DON'T *MIND* THIS OLD THING: THE AGING BRAIN

PARKINSON'S DISEASE

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Lecture 2

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STATISTICS ON PARKINSON'S

- Approximately 60,000 Americans diagnosed each year
- As many as 1 million Americans with Parkinson's disease (PD)
- More than 10 million people living with PD worldwide
- Incidence increases with age, but ~4% of people with PD are diagnosed before the age of 50
- Men and 1.5x likely to have PD than women

Parkinson's Disease Foundation

www.pdf.org

www.parkinson.org

NATIONAL PARKINSON® FOUNDATION

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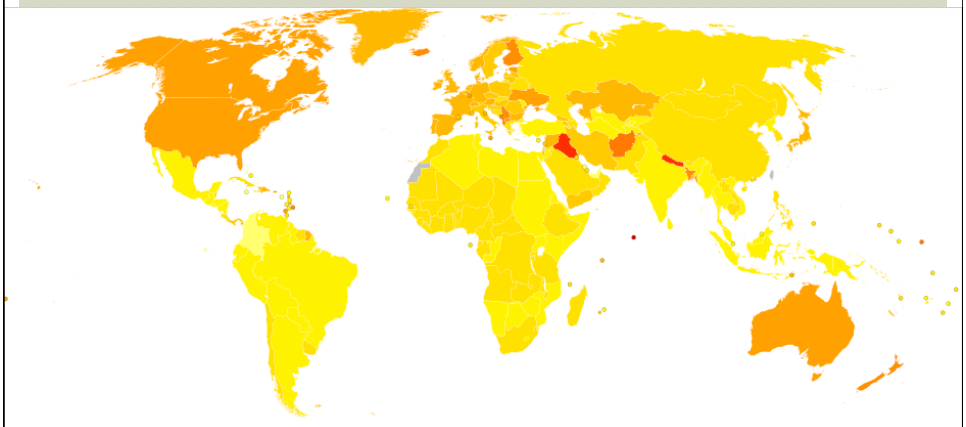
GLOBAL PARKINSON'S

- Incidence of PD highest in countries with longest life expectancies



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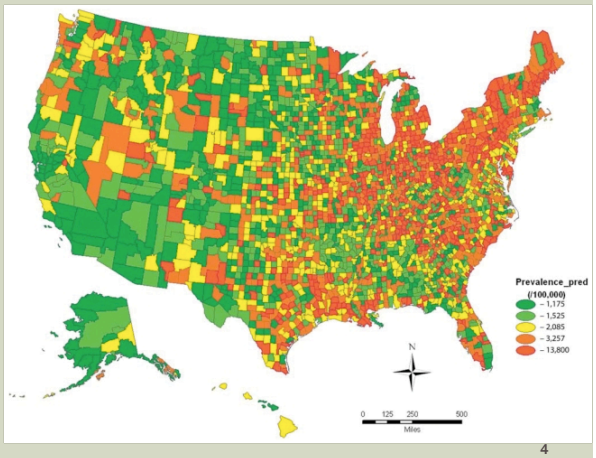
PD IN THE UNITED STATES

- 2010, Washington University
- 36 million Medicare recipients
- PD more common in Midwest and Northeast
- 2x more likely in Caucasians and Hispanics compared to African Americans and Asians

Geographic clusters for PD in US



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PD IN THE UNITED STATES

- Hypothesized that hotspots occur in Midwest and Northeast because these areas of the country are most involved in medal processing and agriculture
  - **Environmental risk**
- Genetic factors could contribute to protection from PD between gender and races
  - **Genetic background**

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RISK FACTORS FOR PD

1. **Advancing age. Aging is the single strongest risk factor for PD.**
2. **Gender**. Males are more likely to get PD then females (suggests a protective effect of estrogen).
3. **Exposure to environmental toxins**. Continued exposure to pesticides increased risk of PD (agriculture, farming).
4. **Heredity**. Having one or more close family members with PD increases your chances of also having PD (minimal).
5. **Genetic factors**. Mutations in specific genes have been linked to PD.
6. **Head injury**. Traumatic brain injury (loss of consciousness) has been associated with an increased risk of developing PD years after injury.

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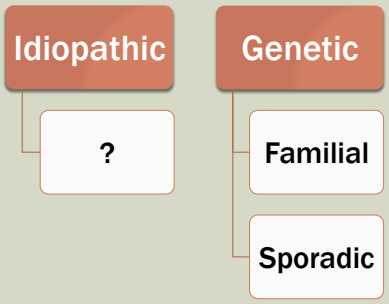
FORMS OF PARKINSON'S DISEASE

- Majority of PD cases are **idiopathic** – there is no known genetic cause
- Only 10% of PD cases are linked to a **genetic** cause
  - **Familial** – inherit disease gene
  - **Sporadic** – random mutation in a gene



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GENETIC LINKS TO PD

PARK	Gene	Inheritance	Phenotype	Pathology
1	α-Synuclein	Dominant	Complex mix of Parkinsonism and dementia	Lewy bodies **1997**
2	Parkin	Recessive	Juvenile onset Parkinsonism	Nigral cell death, some with Lewy body pathology
6	PINK1	Recessive	Juvenile onset Parkinsonism	One reported case with Lewy bodies
7	DJ1	Recessive	Juvenile onset Parkinsonism	No reported pathology
8	LRRK2	Dominant	Typical Parkinson's disease	Mixed pathology: Lewy bodies tangles and TDP43
9	ATP13A2	Recessive	Juvenile onset Parkinsonism	No reported pathology
14	PLA2G6	Recessive	Juvenile onset Parkinsonism dystonia	Lewy bodies
15	FBXO7	Recessive	Juvenile onset Parkinsonism	No reported pathology
	GBA	Dominant	Typical Parkinson's disease	Lewy bodies
	PANK2	Recessive	Juvenile onset Parkinsonism dystonia	Lewy bodies in NBIA-1 cases
	Tau	Dominant	Frontal temporal dementia with Parkinsonism	Tangles

UCHL1, HTRA2, NR4A2 have all been linked to Parkinson's disease but are of uncertain provenance. The causative genes for PARK 3, 10, 11, 12, 13, 16 remain to be identified.

