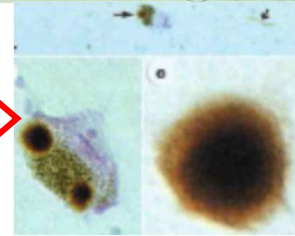
What is Parkinsonism?



Normal



PD



Lewy body

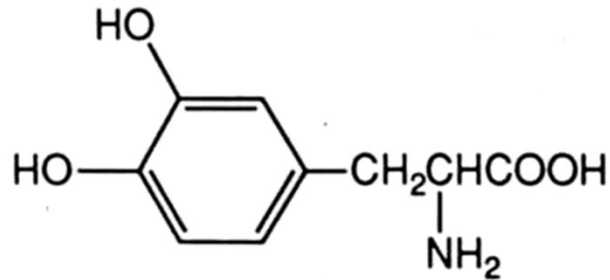
DIFFERENTIAL DIAGNOSIS

- Idiopathic Parkinson disease
 - Genetic etiologies
- Drug induced parkinsonism
- Other degenerative parkinsonism
- Wilson's disease



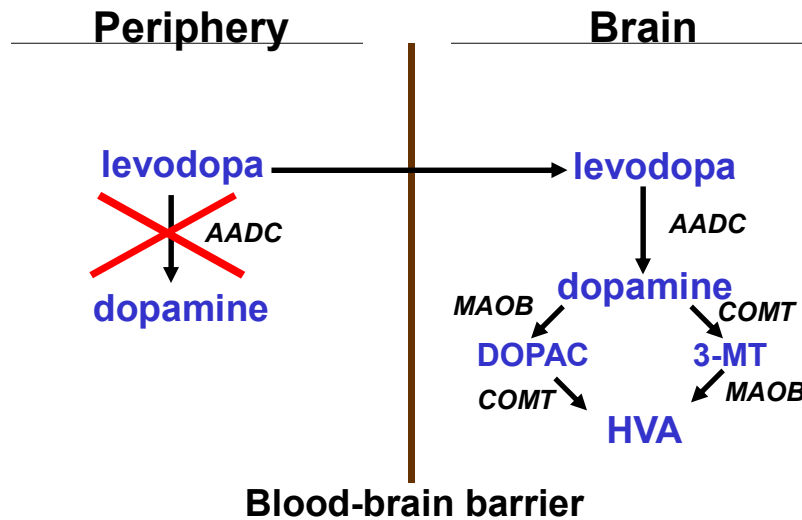
Levodopa dopamine

aaa decarboxylase



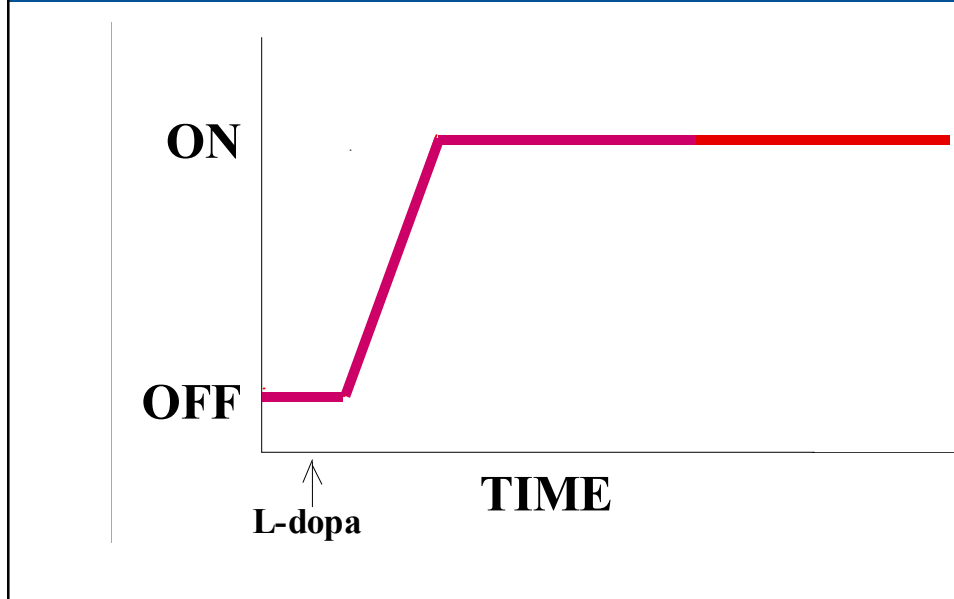
