FBN CASE STUDY 2017

By MedSoc Teaching

CASE

A 75-year old man with Parkinson's disease was seen by his doctor complaining that the tremor in his left arm and muscular stiffness was no longer well-controlled by the drugs he had been prescribed. Examination revealed that his affect was generally flat and he spoke with a weak voice. His wife was worried that he might be depressed. At rest the fingers of his left hand alternated between contracted and relaxed and there was a fine tremor of the wrist and elbow. His everyday behaviour had become increasingly disorganised and he found it difficult to successfully complete any goal-directed tasks.

DEPRESSION

See FBN case study 2014

https://www.su.nottingham.ac.uk/resources/medsocteaching/MedSoc-Teaching-2014-Neuroanatomy-Case-Study-Slides/

NB: Contains info on both depression and post-partum depression (PPD)

PARKINSONISM

Clinical diagnosis: 2 out of 4 symptoms below, improve with medications

1. Bradykinesia → mask-like face (hypomimia), hypophonia, micrographia
2. Rigidity → increased tone, lead-pipe vs cogwheel rigidity
3. Tremor → resting tremor, pill-rolling
4. Postural instability → shuffling gate, slow to initiate, festinating gate

"tremor in left arm", "muscular stiffness"

"at rest the fingers of his left hand alternated between contracted and relaxed"

NON-MOTOR SYMPTOMS

Cognition – dementia at later stage of the disease

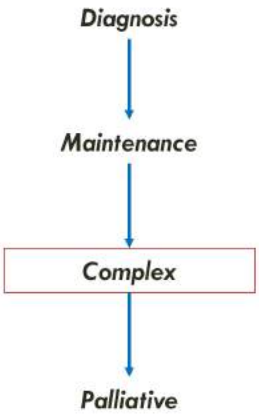
Mood – depression

Sleep disturbances

Autonomic dysfunctions: constipation, postural hypotension,…

"his affect was generally flat and he spoke with a weak voice"

"increasingly disorganised", "difficult to complete goal-directed tasks"



DIFFERENTIALS

Parkinson-plus syndromes: multisystem atrophy (significant autonomic dysfunction), progressive supranuclear palsy (eye movements affected)

Lewy body dementia: dementia from early on

Secondary Parkinson's: drug-induced (antipsychotics), vascular parkinsonism,…

Advanced imaging:

- DaT scan: assess dopamine activity in the striatum
- MRI: distinguish PD and Parkinson's plus syndromes

PARKINSON'S DISEASE

- Prevalence: 65.6 per 100,000 to 125 per 100,000.
- UK Incidence= approx. 128,000 cases
- Incidence increases severely with age
- Slightly more common in men
- Insidious onset and progression

"75-year-old man"

PARKINSONISM

Clinical diagnosis: 2 out of 4 symptoms below, improve with medications

1. Bradykinesia	→ mask-like face (hypomimia), hypophonia, micrographia
2. Rigidity	→ increased tone, lead-pipe vs cogwheel rigidity
3. Tremor	→ resting tremor, pill-rolling
4. Postural instability	→ shuffling gate, slow to initiate, festinating gate

"tremor in left arm", "muscular stiffness"

"at rest the fingers of his left hand alternated between contracted and relaxed"

Although clinical manifestation of Parkinson's disease can vary from person to person, the cardinal symptoms are a triad of motor impairments: tremor, rigidity, and bradykinesia

During walking, the head and shoulders are stooped, the gait is short and shuffling, and there is a loss of automatic movements, such as arm swinging.

"AT REST THE FINGERS OF HIS LEFT HAND ALTERNATED BETWEEN CONTRACTED AND RELAXED AND THERE WAS A FINE TREMOR OF THE WRIST AND ELBOW"

- Usually unilateral → Becomes bilateral
- Worsens with stress
- Usually the first symptom to arise
- Occurs in the hands or arms
- Disappears with purposeful movement; such as picking up an object
- Frequency of PD tremor is between 4 and 6 hertz (cycles per second). It is a pronation-supination tremor that is described as "pill-rolling," that is the index finger of the hand tends to get into contact with the thumb and perform a circular movement together

NON-MOTOR SYMPTOMS

Cognition – dementia at later stage of the disease

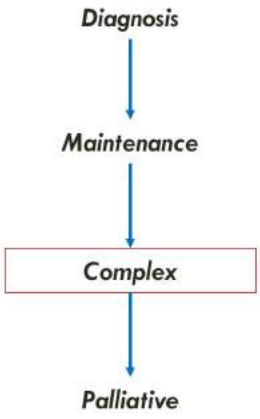
Mood – depression

Sleep disturbances

Autonomic dysfunctions: constipation, postural hypotension,…

"his affect was generally flat and he spoke with a weak voice"

"increasingly disorganised", "difficult to complete goal-directed tasks"



GENETIC FACTORS

PD may be multifactorial in aetiology with genetic contributions

Familial cases are relatively rare (5-10%)

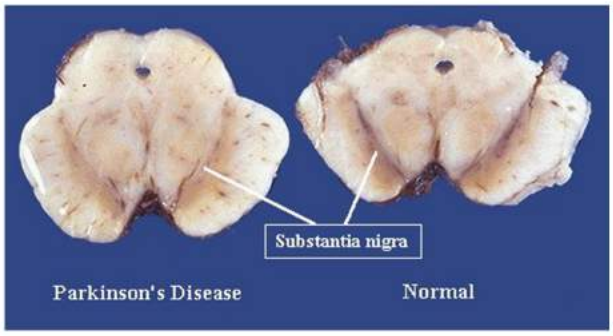
Ten singles gene mutations identified – associated with ubiquitin-proteasome system

Mutations in specific genes have been conclusively shown to cause Parkinson's (all cases of familial Parkinson's are caused by one of these genes):

- **PARK1** codes for **α-synuclein**
- **PARK2** codes for **parkin protein**
- **PARK7** codes for **DJ-1 protein**
- **Leucine-rich repeat kinase 2** (LRRK2) – heavily associated with sporadic cases of Parkinson's Disease
- **PTEN-induced putative kinase 1** (PINK1)

Hereditary autosomal dominant early-onset Parkinson's can be cause by defects in PARK1 gene, which encodes for alpha-synuclein with Lewy bodies and marked rigidity

Leucine-rich repeat kinase 2 (LRRK2 or dardarin) is a mutation found in many sporadic cases of Parkinson's disease and may be a risk factor – this may be relevant to the case study as this is highly prevalent and it is likely to be a mutation the patient may have.



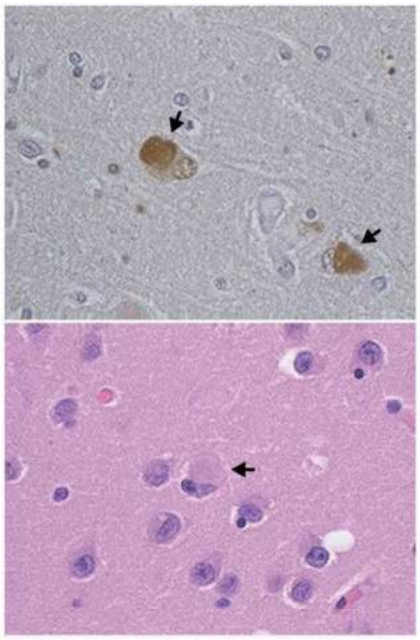
Parkinson's disease = Loss of dopaminergic pigmented neurons in substantia nigra pars compacta

NEUROPATHOLOGY

Cell loss in other pigmented nuclei
- Ventral tegmental area
- Locus coeruleus
- Raphe nucleus

Intraneuronal eosinophilic inclusion bodies (Lewy)
- Brainstem
- Diffuse distribution in cortex
- **Protein aggregates** with cores **of α-synuclein**
- Occur in other diseases
- Aggregates can form fibrils and may contribute to dementia in 50% of patients
- Causal or symptomatic?

Reactive gliosis = proliferation or hypertrophy of several different types of glial cells, including astrocytes, microglia, and oligodendrocytes

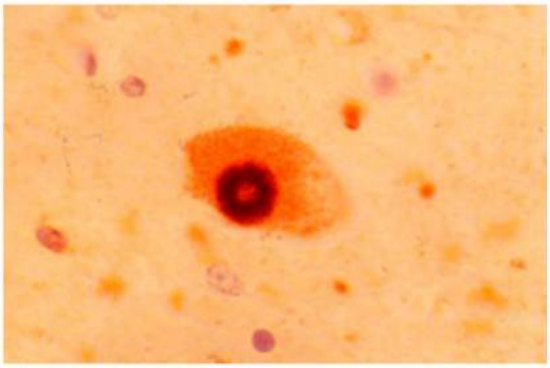


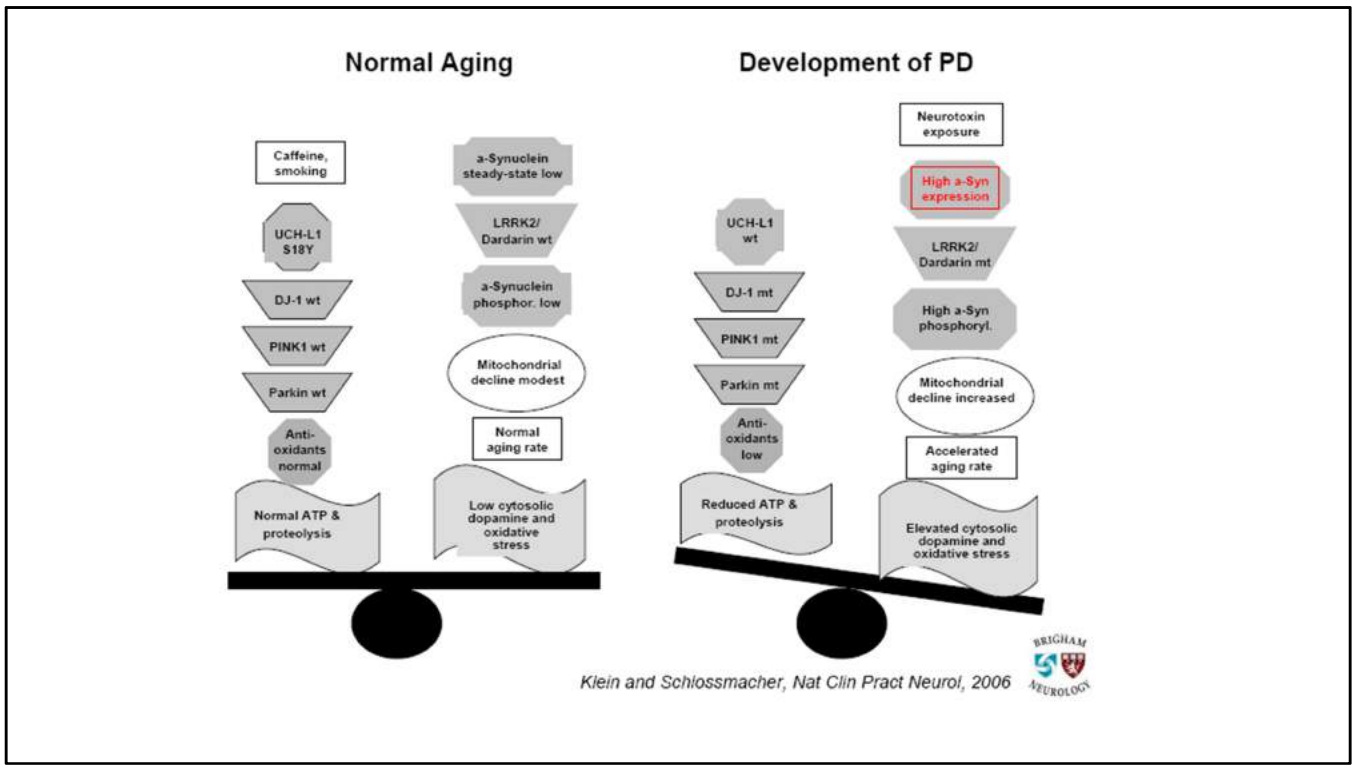
Lewy bodies are abnormal aggregates of protein that develop inside nerve cells in Parkinson's disease (PD), Lewy body dementia (which can be considered a separate disease), and some other disorders