- Multiple genes have been identified that *contribute* to PD
- Typical Parkinsonism – Onset in 60's
- Juvenile onset Parkinsonism – diagnosed before the age of 40 or 50
- Juvenile onset more strongly linked to genetic cause
- LRRK2 most common cause of PD in genetic cases

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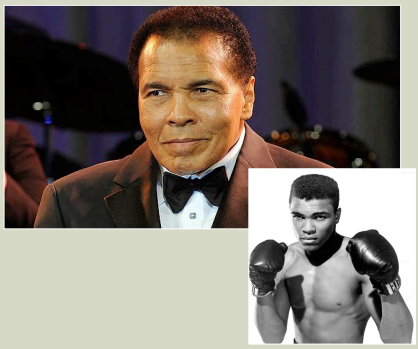
PARKINSON'S DISEASE

Michael J. Fox

Successful Actor

Juvenile Onset Parkinsonism

Muhammad Ali



Boxing Champion

Typical Parkinsonism

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MICHAEL J. FOX AND PD

28 years old
Symptom:
Twitching pinky

→

29 years old (1991)
Diagnosed with PD

- Very early onset
- Hid his diagnosis from the public for years
- PD is a slowly progressing neurodegenerative disease
- Able to control his symptoms with medication
- Spin City (1996)- Emmy and 3 Golden Globes
- 1998 – retired from acting, became an advocate for PD research

THE MICHAEL J. FOX FOUNDATION FOR PARKINSON'S RESEARCH

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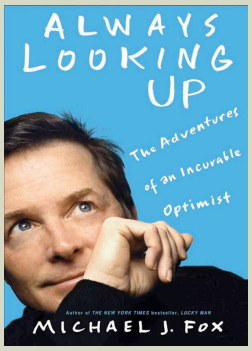
MICHAEL J. FOX AND PD

- PD continued to progress and the motor symptoms that characterize the disease worsened



https://www.youtube.com/watch?v=ECkPVTZIfP8

"Grasping the toothpaste is nothing compared to the effort it takes to coordinate the two-handed task of wrangling the toothbrush and strangling out a line of paste onto the bristles. By now, my right hand has started up again, rotating at the wrist in a circular motion, perfect for what I'm about to do. My left hand guides my right hand up to my mouth, and once the back of the Oral-B touches the inside of my upper lip, I let go. It's like releasing the tension on a slingshot and compares favorably to the most powerful state-of-the-art electric toothbrush on the market."

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PD IS A MOVEMENT DISORDER

"At the turn from our bedroom into the hallway, there is an old full-length mirror in a wooden frame. I can't help but catch a glimpse of myself as I pass. Turning fully toward the glass, I consider what I see. This reflected version of myself, wet, shaking, rumpled, pinched, and slightly stooped, would be alarming were it not for the self-satisfied expression pasted across my face."

- Michael J. Fox, *Always Looking Up*

- Passages illustrate his struggles with the most common motor symptoms

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Motor symptoms of PD

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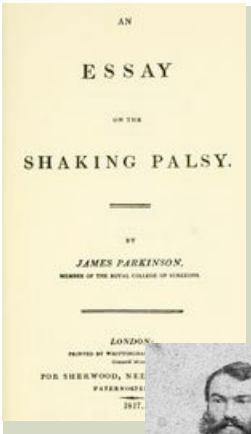
PD IS A MOVEMENT DISORDER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ESSAY

ON THE

SHAKING PALSY.

BY

JAMES PARKINSON.

- 1817- James Parkinson describes the disease
- *Paralysis agitans* (shaking palsy) due to characteristic motor symptoms
- Most common movement symptoms:
  1. **Tremor**
  2. **Rigidity**
  3. **Bradykinesia**
  4. **Balance and posture**

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MOVEMENT SYMPTOMS OF PD

1. **Tremors/Shaking**
   - Often first signs of the disease
   - Begin in hands or feet
   - "Resting tremors" can disappear after voluntary movement
   - Pill-rolling hand tremor characteristic of disease

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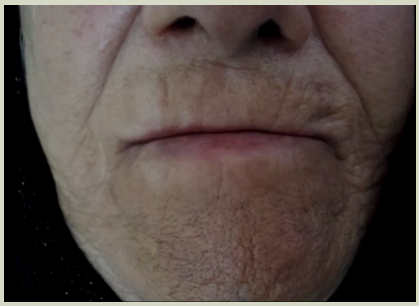
MOVEMENT SYMPTOMS OF PD

- Tremors/Shaking
  - Spread elsewhere with disease progression

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MOVEMENT SYMPTOMS OF PD

2. **Rigidity/Stiffness**
   - Occurs because muscles often contract involuntarily
   - Stay rigid for an extended period of time
   - Limits mobility
   - Constant or intermittent
   - Sustained contractions are painful

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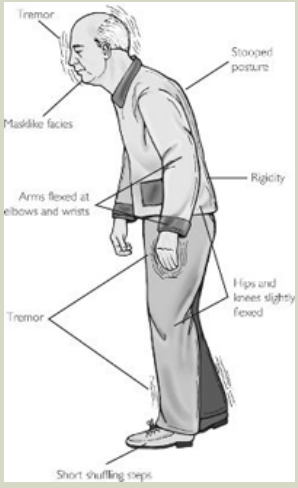
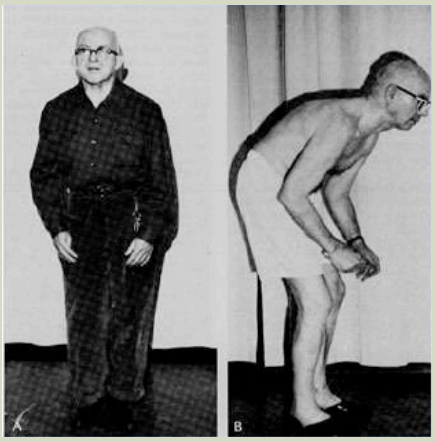
MOVEMENT SYMPTOMS OF PD





- Examples of rigidity

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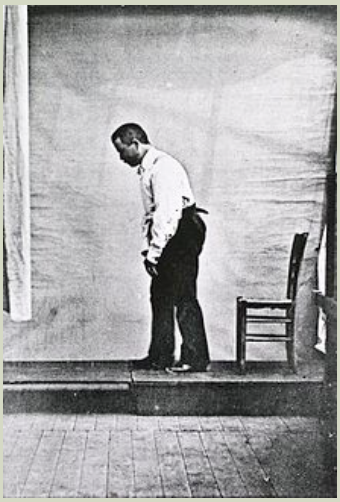
MOVEMENT SYMPTOMS OF PD



A man with PD displaying a flexed walking posture pictured in 1892.

Nouvelle Iconographie de la Salpètrière, vol. 5., p.226

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MOVEMENT SYMPTOMS OF PD

3. **Bradykinesia** → slowing of movement
   - Slower at daily motor tasks (ie: buttoning a shirt, brushing teeth, cutting food)
   - Change in gait- Parkinsonian shuffle
   - Reduction in spontaneous movement
     - Dysarthria: reduced speech volume and intelligibility
     - Dysphasia: difficulty swallowing
   - Can be provoked into quick action by external stimuli

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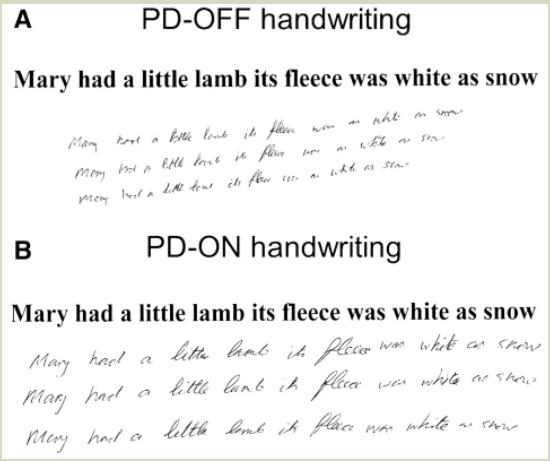
MOTOR SYMPTOMS OF PD

- Micrographia – progressive shrinking of handwriting
  - Early sign of the disease



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MOTOR SYMPTOMS OF PD

- Shuffle

- Gait "Freezing"

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MOTOR SYMPTOMS IN PD

4. **Balance and posture**
   - Problem late stages of disease
   - Concern about falls

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5 STAGES OF PD

- PD impacts everyone differently. Even so, there are typical patterns of progression that are defined in stages.