LEVODOPA

CARBIDOPA INHIBITS DECARBOXYLASE



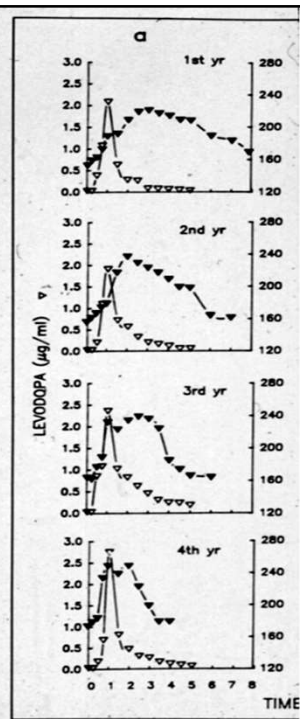
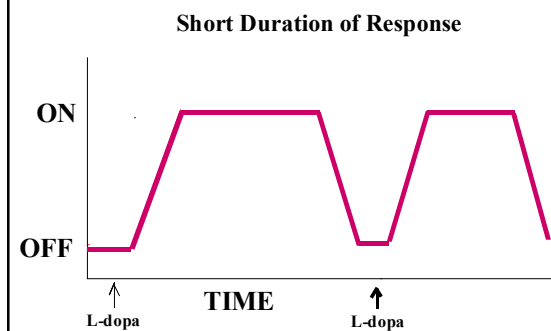


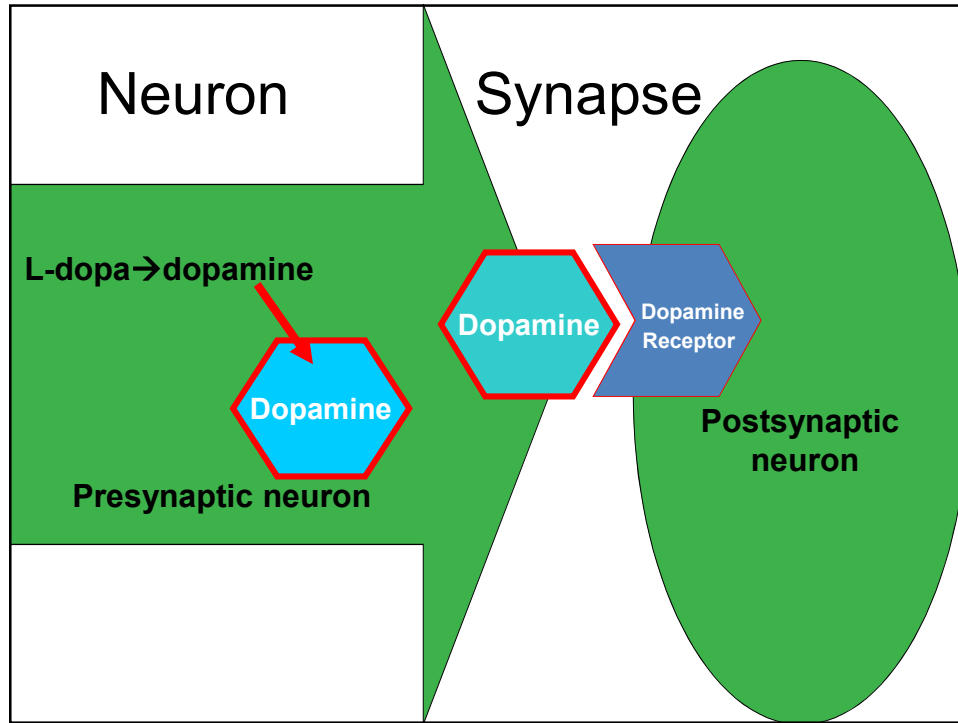
TREATMENT RESPONSE: EARLY



DURATION OF BENEFIT

-decreases as disease progresses





DOPAMINE AGONISTS

- Orthostasis
- Psychosis
- Compulsive behaviors
- Daytime sleepiness
- Daytime somnolence/insomnia
- GI upset