NEURONAL CELL DEATH

Cell death could be due to:

- Oxidative stress
- Mitochondrial dysfunction
- Proteasome dysfunction



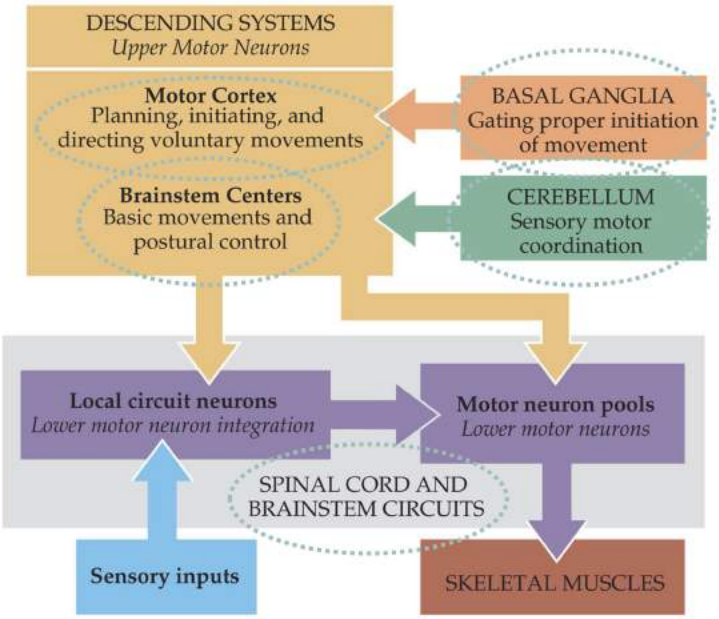


A model of known pathogenetic events in PD shows a principal imbalance between factors that promote PD (e.g. increased total metal content in the substantia nigra, altered steady-state levels of alpha-synuclein proteins, including its phosphorylation, rise in dopamine-metabolism-related stress, and exposure to neurotoxins, LRRK2 MUTATION) and factors that prevent PD (e.g. cigarette smoking, caffeine consumption, expression of wild-type Parkin, DJ1, and PINK1, and normal levels of glutathione)

BASAL GANGLIA

- Components of the basal ganglia
- Function of the basal ganglia
- Functional circuitry of the basal ganglia
  - Direct and indirect pathways
- Circuitry involved in Parkinson's Disease

Neural structures involved in the control of movement



NEUROSCIENCE, Third Edition, Figure 15.1 © 2004 Sinauer Associates, Inc.

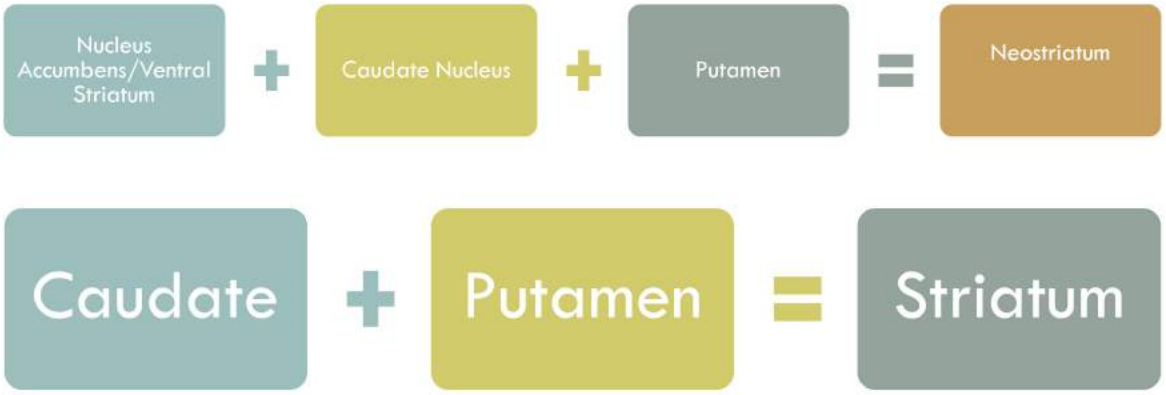
BASAL GANGLIA

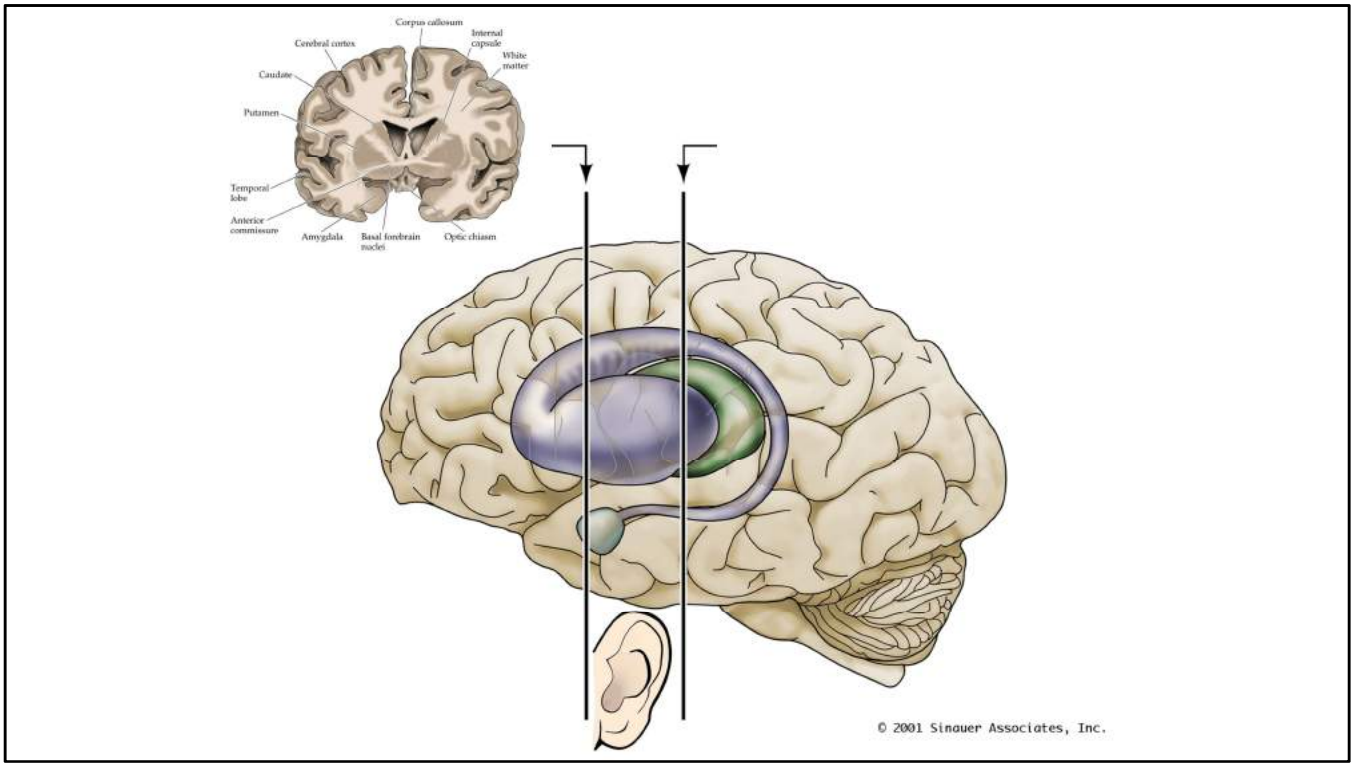
- Basal ganglia = collections of neuronal cell bodies in the brain
- 4 key functions/loops:
  - **Motor Loop** – modulate the motor function of the pyramidal tracts e.g. smooth out movement
  - Occulomotor loop – saccades (visual tracking movements)
  - Limbic loop – motor movements of emotions
  - Cognitive/Prefrontal loop