Stage 1
- Mild symptoms that generally do not interfere with daily activities
- Tremors occur on a single side of the body.
- Some changes in facial expression, posture, and walking.

Stage 2
- Tremor, rigidity and other movements symptoms affect both sides of the body.
- Live alone, but daily tasks become slower and more difficult

Stage 3
- Loss of balance and slowness
- Independent, but symptoms impair daily living activities like dressing and eating

Stage 4
- Symptoms are severe and limiting
- Stand without assistance but movement may require a walker
- Help required for daily activities and unable to live alone

Stage 5
- Stiffness in legs makes it difficult to walk, wheelchair required
- Around-the-clock care required for activities
- Severe non-motor symptoms such as depression and hallucinations can occur

www.parkinson.org

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MOTOR SYMPTOMS VIDEO

- https://www.youtube.com/watch?v=aOSB6ytMk20

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NON-MOTOR SYMPTOMS OF PD

- Can occur prior to motor symptom onset
- Non-motor symptoms can be as troublesome as motor symptoms and impact activities of daily living
- Often under-recognized by health care professionals

- Constipation
- Urinary dysfunction
- Excessive sweating
- Dementia
- Executive function
- Weight changes
- Sexual dysfunction

- Depression
- Anxiety
- Sleep disturbances
- Fatigue
- Pain
- Reduced sense of smell and taste
- Orthostatic Hypotension

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NON-MOTOR SYMPTOMS OF PD

- UPDRS questionnaire after diagnosis
- Parts of the PD brain might be affected before motor symptom onset
- Frequency of non-motor symptoms increases with disease severity

Table 1. Proportion of affected PD patients

Nocturia	59.5%
Urinary urgency	53.6
Constipation	50.2
Blues/depression	48.2
Insomnia	44.3
Concentration	44.0
Anxiety	43.4
Memory	43.1
Restless legs	40.3
Dribbling	40.1

Table 2. Non-motor symptoms suggested as preclinical (motor) characteristics in PD

Strong evidence
> Constipation
> Olfactory deficit
> REM sleep behaviour disorder
> Depression

Suggested links (weaker evidence base)
> Restless legs syndrome
> Apathy
> Fatigue
> Anxiety

(Table adapted from Chaudhuri *et al*, 2006[5])

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What happens in the brain that leads to these symptoms?

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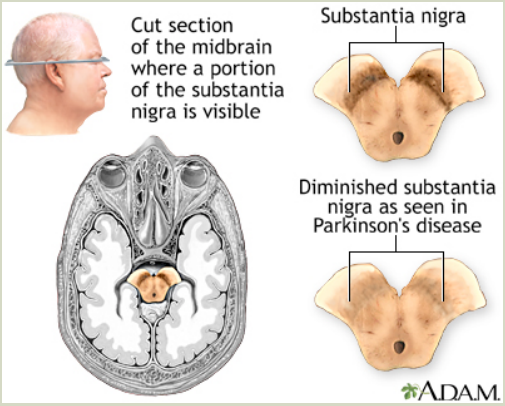
THE PD BRAIN

- Motor symptoms arise from death of neurons in the **substantia nigra** (black substance)
- Located in the brain stem



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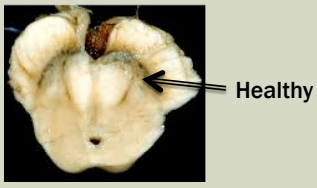
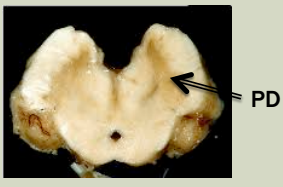
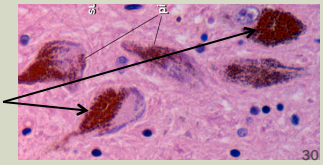
DOPAMINERGIC NEURONS





- Substantia nigra neurons contain neuromelanin
- Visualize without staining
- Neurons make the chemical messenger DOPAMINE
- Neurons communicate with movement centers using dopamine
- Dopamine is crucial for voluntary movement



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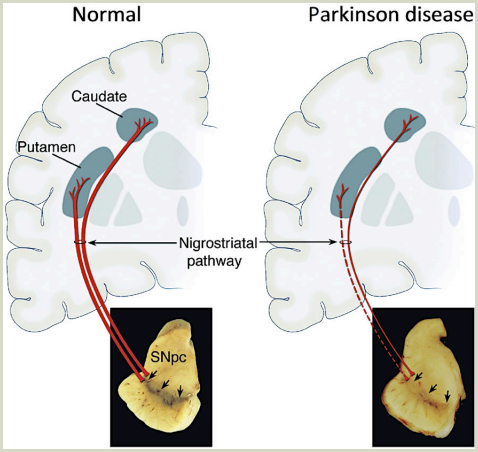
BRAIN AREAS COMMUNICATE WITH DOPAMINE



- Substantia nigra neurons produce dopamine
- Axons project to the Caudate and Putamen
- Collectively referred to as the "striatum"
- When neurons die, dopamine is no longer delivered

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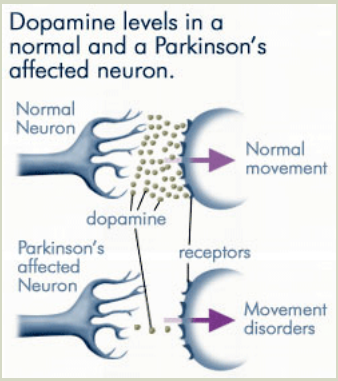
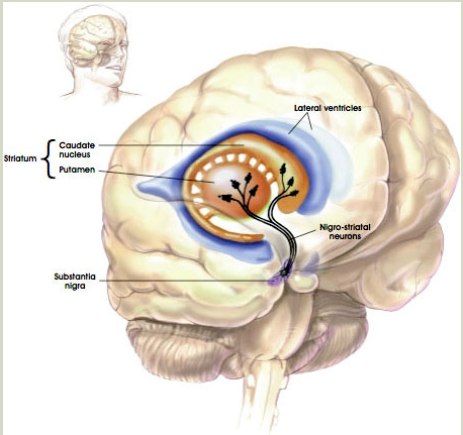
DOPAMINE LOSS IN THE STRIATUM RESULTS IN MOTOR SYMPTOMS





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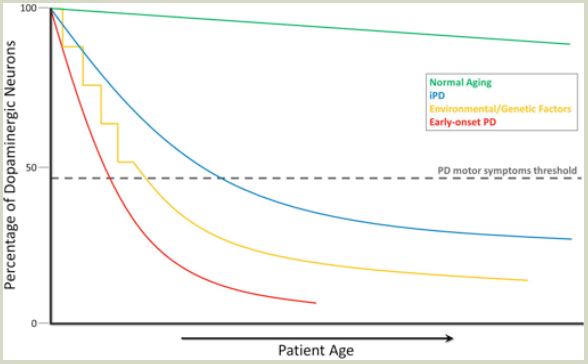
DOPAMINE NEURON LOSS LEADS TO PD

- As we age, dopamine neurons die
- Selectively vulnerable
- Rate of 5-10% every decade
- Gradual loss has little impact on motor function



- In PD, neurons die at a much faster rate
- When ~70% of neurons have died, motor problems begin to appear

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WHY DO DOPAMINE NEURONS DIE QUICKLY IN PD?