Bromocriptine
Pramipexole
Ropinirole
Rotigotine

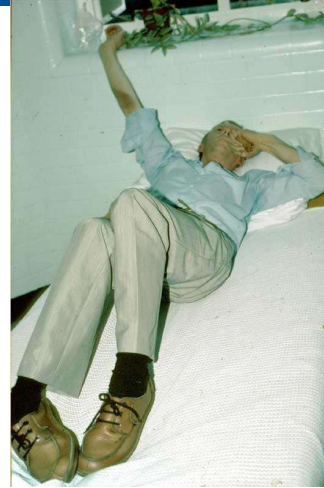
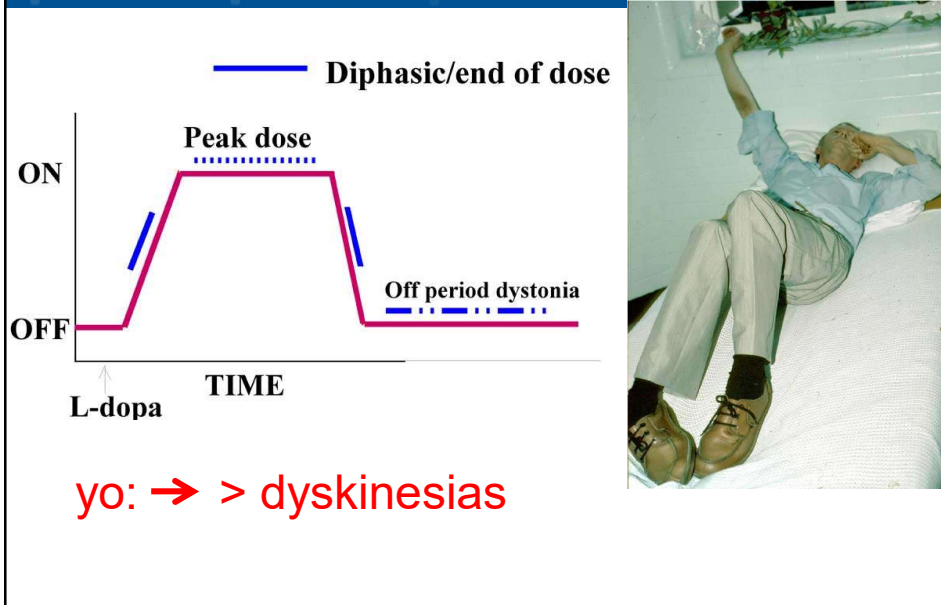
- Transcutaneous administration

Apomorphine

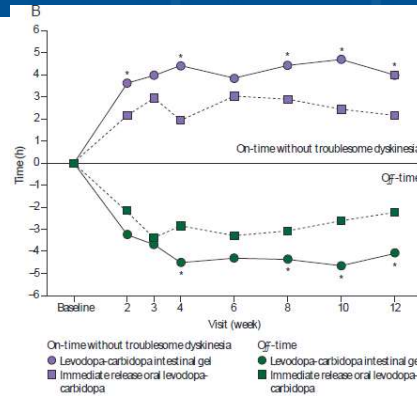
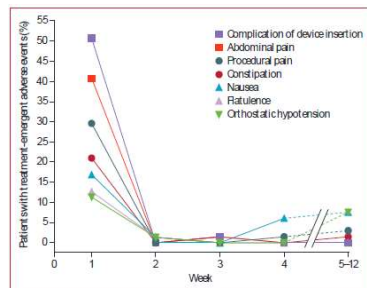
- Rapid action
- Injection
- Nausea & vomiting