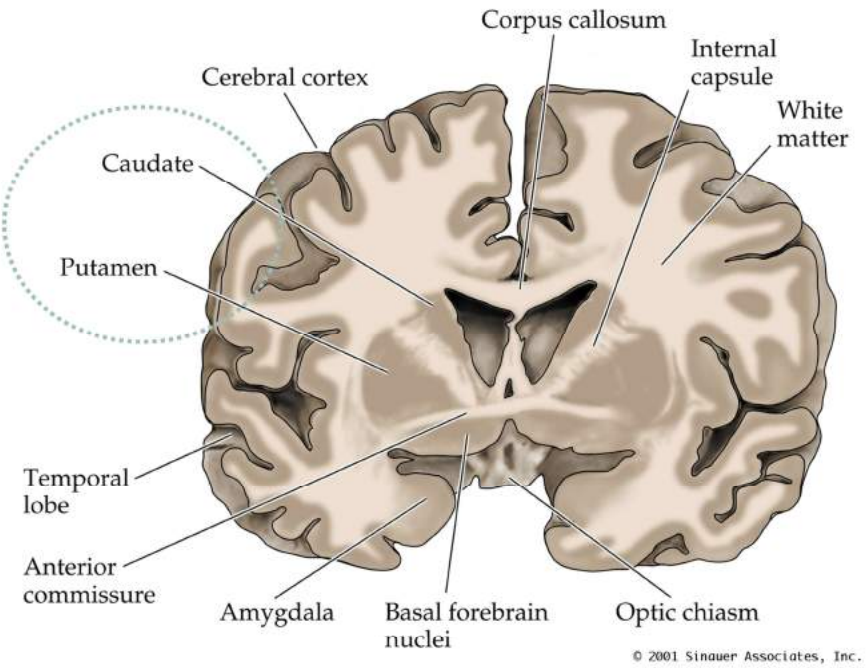
ANATOMY OF THE BASAL GANGLIA

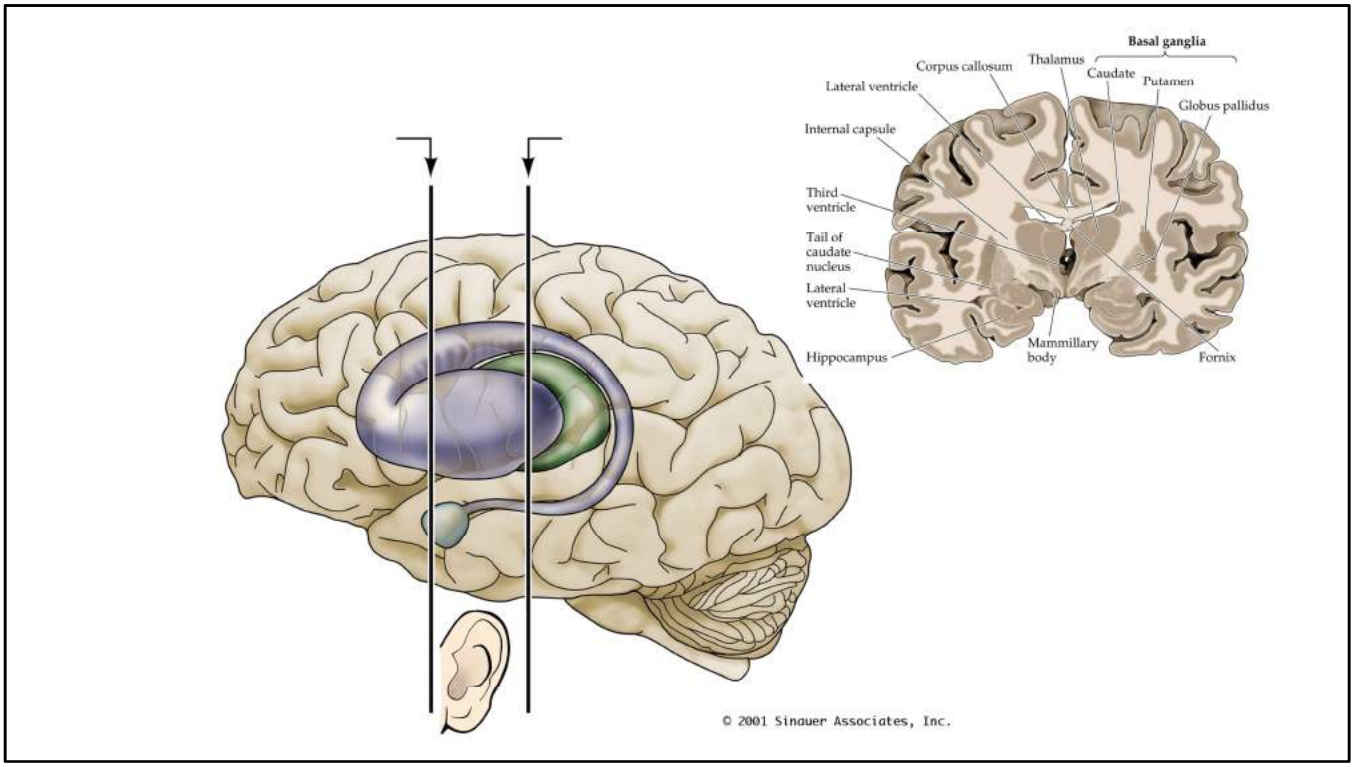
- Caudate
- Putamen
- Ventral striatum/Nucleus Accumbens
- Globus Pallidus
  - Internus
  - Externus
- Subthalamic Nucleus
- Substantia Nigra
  - Pars Compacta
  - Pars Reticularis

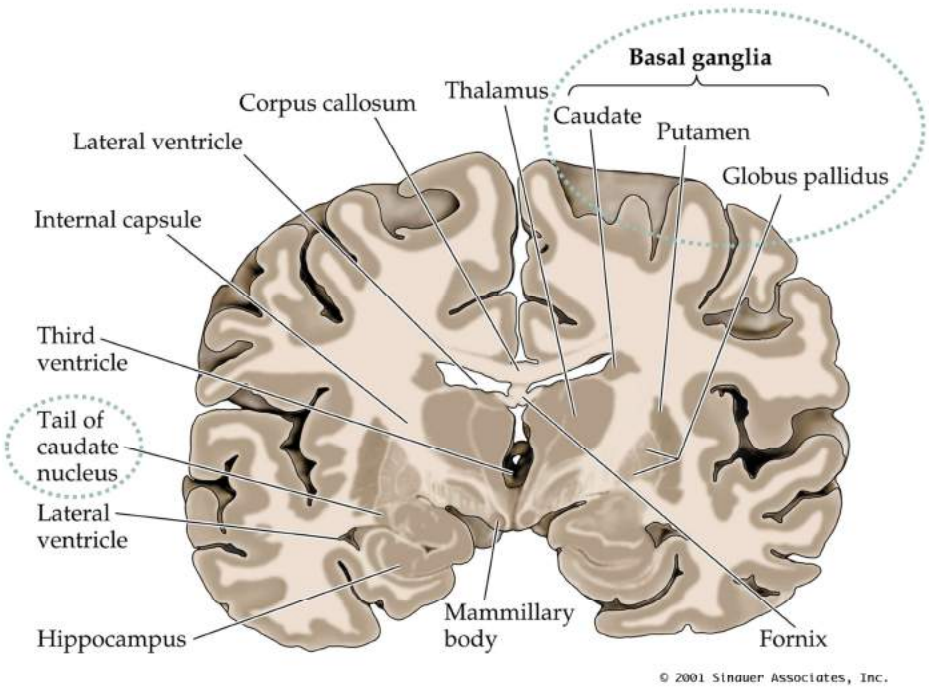
SOME NOMENCLATURE!

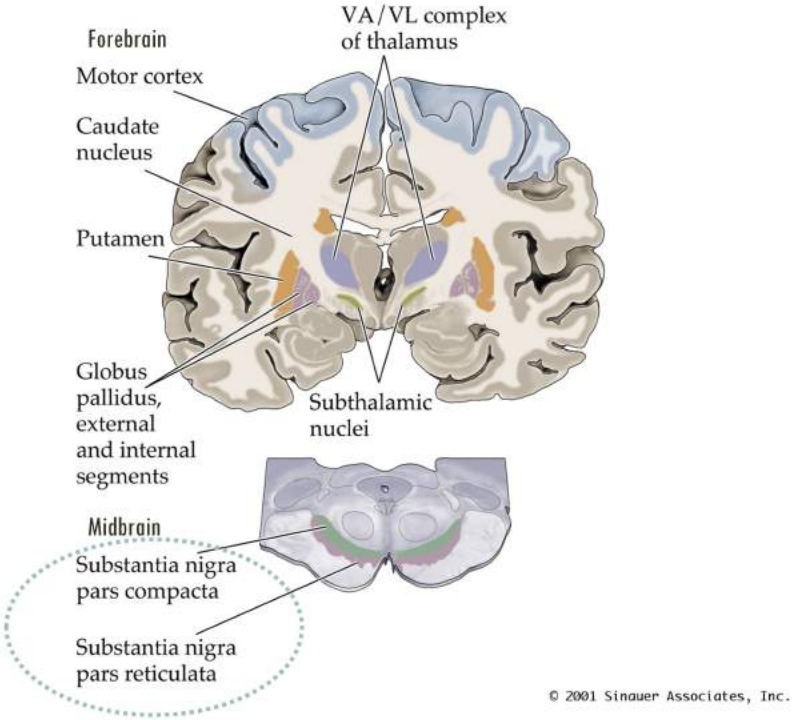


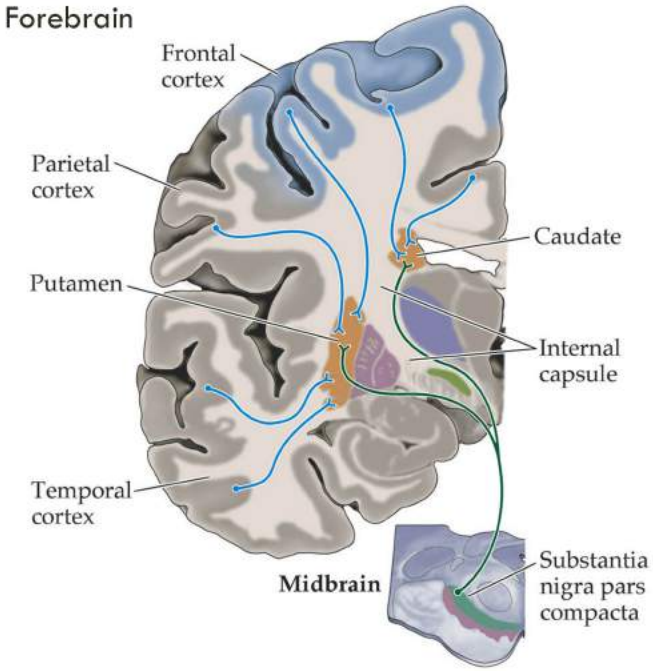

Corpus callosum
Cerebral cortex
Internal capsule
White matter
Caudate
Putamen
Temporal lobe
Anterior commissure
Amygdala
Basal forebrain nuclei
Optic chiasm
© 2001 Sinauer Associates, Inc.


Corpus callosum
Internal capsule
Cerebral cortex
White matter
Caudate
Putamen
Temporal lobe
Anterior commissure
Amygdala
Basal forebrain nuclei
Optic chiasm
© 2001 Sinauer Associates, Inc.


Basal ganglia
Thalamus
Corpus callosum
Caudate
Putamen
Lateral ventricle
Globus pallidus
Internal capsule
Third ventricle
Tail of caudate nucleus
Lateral ventricle
Hippocampus
Mammillary body
Fornix
© 2001 Sinauer Associates, Inc.


Basal ganglia
Thalamus
Corpus callosum
Caudate
Putamen
Lateral ventricle
Globus pallidus
Internal capsule
Third ventricle
Tail of caudate nucleus
Lateral ventricle
Hippocampus
Mammillary body
Fornix
© 2001 Sinauer Associates, Inc.


Forebrain
Motor cortex
Caudate nucleus
Putamen
Globus pallidus, external and internal segments
VA/VL complex of thalamus
Subthalamic nuclei
Midbrain
Substantia nigra pars compacta
Substantia nigra pars reticulata
© 2001 Sinauer Associates, Inc.

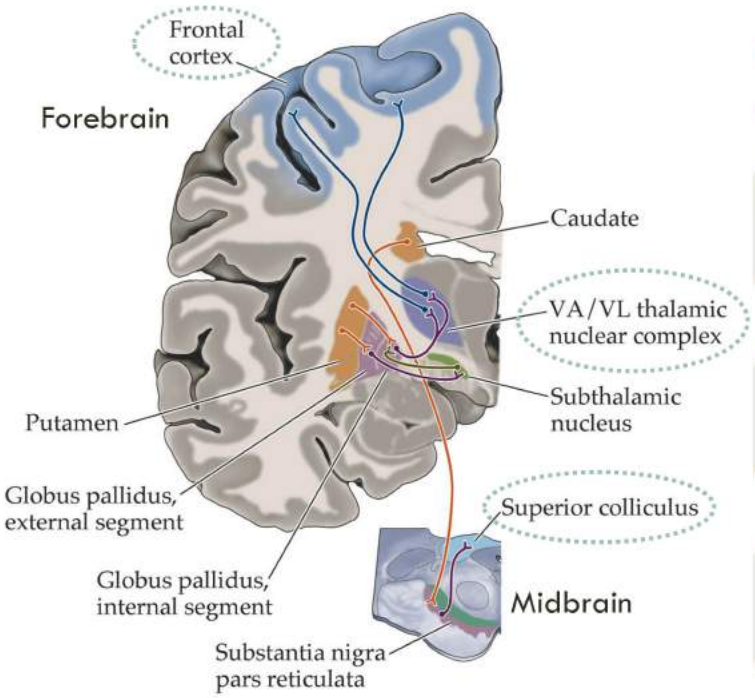


INPUT OF THE BASAL GANGLIA

Cortex

Striatum

NEUROSCIENCE, Third Edition, Figure 17.2 © 2004 Sinauer Associates, Inc.