We don't know.

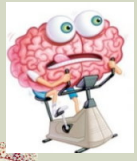
DA neurons fire rhythmically

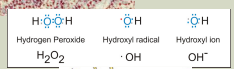
Burn a lot of energy, under metabolic stress

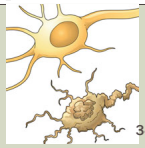
Impacts mitochondria (energy producers of cells)

Oxidative stress produces reactive oxygen species (chemical species containing oxygen)

ROS causes cell death







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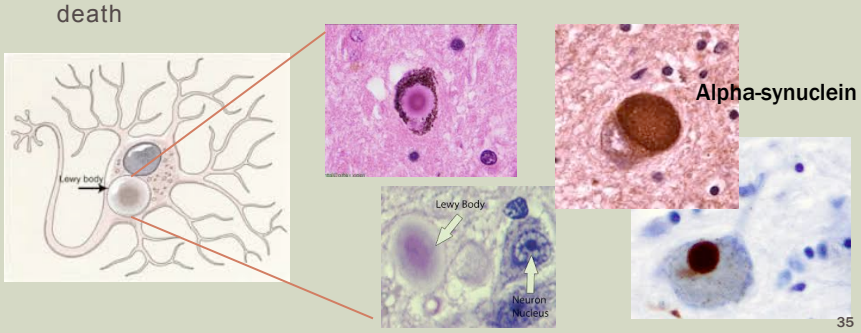
HISTOPATHOLOGY OF PD

1. DA neuron death in the substantia nigra
2. Lewy bodies- abnormal protein aggregates inside neurons
   - Made of mutated ALPHA-SYNUCLEIN protein
   - Misfolded protein sticks to other protein fragments to form clumps
   - Clumps activate a signal cascade that eventually leads to cell death



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SUBSTANTIA NIGRAL NEURONS ARE ONLY THE TIP OF THE ICEBERG

- Other brain regions are impacted with PD progression

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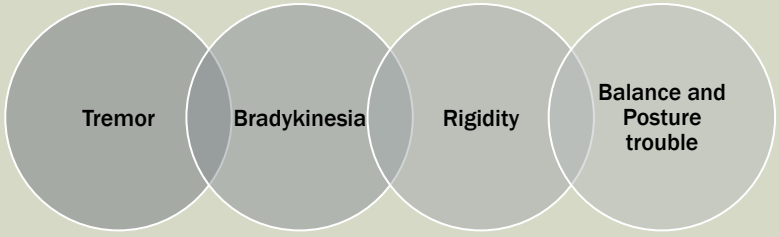
DIAGNOSIS OF PD

- No single way to diagnose PD
- Combination of symptoms and diagnostic tests
- There must be 2 of the 4 main motor symptoms present over a period of time for a neurologist to consider a PD diagnosis



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HOW DOES YOUR DOCTOR MAKE A PD DIAGNOSIS?

- Bedside examination
  1. Detailed medical history and physical examination
  2. Detailed medication history – to make sure you are not taking medications that can cause symptoms similar to PD
  3. Neurological examination – agility, muscle tone, gait and balance
  4. United Parkinson's Disease Rating Scale (UPDRS) – universal scale of Parkinson's symptoms
  5. Response to medications that mimic the action of dopamine (Levodopa)

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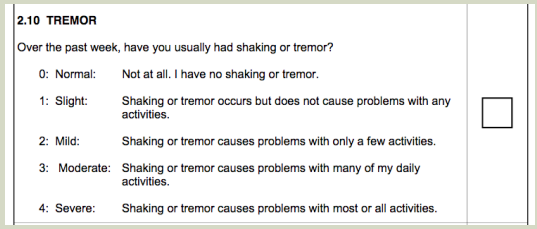
UPDRS

- Non-motor Aspects of Experiences of Daily Living
  - Cognitive impairment, Hallucinations and Psychosis, Depression, Anxiety, Apathy, Sleeping habits, Pain, Urinary problems, Constipation, Lightheadedness, Fatigue
- Motor Aspects of Experiences of Daily Living
  - Speech, Saliva and Drooling, Chewing and Swallowing, Eating Tasks, Dressing, Hygiene, Handwriting, Hobbies, Turning in Bed, Tremor, Exiting bed, Walking and Balance, Freezing
  - Complete copy: http://www.movementdisorders.org/MDS/About/Committees--Other-Groups/MDS-Task-Forces/Task-Force-on-Development-of-MDS-UPDRS.htm



2.10 TREMOR

Over the past week, have you usually had shaking or tremor?

0: Normal:	Not at all. I have no shaking or tremor.	☐
1: Slight:	Shaking or tremor occurs but does not cause problems with any activities.	
2: Mild:	Shaking or tremor causes problems with only a few activities.	
3: Moderate:	Shaking or tremor causes problems with many of my daily activities.	
4: Severe:	Shaking or tremor causes problems with most or all activities.	

Demonstration of UPDRS with Bradykinesia: https://www.youtube.com/watch?v=CH7UTwQgMm8

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Clinical Treatments for Parkinson's Disease

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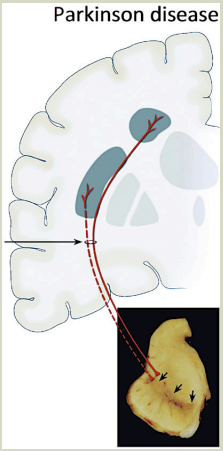
PARKINSON'S THERAPY

- There is no cure for Parkinson's
- Medications, surgery, and multidisciplinary management can provide symptom relief
- Most common treatment is based on **replacing dopamine** that is lost because of neuron death in the substantia nigra



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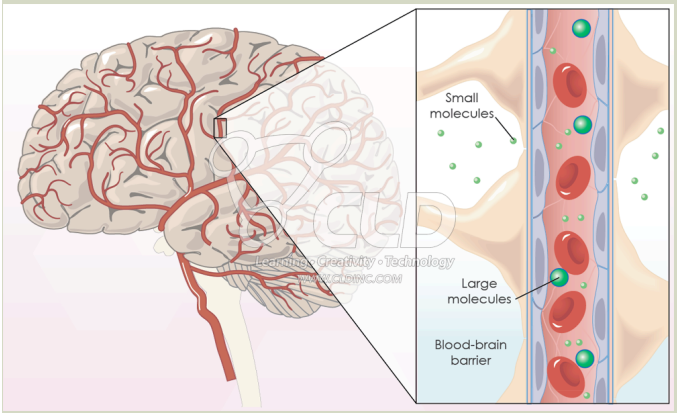
DOPAMINE CANNOT CROSS THE BBB