DRUG RESPONSES: DYSTONIA & DYSKINESIA



LEVODOPA GEL VIA PEG

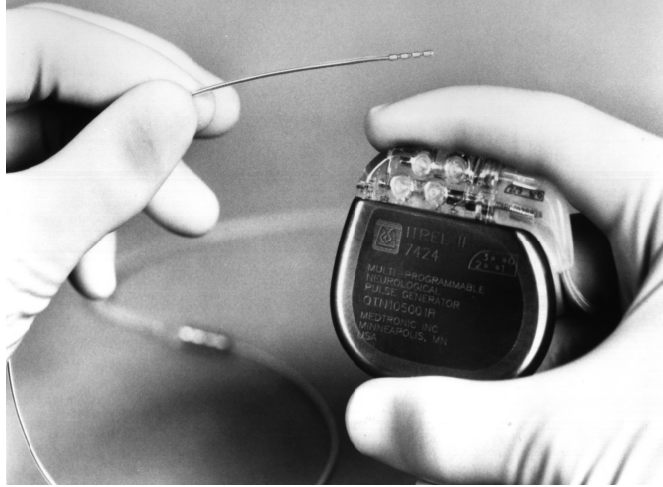


Olanow et al, 2013
Abbruzzese et al, 2012

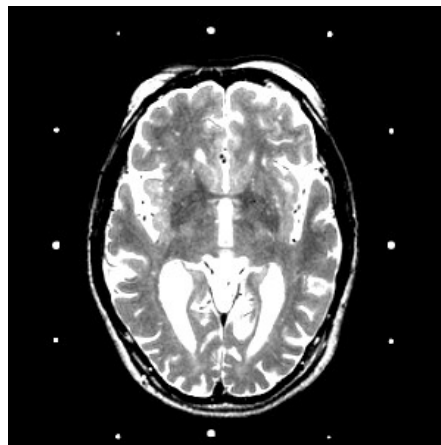
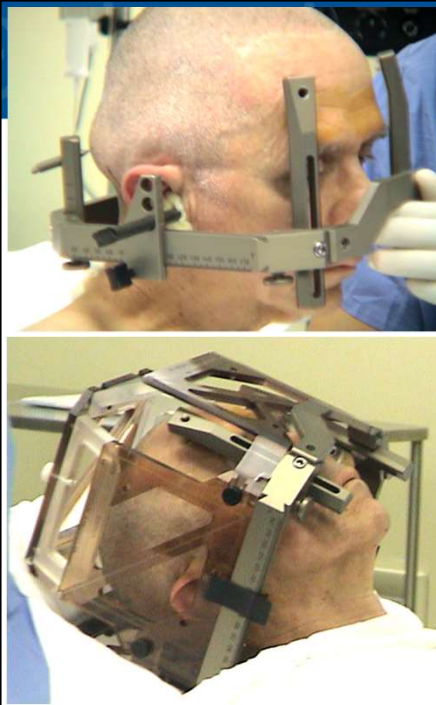