Output to thalamus and cortex

Substantia nigra pars reticulata (SNr) + Internal segment of globus pallidus (GPi)

↓

Thalamus

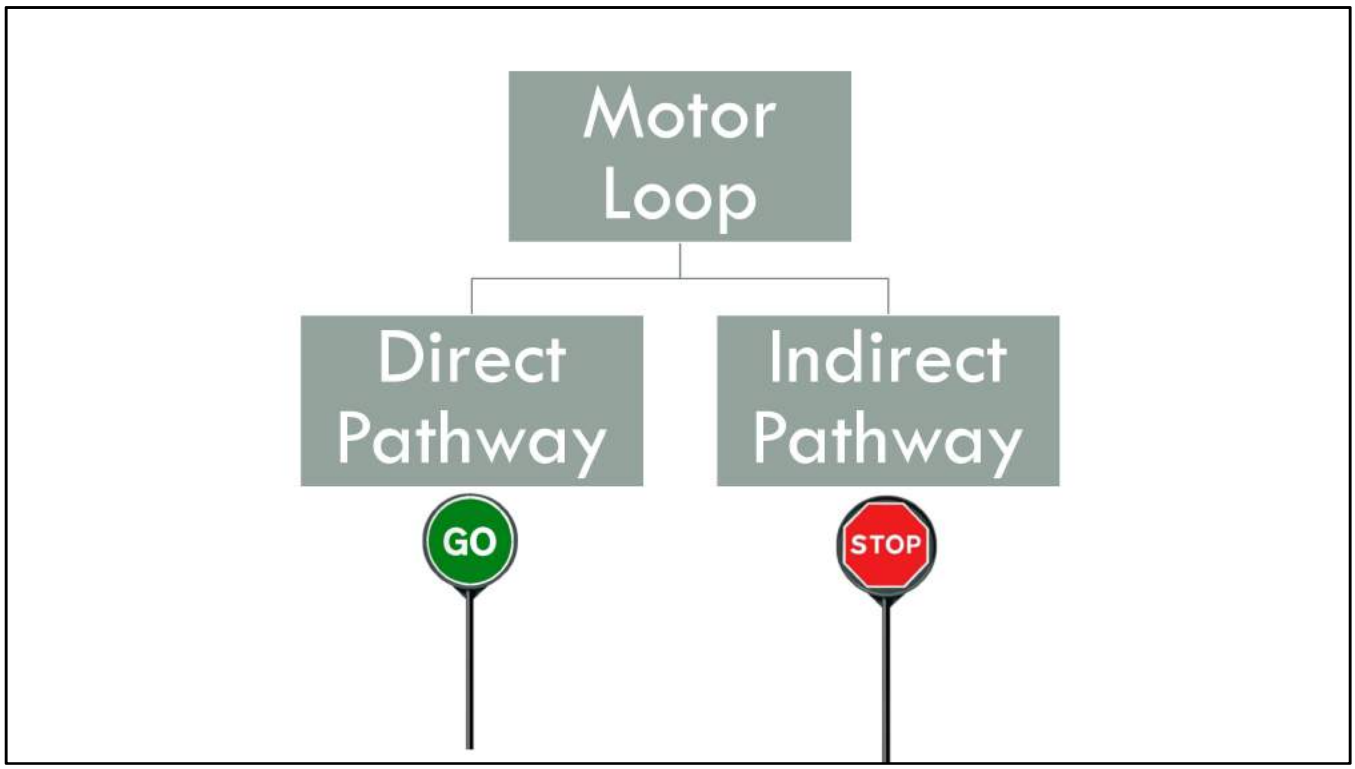
↓

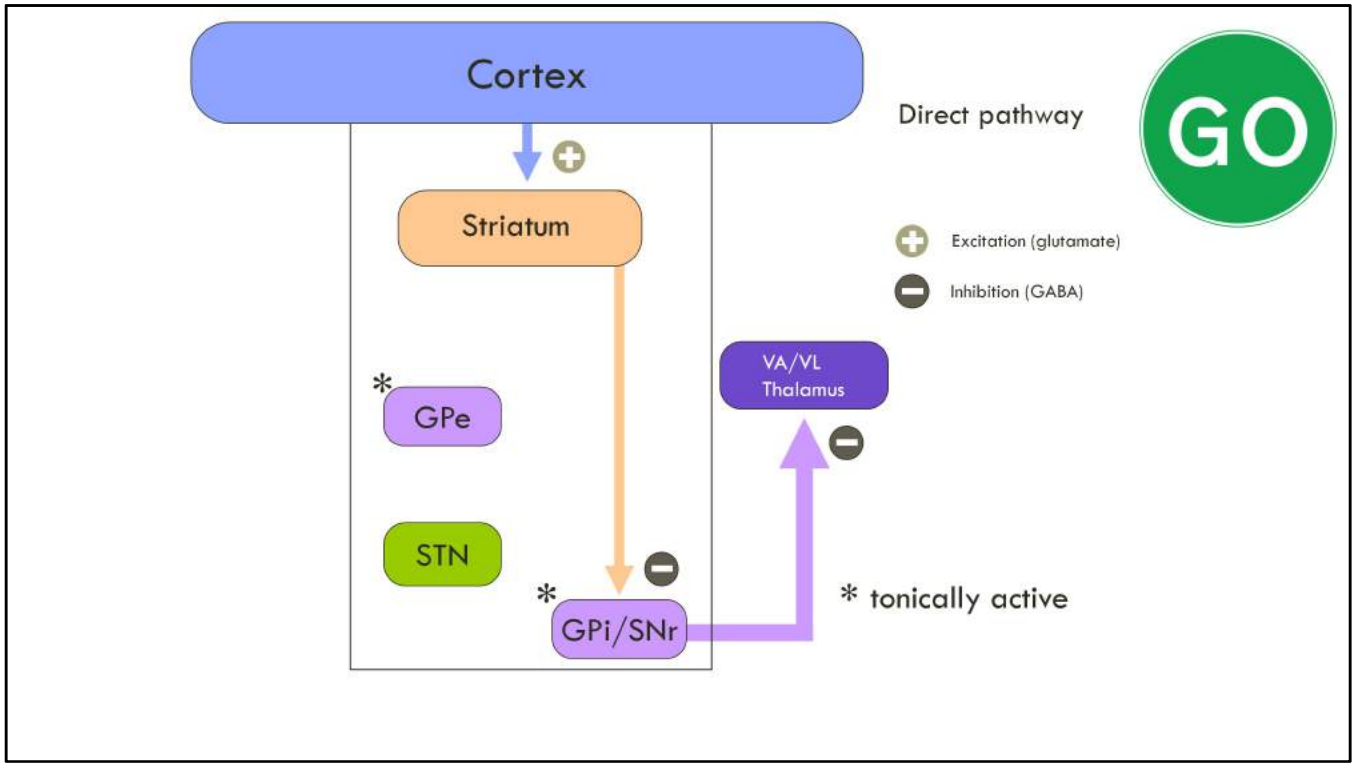
Cortex

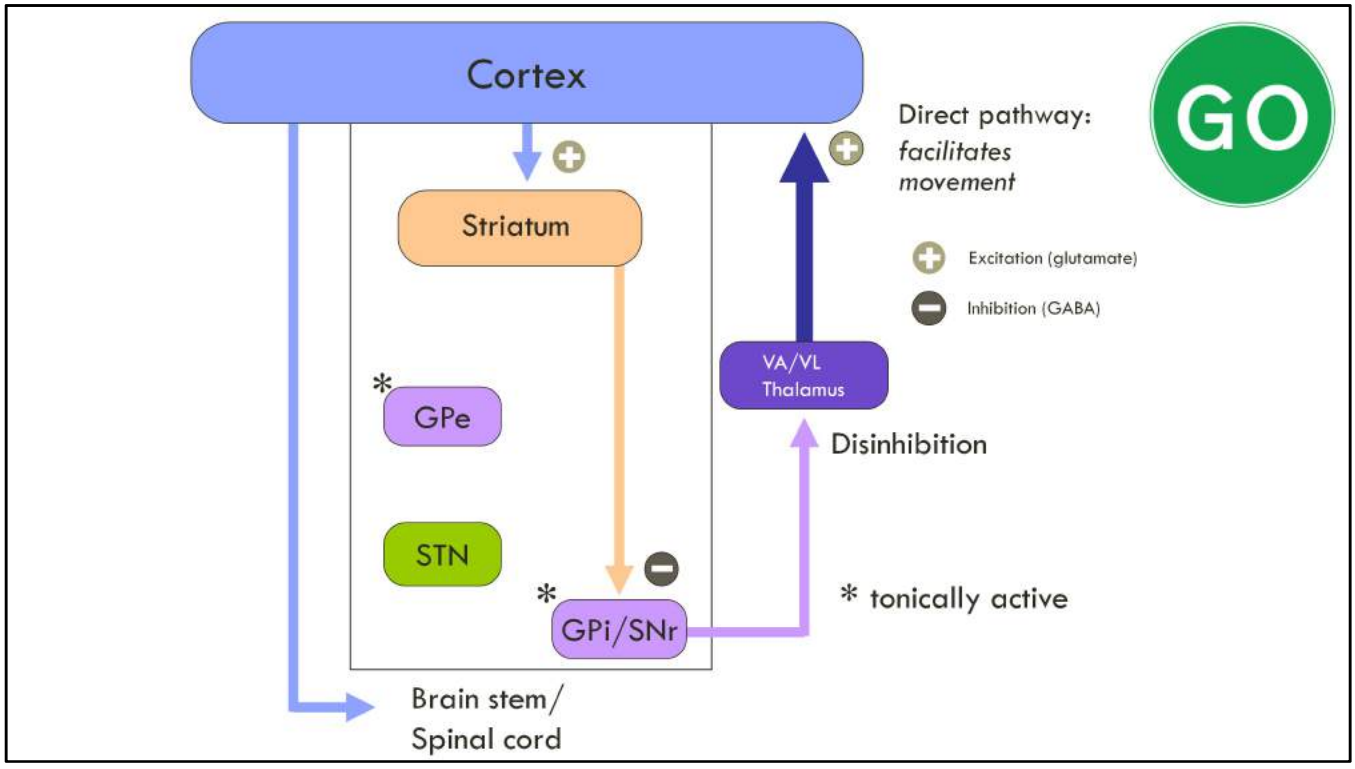
NEUROSCIENCE, Third Edition, Figure 17.5 (Part 2)