- Dopamine cannot cross the Blood Brain Barrier



- Protective layer around blood vessels in the brain that prevents large molecules from entering the brain

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LEVODOPA (L-DOPA)

- Developed in the 1960's
- Most effective treatment of PD's major symptoms today
- Levodopa can cross the BBB and get to substantia nigra neurons
- Neurons are able to convert to useful dopamine
- Almost always used in combination with **Carbidopa**
- Carbidopa helps prevent the breakdown of L-dopa
- Combining L-dopa and Carbidopa allows for smaller doses

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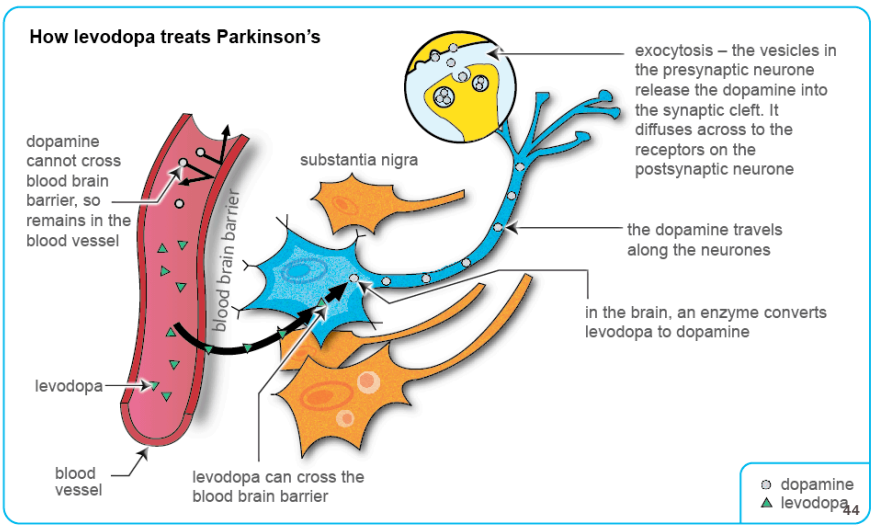
LEVODOPA



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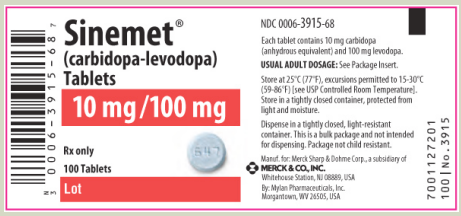
LEVODOPA (L-DOPA)



Response to a dopamine replacement drug is one if the criteria for diagnosing PD.

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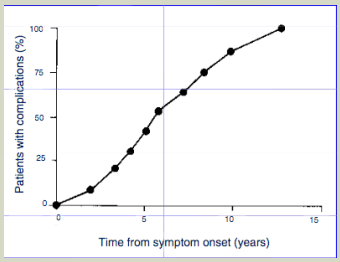
LONG-TERM USE OF LEVODOPA

- As PD progresses, patients have to take <u>increased doses</u>
- Develop more significant side effects
  - Involuntary movements (<u>dyskinesia</u>)
  - Motor ticks
- Experience "<u>Off periods</u>" when they no longer respond to the drug and have difficulty initiating movement
- Doctors often delay the use of L-dopa as long as possible



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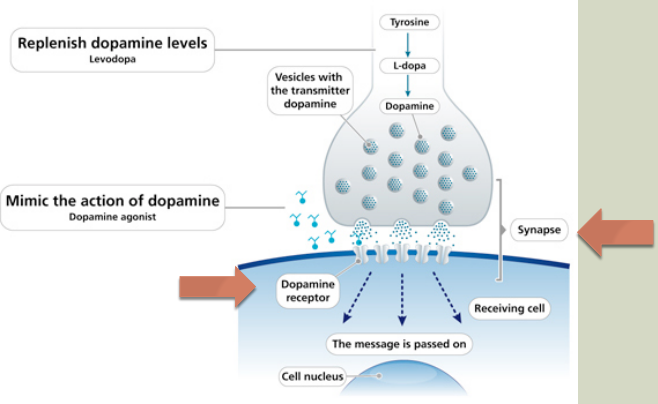
DOPAMINE AGONISTS

- Commonly used during earliest stages of disease
- Rather then trying to replace dopamine, these drug mimic dopamine's effects



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DOPAMINE AGONISTS

- Signal to downstream neurons like dopamine
- Can help improve motor function that is dependent on dopamine

Medscape® www.medscape.com

	Indications			Possible severe side-effects		Titration (weeks)
	Mono-therapy	Early combination with levodopa	Late combination with levodopa	Ergot side-effects(3)	Sleep attacks	
Bromocriptine	+	+	+	+	NS	3–33
Pergolide			+	+	+	3–33
Piribedil	+	+	+		NS	3–7
Pramipexole	(1)		(2)		+++	3–7
Ropinirole	+		+		+++	4–18

(1) in only four countries
(2) 13 countries
(3) Ergot side-effects:
coronary vasoconstriction in case of severe cardiovascular pasts
Raynaud's phenomenon
Retroperitoneal fibrosis
Pleural pulmonary fibrosis
NS: Non-significant

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DOPAMINE AGONISTS

- Side Effects:
  - Drowsiness
  - Increased risky behavior (hypersexuality, compulsive gambling)
  - Hallucinations
- Doctors use agonists to delay start of Levodopa

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For patients who are non-responsive to pharmacological therapies, or experience severe side effects to medications, surgical approaches may be used.

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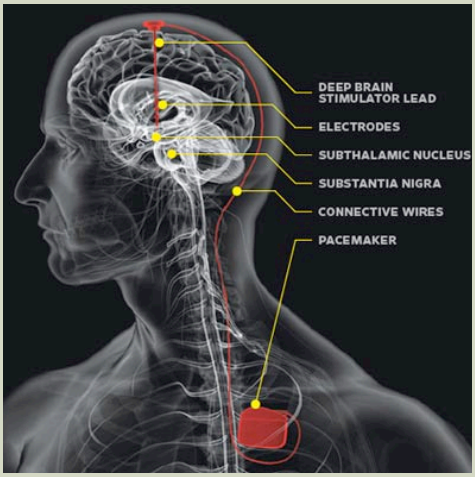
DEEP BRAIN STIMULATION (DBS)



- Most common surgical treatment of PD
- Implant a <u>neurostimulator</u>
  - Pacemaker for neurons
  - Sends electrical signals to patient's motor system
  - Changes neurons' firing patterns
- Alleviates some disease symptoms