DEEP BRAIN STIMULATION

Hardware

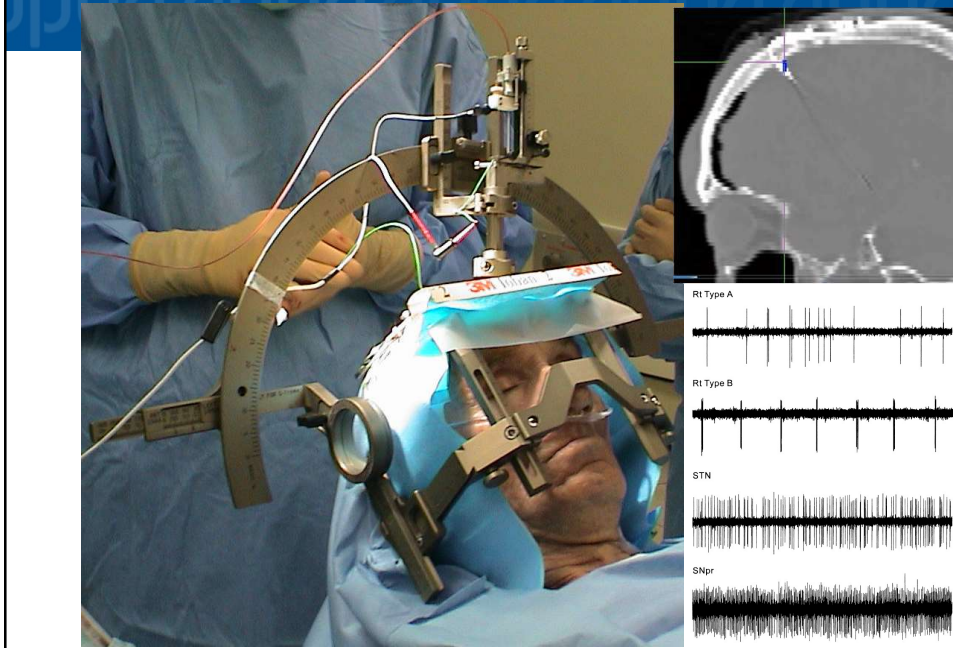


STEREOTAXIC FRAME

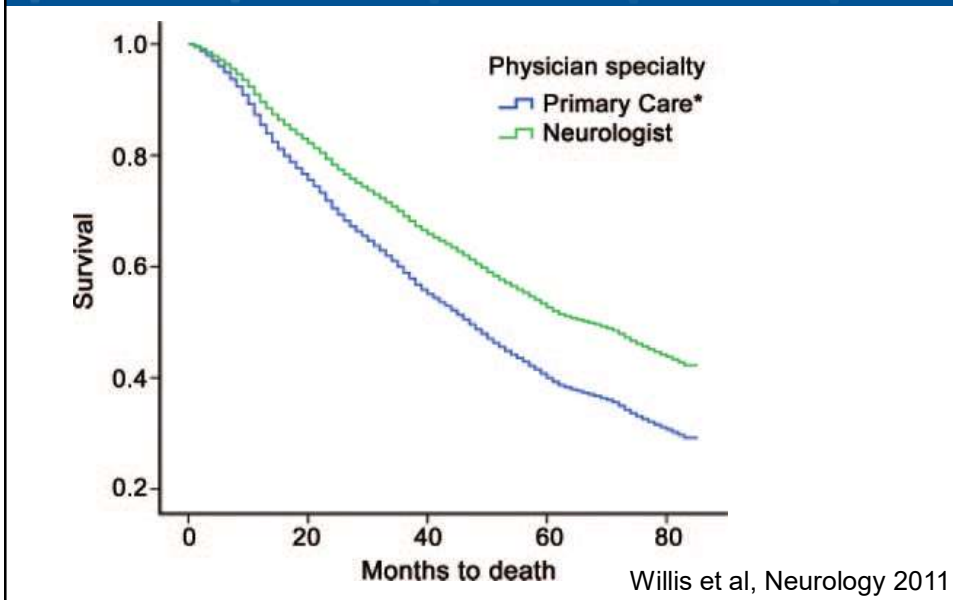




MICROELECTRODE TARGETING



TREATING PHYSICIAN EFFECTS





YOUNG ONSET CLINICAL FEATURES

- < tremor at onset
- > family history
- > depression
- > dopa-induced dyskinesias
- < dementia
- > survival ~32 yrs vs 9 (> 70)

QUESTION & ANSWER



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CLOSING REMARKS



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**FOR ADDITIONAL INFORMATION,
ANSWERS TO YOUR QUESTIONS,
OR FOR ADDITIONAL RESOURCES**

Please visit our website
apdaparkinson.org

Or call us
1-800-223-2732