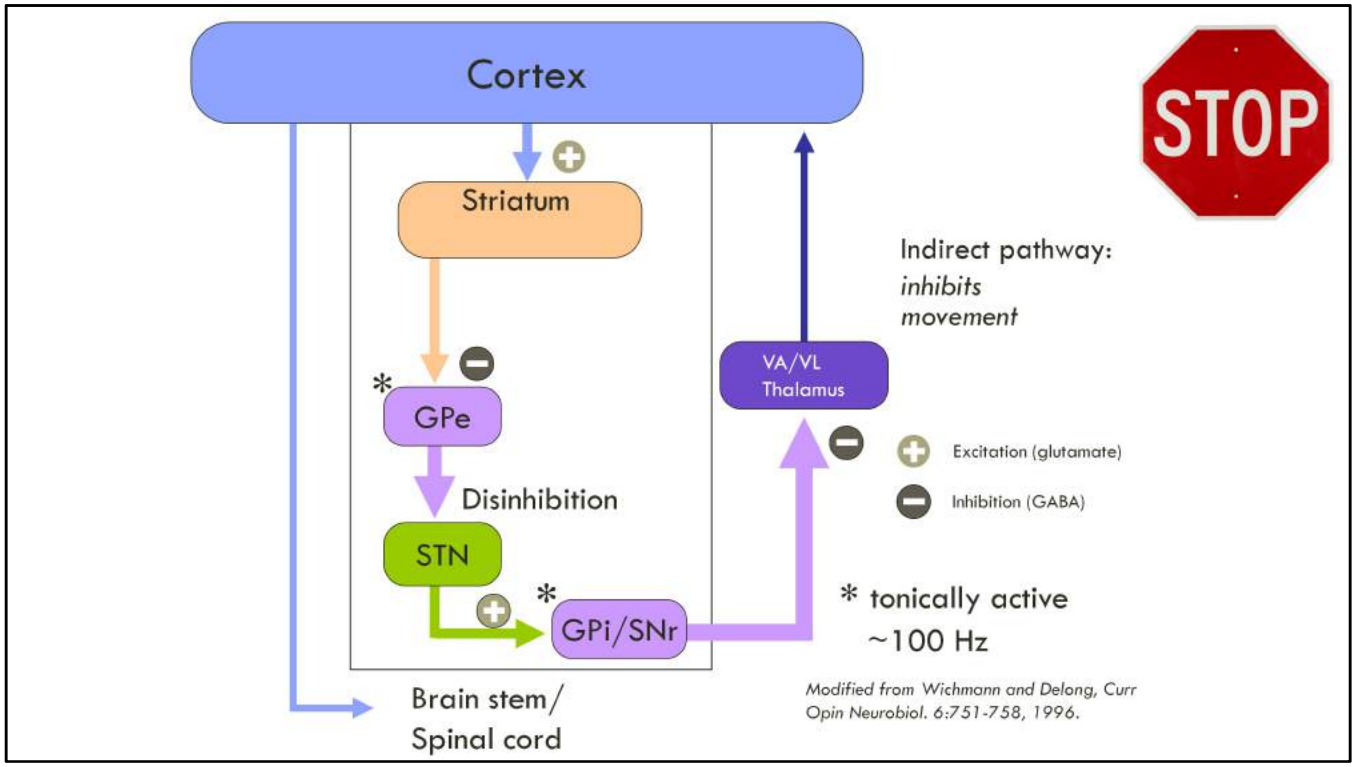
- Basal ganglia are involved in generation of goal-directed voluntary movements:
  - Motor learning
  - Motor pattern selection

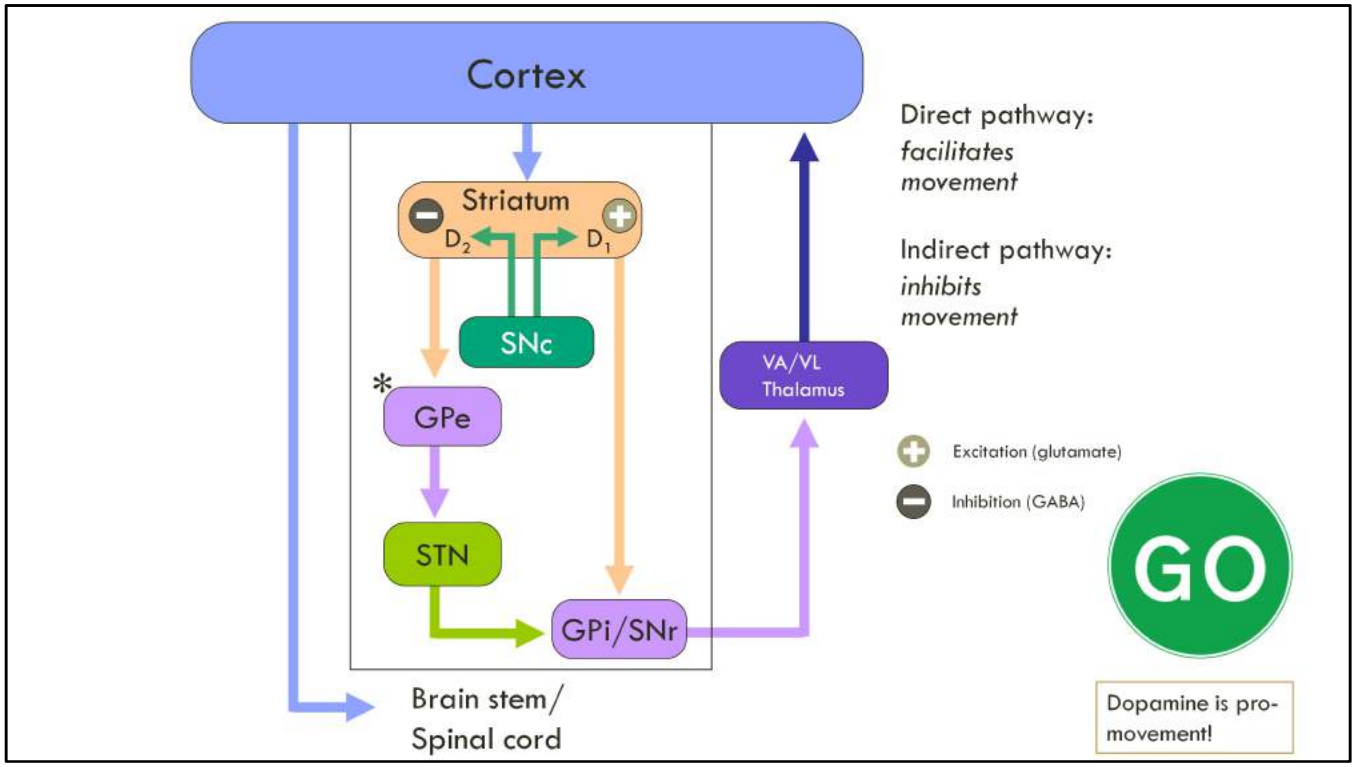
"increasingly disorganised and he found it difficult to successfully complete any goal-directed tasks"


Motor Loop
Direct Pathway
Indirect Pathway
GO
STOP


Cortex
Striatum
GPe
STN
GPi/SNr
VA/VL
Thalamus
Direct pathway
GO
Excitation (glutamate)
Inhibition (GABA)
* tonically active


Cortex
Striatum
GPe
STN
GPi/SNr
VA/VL
Thalamus
Brain stem/
Spinal cord
Direct pathway:
facilitates
movement
GO
Excitation (glutamate)
Inhibition (GABA)
Disinhibition
* tonically active


Cortex
Striatum
GPe
Disinhibition
STN
GPi/SNr
VA/VL
Thalamus
Brain stem/
Spinal cord
Indirect pathway:
inhibits
movement
Excitation (glutamate)
Inhibition (GABA)
* tonically active
~100 Hz
Modified from Wichmann and Delong, Curr Opin Neurobiol. 6:751-758, 1996.
STOP

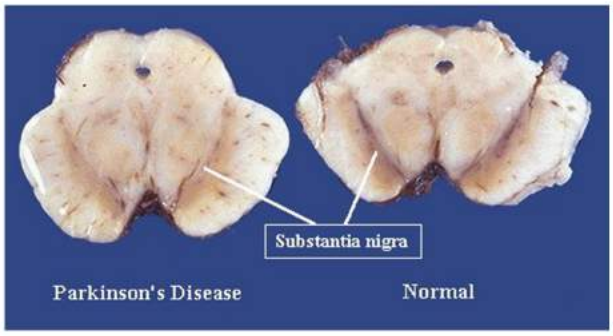


Direct pathway striatal neurones have **D_1 dopamine receptors**, which **depolarize** the cell in response to dopamine.

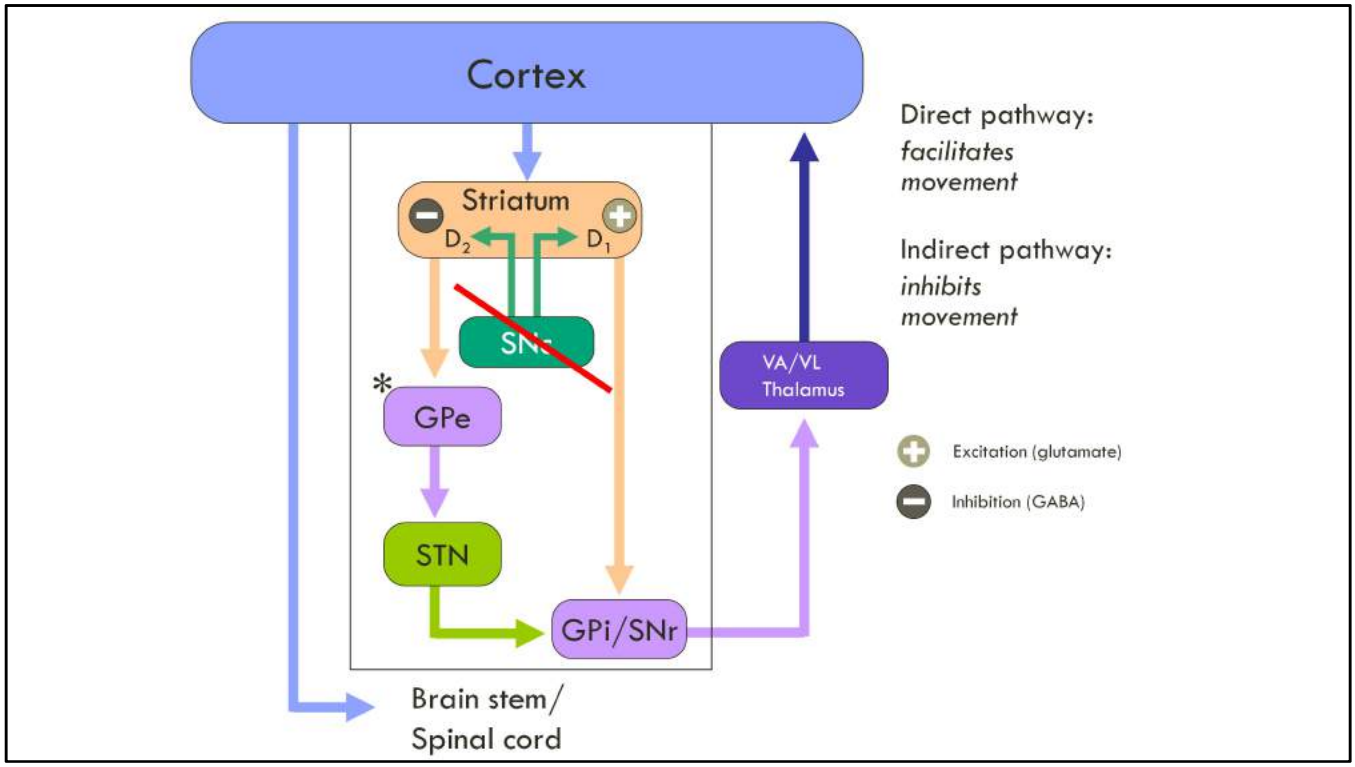
In contrast, indirect pathway striatal neurones have **D_2 dopamine receptors**, which **hyperpolarize** the cell in response to dopamine.