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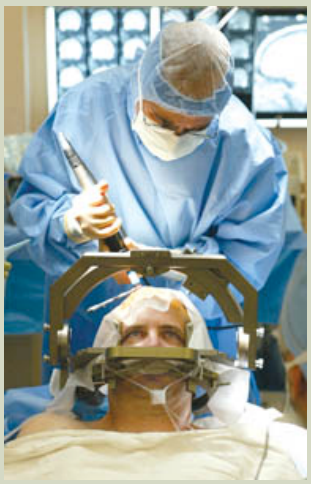
DEEP BRAIN STIMULATION SURGERY

- Invasive neurosurgery
- Not every PD patient is a candidate
  - Clear diagnosis of idiopathic PD
  - Intact cognitive function
  - Clear evidence of motor improvement with levodopa OR
  - Good motor function in an on-medication state
  - Lack of comorbidity
  - Patient age
  - Degree of disability
  - Ability to remain calm and awake during neurosurgery
  - Realistic expectations
  - Willingness to be seen for follow-up



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DEEP BRAIN STIMULATION EFFECTS

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DEEP BRAIN STIMULATION EFFECTS

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OTHER SURGICAL OPTIONS

- Thalamotomy
  - Surgery in which the thalamus is purposefully destroyed
  - Used to treat severe tremor on 1 side of the body
  - Does not help with other motor problems
  - Rarely done today
- Pallidotomy
  - Selectively destroy an overactive brain region called the globus pallidus
  - Reduces tremor and rigidity
  - Patient must be levodopa responsive
  - Rarely performed- replaced by DBS
- Subthalamotomy
  - Subthalamus is destroyed
  - Used to treat tremor
  - Very rarely performed today

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Research for New Parkinson's Therapies

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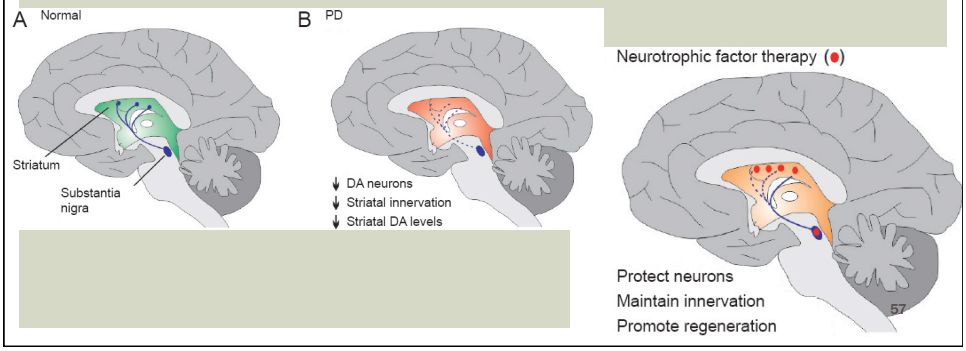
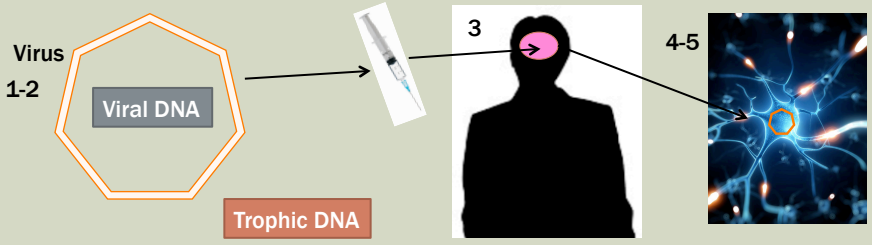
DISEASE MODIFYING: NEUROTROPHIC FACTORS

- Trophic factors are like the brain's natural fertilizer; they help protect and restore neurons
  - Glial Cell-Line Derived Neurotrophic Factor (GDNF)
  - Neurturin (NTN, CERE-120)



GENE THERAPY



1. Viruses are good at getting inside of cells
2. Alter viruses to express neurotrophic factor genes
3. Inject altered (recombinant) viruses into the brain
4. Viruses enter neurons
5. Neurons produce protective neurotrophic proteins

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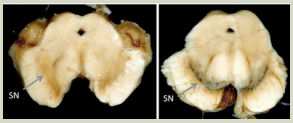
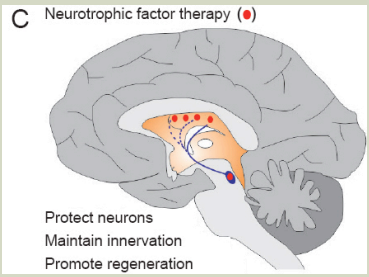
NEUROTROPHIC FACTOR GENE THERAPY IN PARKINSON'S PATIENTS

- Malfunction and death of dopaminerigic neurons in the substantia nigra
- Nigral neurons project to the striatum
- Clinical trials injecting the trophic factor Neurturin



PD Healthy



Clinical Trials

1. Inject Neurturin in the neuron bodies
2. Inject Neurturin in the neuron bodies and in their axons in the striatum

https://www.youtube.com/watch?v=gl2miunHTRI

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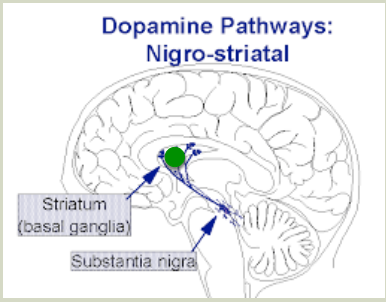
NEUROTROPHIC FACTOR GENE THERAPY IN PARKINSON'S PATIENTS

- Clinical Trial 1- injected Neurturin into striatum where neuron axons are
  - 58 patients, some control
  - Believed that neurturin would be carried through the axons to the cell body
  - Followed patients up to 18 months post surgery
  - No change in patient UPDRS scores



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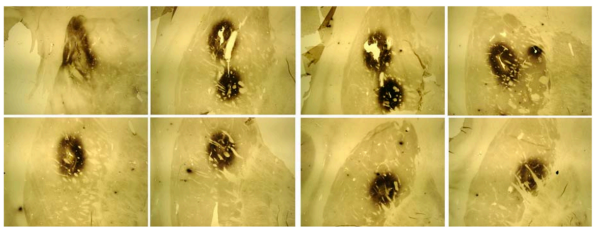
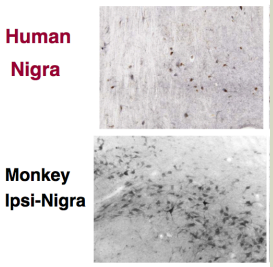
NEUROTROPHIC FACTOR GENE THERAPY IN PARKINSON'S PATIENTS

73 year old male: died of myocardial infarction 47 days post-op



•Quantitative analysis of all 3 brain hemispheres demonstrates a mean of 15% NTN coverage of the putamen

•No clear evidence of NTN in substantia nigra



Note clear NTN signal in
to non-specific stair

- Primate studies suggested that Neurturin (NTN) would be carried back into the neuron cell body
- NTN never made it back to the cell bodies of humans
- Without NTN in cell body, therapy could not work