The **nigrostriatal pathway** thus has the dual effect of **exciting the direct pathway** while simultaneously **inhibiting the indirect pathway**.

Because of this dual effect, excitation of the nigrostriatal pathway has the net effect of exciting cortex by two routes, by exciting the direct pathway (which itself has a net excitatory effect on cortex, the drive) and inhibiting the indirect pathway (thereby disinhibiting the net inhibitory effect of the indirect pathway or the brake on cortex)

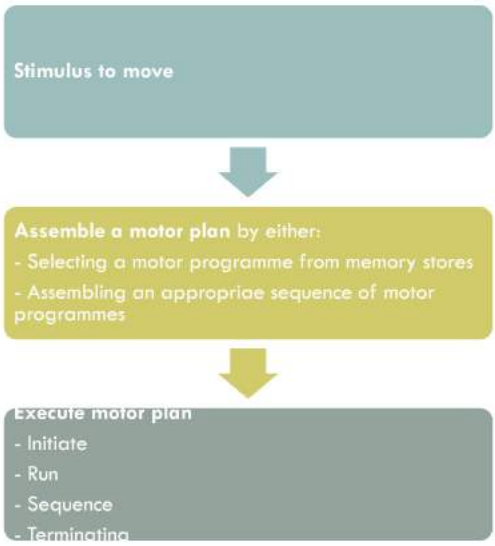


Parkinson's disease = Loss of dopaminergic pigmented neurons in substantia nigra pars compacta



The loss of these dopamine neurones in Parkinson's disease causes a reduction in the ability to initiate movement, as the balance between direct pathway excitation of cortex and indirect pathway inhibition of cortex is tipped in **favour of the indirect pathway**, resulting in **pathological inhibition of motor cortex**

Basal ganglia are involved in the **programming of movement**
Decide how, when and where to act
Help us execute **action learned motor plan**



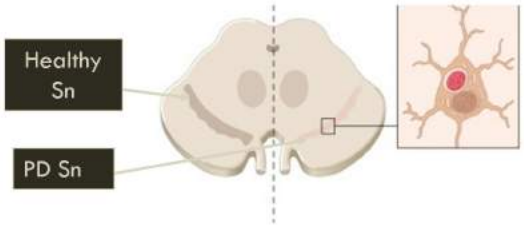
In **Parkinson's disease:**

- Patients **can assemble motor plans**
- But are **unable to specific accuracy of the programme, run or sequence them**

DECREASED DOPAMINE IN THE BASAL GANGLIA RESULTS IN…

- Tremor
- Rigidity
- Bradykinesia → Akinesia
- Postural Instability
- Hypomimia: a mask-like face – can't contract facial muscles
- Micrographia: small, cramped handwriting
- Dysphagia: impaired ability to swallow; which in the case of PD is probably related to an inability to initiate the swallowing reflex
- Hypophonia: soft speech
- Dystonia: abnormal, sustained, sometimes painful twisting muscle contractions, often affecting the foot and ankle (mainly toe flexion and foot inversion) which often interferes with gait
- Scoliosis: abnormal curvature of the spine

Only when the stores are depleted by 60-70% do Parkinsonian symptoms arise



Cells degenerate in substantia nigra (Sn)

⇩

Substantia nigra destroyed

⇩

Dopamine decreases

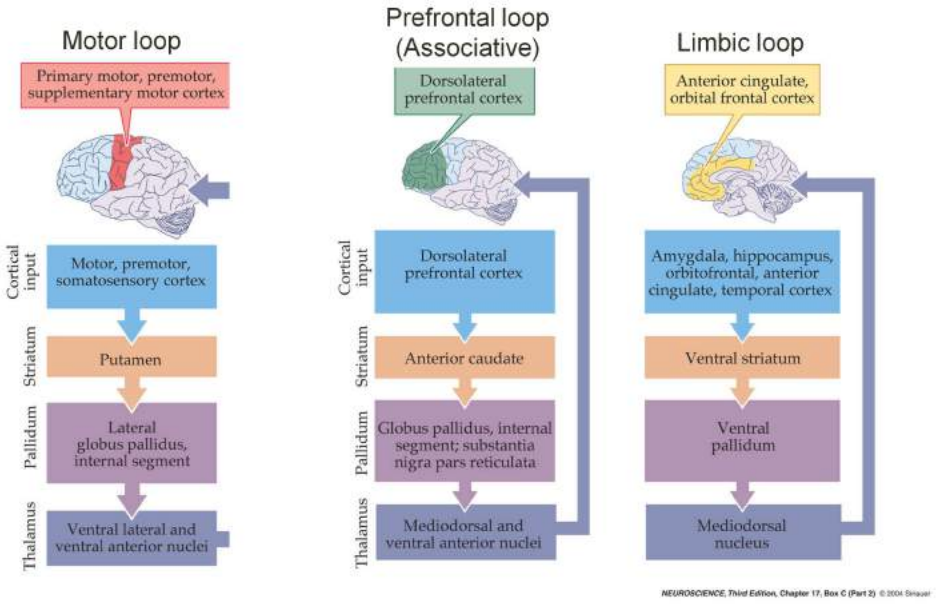
⇩

Muscle cell activation decreases

⇩

Movement control decreases

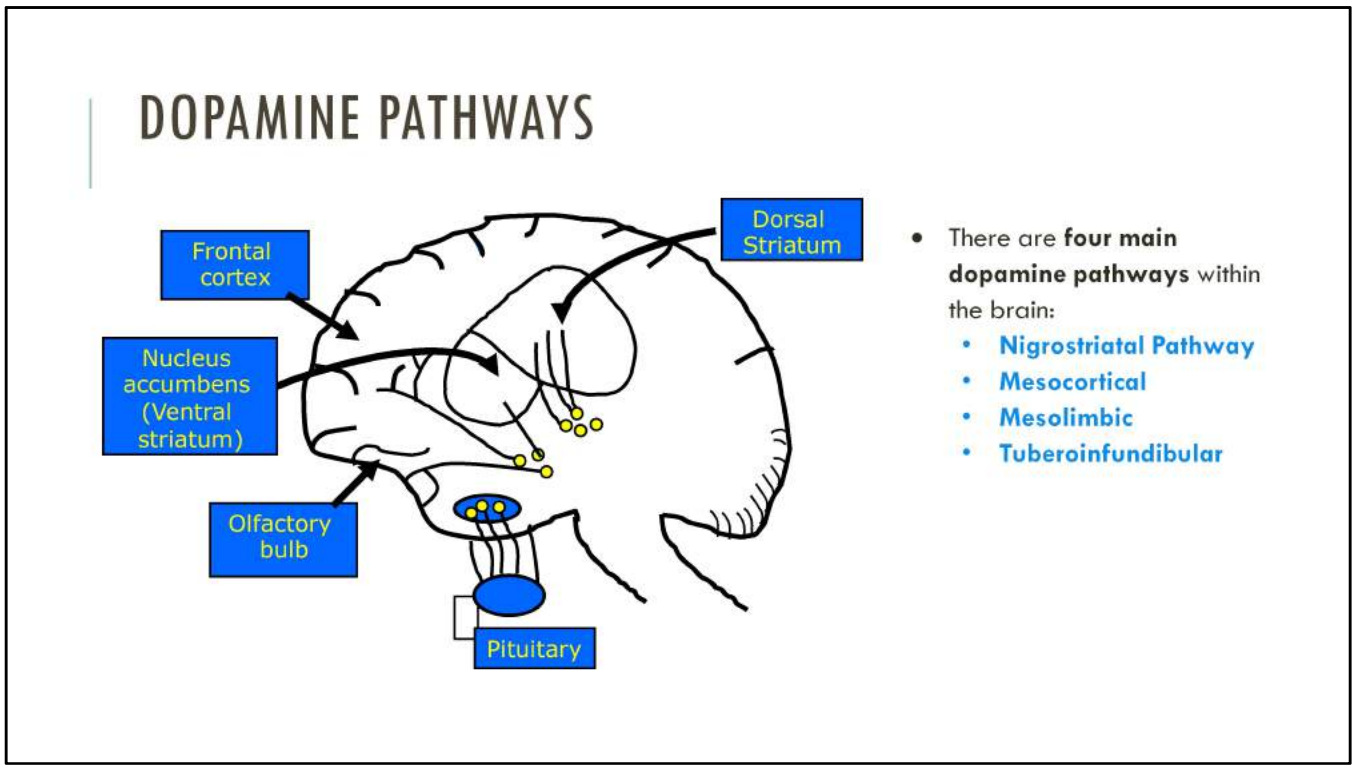
Basal ganglia loops – motor and non-motor



NEUROTRANSMITTERS & PARKINSONISM

1. Dopamine in striatum ↓
2. Loss of dopamine in mesolimbic areas
3. Hypothalamic amines ↓
4. Cortical noradrenaline and Ach ↓
5. Neuropeptides in striatum ↓ (CCK-8, Substance P, Enkephalins)

.



- **Nigrostriatal Pathway**
  - Transmits dopamine from the **substantia nigra pars compacta** (SNc) → **striatum**
  - Associated disorder: Parkinson's Disease

- **Meso = VTA/Nucleus Accumbens**

- **Mesocortical** and **Mesolimbic Pathways**
  - Mesolimbic pathway transmits dopamine from the ventral tegmental area (**VTA**) in the midbrain → **limbic system** via the **nucleus accumbens**
  - Mesocortical pathway transmits dopamine from the **VTA** → **frontal cortex**

- **Tuberoinfundibular Pathway**
  - Transmits dopamine from **arcuate nucleus** of **hypothalamus** → **pituitary gland**
  - Dopamine **inhibits** pituitary release of **prolactin**

Reward/ Mesolimbic Pathway

Function – this pathway has a role in reward + addiction

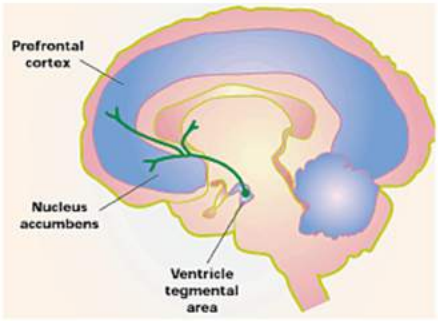
Ventral Tegmental Area

↓

Nucleus Accumbens

↓

Orbitofrontal Cortex (part of the prefrontal cortex)



Orbitofrontal cortex – brake/accelerator.