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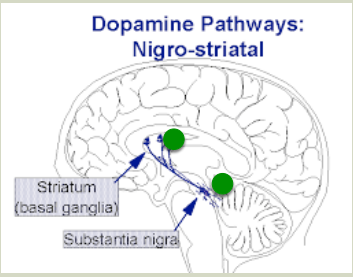
NEUROTROPHIC FACTOR GENE THERAPY IN PARKINSON'S PATIENTS

- Clinical Trial 2 – injected Neurturin into nigral neuron cell bodies and their axons in the striatum
  - 52 patients including controls
  - Late-stage PD patients
  - Followed for 1 year after surgery
  - No change in patient UPDRS scores



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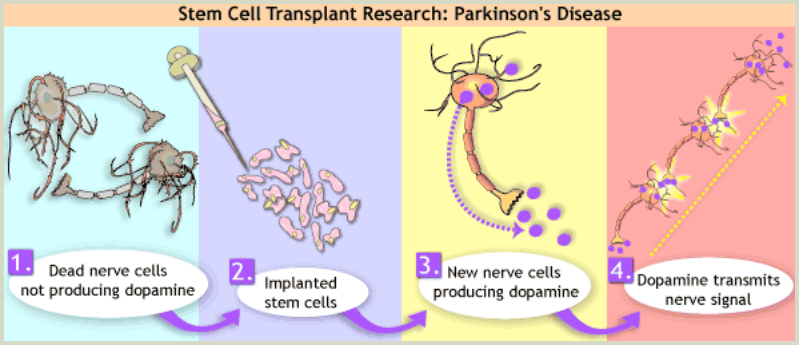
DISEASE MODIFYING: STEM CELL THERAPY FOR PD



- Stem cells: a renewable source of tissue that can be coaxed to become different cell types within the body
- Induce stem cells to become dopamine producing neurons
- Replace dead dopamine neurons with newly formed ones

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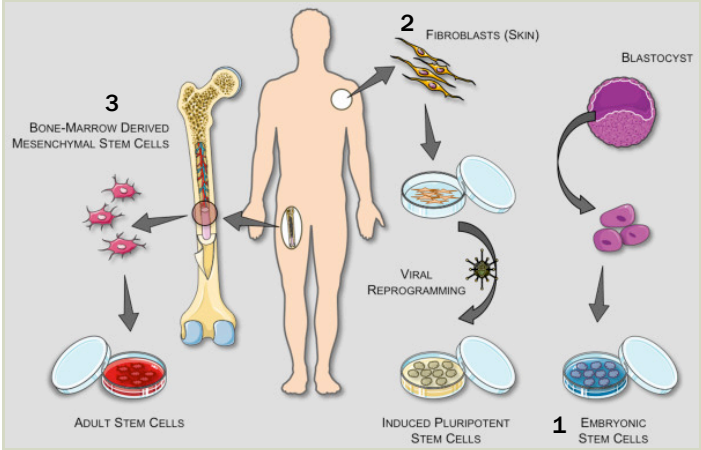
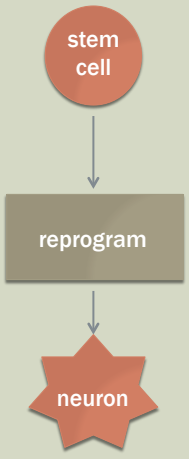
STEM CELL SOURCES





4. Blood
5. Adipose tissue (fat)

Put back into brain

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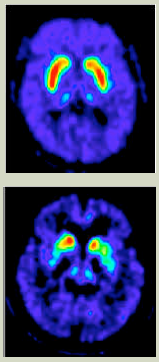
PD STEM CELL CLINICAL TRIAL

- International Stem Cell Corporation Carlsbad, CA
- Phase 1 clinical study to assess safety and efficacy of "ISC-hpNSC"
- ISC-hpNSC's are neural precursor stem cells from unfertilized human eggs
- Enroll 12 patients with moderate-severe PD
- Patients monitored for 12 months
- UPDRS rating scale and PET scans for evaluations
- Study performed at Royal Melbourne Hospital in Australia → June 2, 2016 announcement



PET

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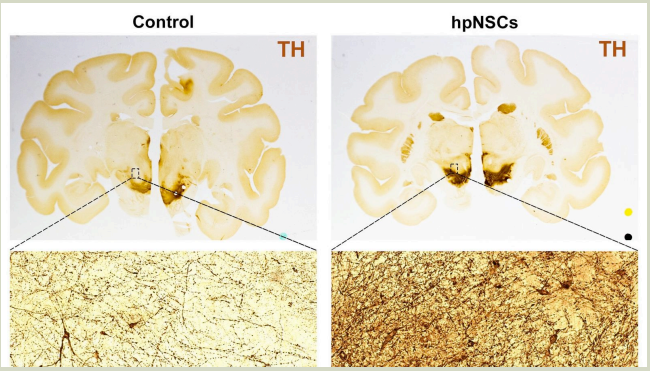
PRE-CLINICAL STUDIES IN NHPS

Pre-clinical Non-Human Primate Trials



- Depleted dopamine neurons in primate brains (MPTP)
- Implanted cells
- Followed for 12 months
- Increase in dopamine neurons
- Decrease in motor symptoms

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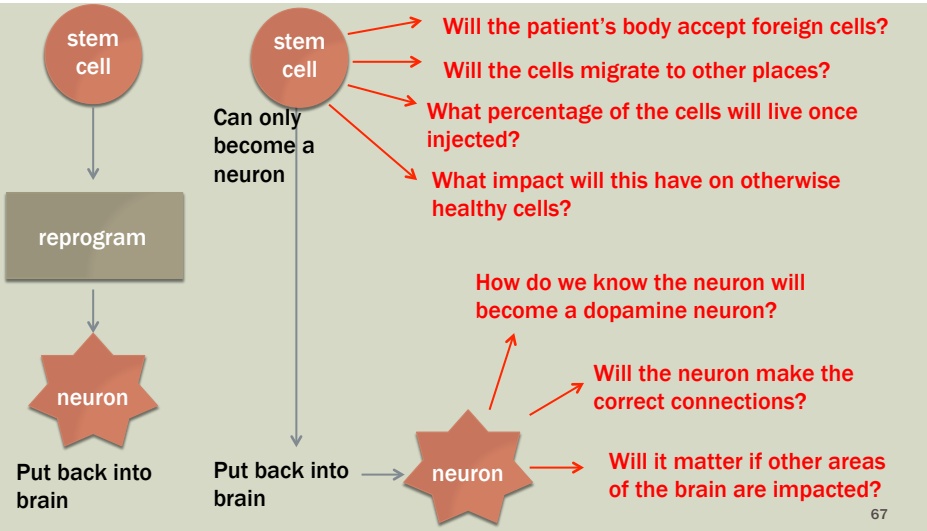
CAUTION: STEM CELL THERAPY FOR PD RED FLAGS