Dysfunction of mesolimbic pathway → Anhedonia → Depression

- Disruption of the limbic loop occurs due to Parkinson's as the disease affects many areas of the brain that control mood (specifically the frontal lobe as well as those areas that produce serotonin, norepinephrine and dopamine), depression may result
- Development of depression proposes that degeneration of mesocortical and mesolimbic dopaminergic neurons causes orbitofrontal dysfunction
- This disrupts serotonergic neurons in the dorsal raphe and leads to dysfunction of depression-related orbitofrontal-basal ganglia-thalamic circuits

The reward circuit involves **midbrain dopaminergic neurones**

When the cortex has received and processed a sensory stimulus indicating a reward, it sends a signal announcing this reward to the **ventral tegmental area (VTA)**–whose activity then increases

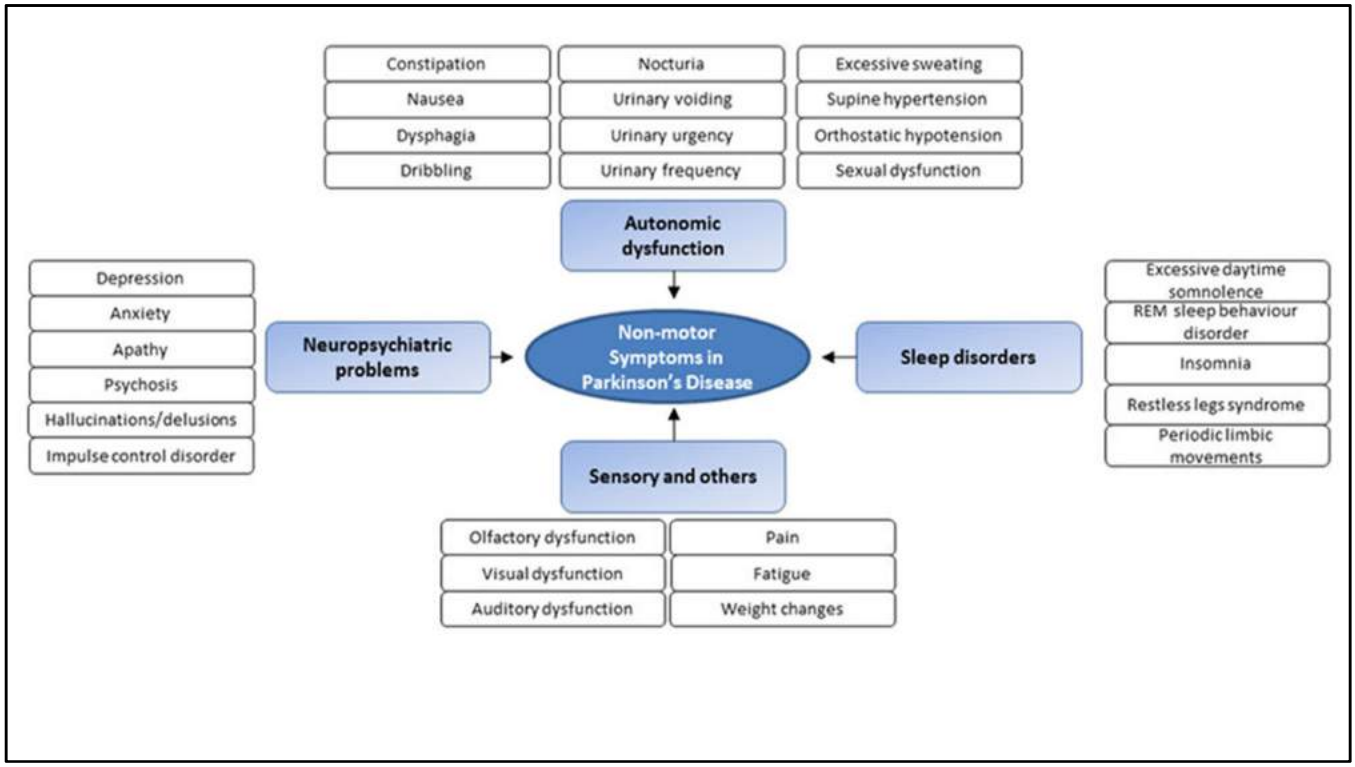
The group of dopaminergic neurons within the ventral tegmental area are labelled **A10**

A10 neurones send axons to the **nucleus accumbens**, the **septum**, the **amygdala**, and the **prefrontal cortex – orbitofrontal and medial frontal cortex**.

The nucleus accumbens then activates the individual's motor functions, while the prefrontal cortex focuses their attention.

CORTICAL NORADRENALINE AND ACH ↓

- Decreases in cortical NA and ACH has been associated with executive dysfunction:
  - Problems with planning, cognitive flexibility, abstract thinking, rule acquisition, inhibiting inappropriate actions and initiating appropriate actions, working memory, and selecting relevant sensory information
  - Fluctuations in attention, impaired perception and estimation of time, slowed cognitive processing speed are among other cognitive difficulties
  - Memory is affected, specifically in recalling learned information



Besides dopamine (DA), three further key neurotransmitters have been described to be involved in the pathogenesis of PD; namely noradrenaline (NA), acetylcholine (ACh), and serotonin (5HT)

Consequentially, non-motor symptoms (NMS) in PD can potentially be related to dopaminergic, non-dopaminergic pathogenesis or a combination of both

However, NMS such as depression, fatigue, weight changes and visual hallucinations may be driven by deficiency in non-dopaminergic transmitters.

DIAGNOSIS

- No definitive tests for PD, it's a clinical diagnosis
- PET scans can aid to determine levels of dopamine
- Difficult to diagnose, many symptoms shared with other disorders.
- Medical history and neurological tests are conducted to diagnose
  - Usually, if two of the cardinal symptoms are present

PARKINSONISM

Clinical diagnosis: 2 out of 4 symptoms below, improve with medications

1. Bradykinesia	→ mask-like face (hypomimia), hypophonia, micrographia
2. Rigidity	→ increased tone, lead-pipe vs cogwheel rigidity
3. Tremor	→ resting tremor, pill-rolling
4. Postural instability	→ shuffling gate, slow to initiate, festinating gate

DIFFERENTIALS

Parkinson-plus syndromes: multisystem atrophy (significant autonomic dysfunction), progressive supranuclear palsy (eye movements affected)

Lewy body dementia: dementia as a result of lewy bodies

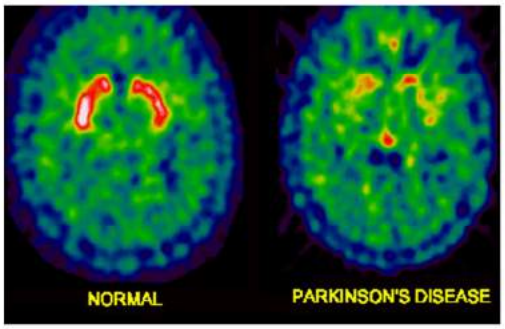
Secondary Parkinson's: drug-induced (antipsychotics), vascular parkinsonism,

YOU MAY USE INVESTIGATIONS TO EXCLUDE OTHER CAUSES:

- To exclude other causes
  - CT/MRI:
    - Exclude:
      - Supratentorial tumours
      - Normal pressure hydrocephalus
      - Extensive subcortical vascular pathology
  - Positron emission tomography (PET) scanning
  - SPECT
  - Transcranial sonography: differentiate PD from atypical or secondary Parkinsonian disorders, for early diagnosis of PD and for detection of subjects at risk for PD

DIAGNOSIS OF PARKINSON'S DISEASE BY IMAGING

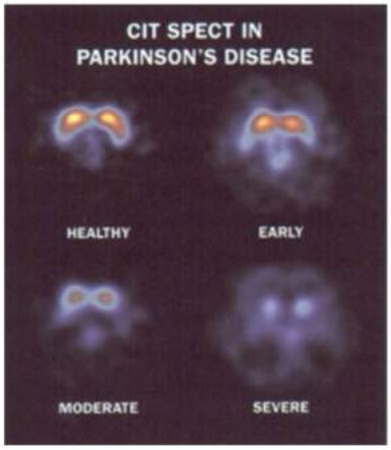
Positron emission tomography (PET)



Visualise and quantify dopaminergic neurones using radioactive ligands which bind to dopamine transporter proteins

fluorodeoxyglucose (18F)

Single photon emission computed tomography (SPECT)



Ioflupane (123I) (DaTSCAN) and iometopane (Dopascan) for SPECT

Computed tomography (CT) and magnetic resonance imaging (MRI) brain scans of people with PD usually appear normal.

Dopaminergic function in the basal ganglia can be measured with different PET and SPECT radioactive tracers. Examples are ioflupane (123I) (trade name DaTSCAN) and iometopane (Dopascan) for SPECT.

A pattern of reduced dopaminergic activity in the basal ganglia can aid in diagnosing PD.

Fludeoxyglucose (18F) (FDG) PET scan of a healthy brain. Hotter areas reflect higher glucose uptake. A decreased activity in the basal ganglia can aid in diagnosing Parkinson's disease.

TREATMENT OF PARKINSON'S DISEASE

"THE TREMOR IN HIS LEFT ARM AND MUSCULAR STIFFNESS WAS ***NO LONGER WELL-CONTROLLED*** *BY THE* ***DRUGS HE HAD BEEN PRESCRIBED****"*

TREAT THE WHOLE PERSON!