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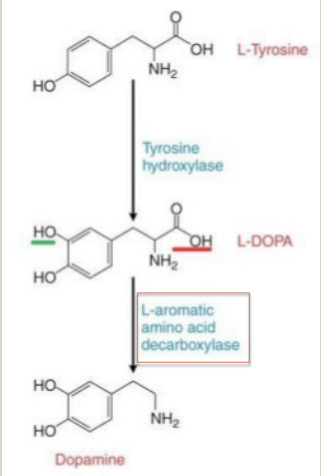
MOTOR SYMPTOMS: ENZYME GENE THERAPY IN PARKINSON'S DISEASE

- Dopamine is produced inside nigral neurons, but those neurons die
- Loss of dopamine = motor symptoms
- Neuron death also causes a loss in **Aromatic L-Amino Acid Decarboxylase** (AADC)
- AADC is an enzyme important for converting levodopa to dopamine



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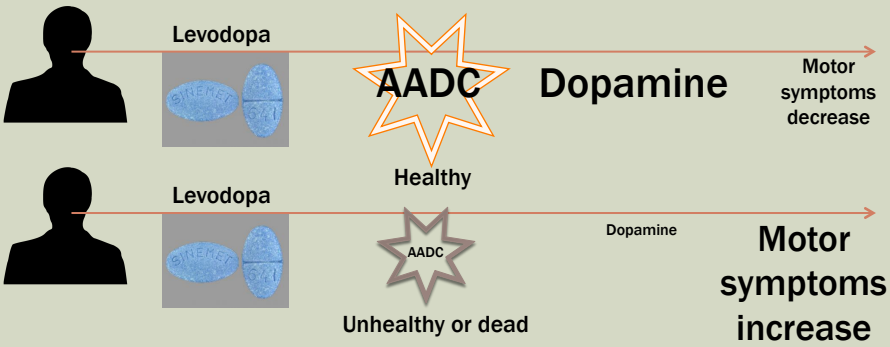
ENZYME GENE THERAPY FOR MOTOR SYMPTOMS IN PARKINSON'S DISEASE



- When dopamine neurons die, they take the enzyme that makes levodopa treatment works with them
- We can replace that missing enzyme with gene therapy

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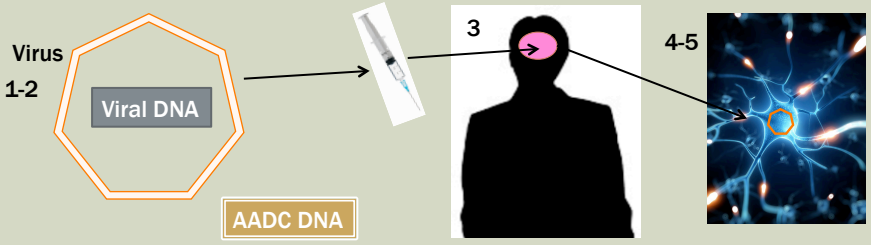
GENE THERAPY



1. Viruses are good at getting inside of cells
2. Alter viruses to express enzyme genes
3. Inject altered (recombinant) viruses into the brain
4. Viruses enter neurons
5. Neurons produce required enzyme

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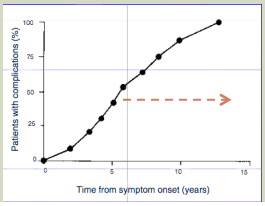
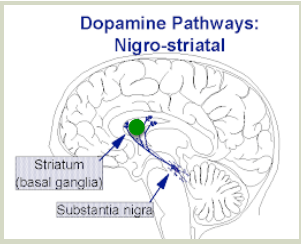
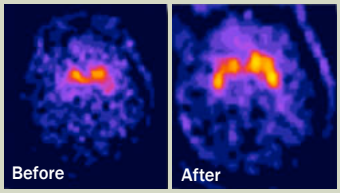
ENZYME GENE THERAPY FOR MOTOR SYMPTOMS IN PARKINSON'S DISEASE

- Clinical trial looking at safety and efficacy
- Injected virus with AADC into the striatum
- 5 patients with advanced PD
- Evaluated 6 months post injection
- UPDRS scores only improved while patients were not taking L-dopa (acting on endogenous dopamine)







FMT-PET image from a human subject after receiving a low dose of AAV2-hAADC gene therapy bilaterally. The warm colors indicate successful AADC gene transfer.

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MOTOR SYMPTOMS: EXERCISE

- For PD patients, exercise is a vital component for maintaining balance, mobility, and daily living activates
- Exercise can benefit in 2 ways:
  - Symptom Management – improve gait, balance, tremor, flexibility
  - Possibly slowing disease progression – reduces risk of PD complications by practicing movement
- Animal studies have shown
  - mice that exercised regularly, then were made Parkinsonian, had neurons that used dopamine more efficiently
  - exercise increases expression of trophic factors which reduces vulnerability of dopamine neurons to damage

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PARKINSON'S OUTCOMES PROJECT

- Largest ever clinical study of PD, 10,000 patients in 4 countries
- Investigating:
  - Most effective treatments,
  - benefits from therapy,
  - best candidates for treatment,
  - impact on caregivers, and
  - benefits of various exercise programs

MIAMI, June 17, 2015—Data released today from the National Parkinson Foundation's (NPF) *Parkinson's Outcomes Project* shows that people with Parkinson's disease (PD) who start exercising earlier experience a significant slower decline in quality of life than those who start later. The study is being presented today by NPF researchers at the 19th International Congress of Parkinson's Disease and Movement Disorders in San Diego, CA.

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PARKINSON'S OUTCOMES PROJECT

- Data from 3,000 PD patients
- 1,300 study participants regularly exercised at start
- 500 of those participants began exercising greater then 2.5 hours/week
- Followed for 2 years

Exercised the entire time

Started to exercise regularly

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PARKINSON'S OUTCOMES PROJECT

- Examined TOTAL exercise done, not type
- Compared quality of life scores with the Parkinson's Disease Questionnaire (PDQ-39)
- PDQ-39: self-reported; measures the impact of PD on daily life through multiple factors, including mood, movement, and social interaction

Exercised regularly	PDQ-39 dropped 1.4 points
Started to exercise later	PDQ-39 dropped 3.2 points

- People who start early exercise get more benefit than those who start late
- The difference in points is enough to impact ease of daily activities

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PARKINSON'S OUTCOMES PROJECT

- Patients suffer when they delay starting their exercise
- Just need to be up and moving

"This is great news that people can have a positive impact on the course of their own disease," said Joyce Oberdorf, NPF's President and CEO. "It is tremendously empowering."

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PD RESOURCES

- National Parkinson's Foundation- Patient Care and Disease Information
  - www.parkinson.org
  - Resources in your community http://www.parkinson.org/find-help/resources-in-your-community
  - Ohio Chapter
- Michael J. Fox Foundation- Ongoing Research in PD
  - www.michaeljfox.org
  - Podcast
- Parkinson's Disease Foundation- Information for patients and about research
  - www.pdf.org
  - Online Seminars
- Davis Phinney Foundation- New, Research, Events in PD
  - www.davisphinneyfoundation.org

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