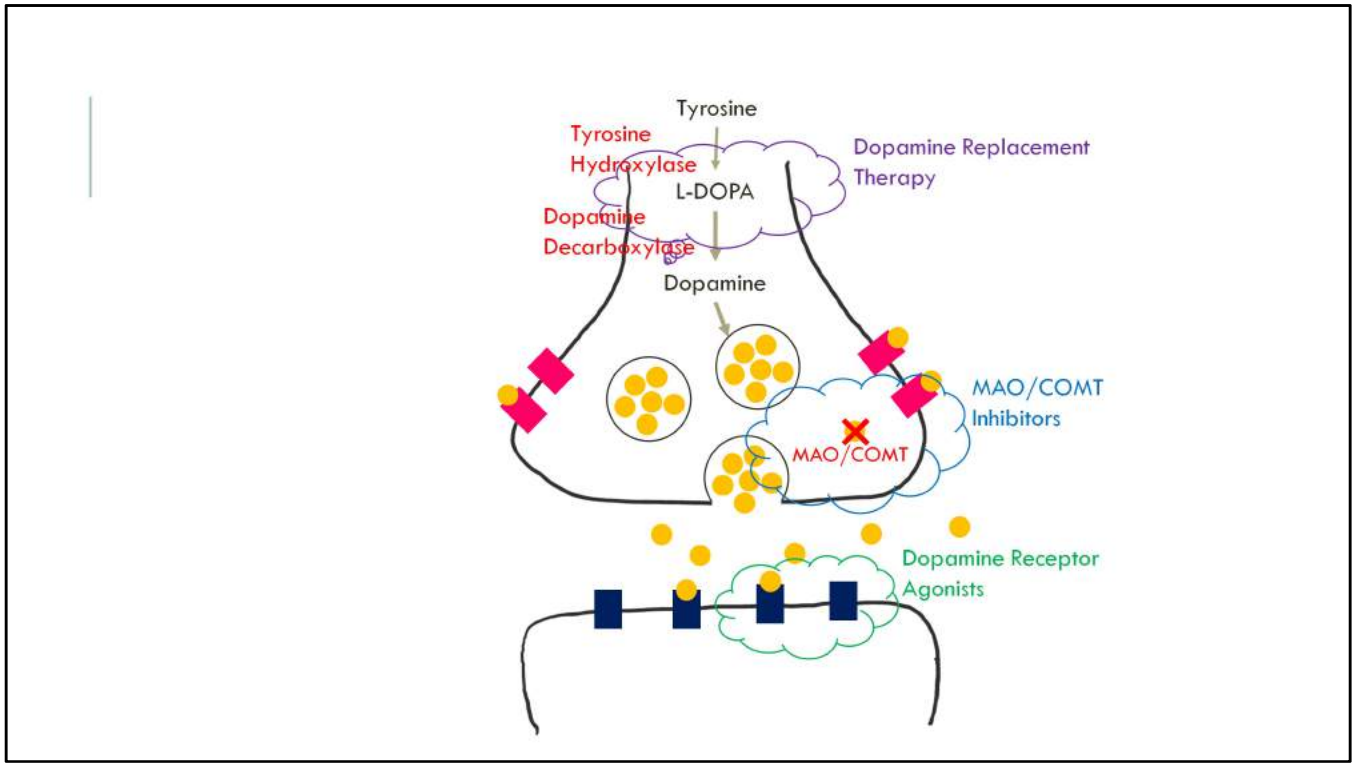
Treat motor features

Treat non-motor features
- Mental health problems
- Sleep disturbance
- Falls

Palliative care

MDT (Multi Disciplinary Team) approach

Motor features = tremor, bradykinesia, rigidity, postural instability, gait problems



G protein coupled receptor

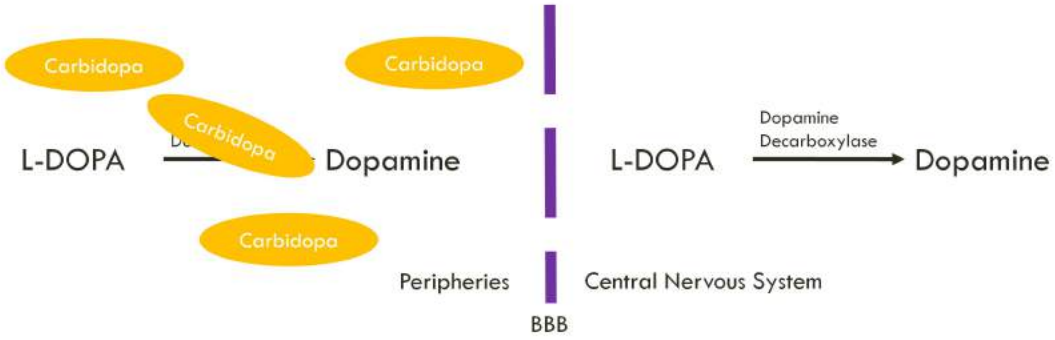
DOPAMINE REPLACEMENT THERAPY

Levodopa PLUS *Carbidopa*

Given as combined tablet

Carbidopa is a **dopamine decarboxylase inhibitor**

- Inhibits metabolism of L-DOPA outside the BBB
- **Charged at physiological pH** – cannot cross BBB into brain



SIDE EFFECTS

Hypotension

Nausea and vomiting

Loss of appetite

Trouble sleeping

Hallucinations

DOPAMINE AGONISTS

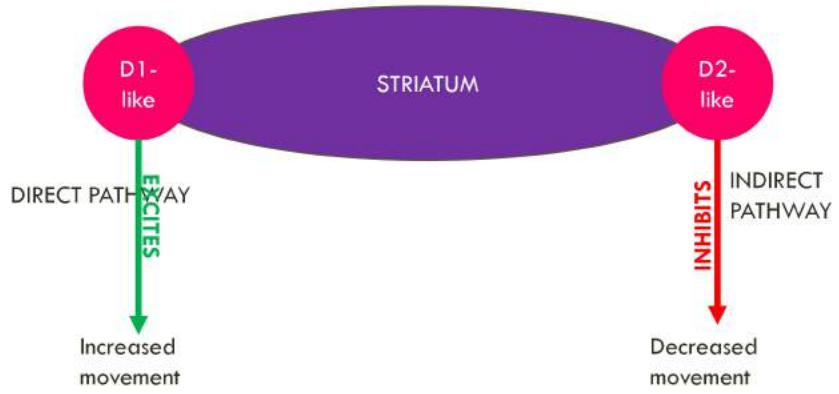
5 types of dopamine receptor: D1, D2, D3, D4, D5

All 7 membrane spanning G-Protein Coupled Receptors

Classified into 2 main subtypes:

- **D1-like receptors** (D1/5)
  - Excitatory – excites direct pathway
  - Located in CNS including basal ganglia
- **D2-like receptors** (D2/3/4)
  - Inhibitory – inhibits indirect pathway
  - Located in basal ganglia, substantia nigra, nucleus accumbens, ventral tegmental area

D2-like receptors are targeted by agonists



Both receptors increase movement when activated!!

DOPAMINE AGONISTS

E.g. ropinirol, bromocriptine

Parkinson's affects the production of dopamine, NOT the post-synaptic receptors

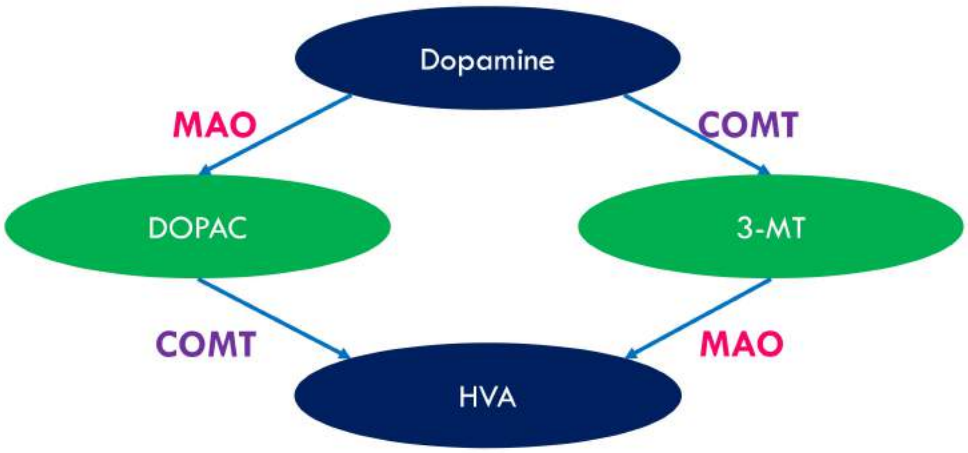
D2 receptors targeted to

Increase Inhibition of the Inhibitory Indirect pathway

Often used in younger patients to put off dopamine replacement therapy

Lots of neuropsychiatric side effects

PREVENTION OF DOPAMINE METABOLISM



MAO-B INHIBITORS

(Mono-Amine Oxidase)

E.g. *Selegiline, Rasegeline*

Prevents breakdown of dopamine

In NICE guidelines as an option for symptomatic relief

NB hypertensive crisis with tyramine!

COMT INHIBITORS

(Catechol-O-methyltransferase)

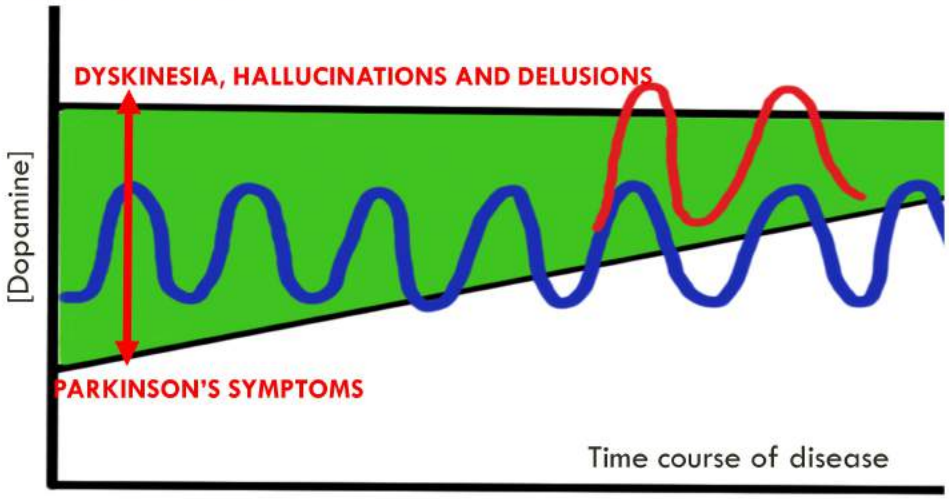
E.g. entacapone

Inhibits the breakdown of dopamine

Used to increase the half-life of L-DOPA – lessens end of dose effect

Only given in combination with L-DOPA and Carbidopa – combined pill available

ON-OFF EFFECT



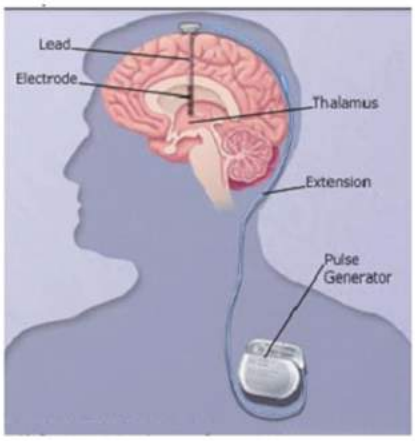
ALTERNATIVE THERAPIES

Deep Brain Stimulation

Modified release L-DOPA

Amantadine (reduces dyskinesia)

Apomorphine – subcutaneous injection
reduces fluctuations



Normal dopamine has half life of 1.5 hours
Amanatadine NMDA-R antagonist and blocks dopamine reuptake
Apomorphine = non-selective dopamine R agonist, made from morphine breakdown products historically, DOESN'T CONTAIN MORPHINE
Similar to l dopa has on off effect but can be used between l dopa to maintain on period

TREATMENT OF NON-MOTOR FEATURES

Mental health problems

- Depression, caution diagnosing as some symptoms are similar
- Psychosis is a side effect – reduce dose!
- Dementia – anticholinesterase inhibitors

Sleep disturbances

- Cant sleep? Sleep hygiene, melotonin?
- Sleeping during day? Modafinil

Falls

MDT APPROACH!

Consultant

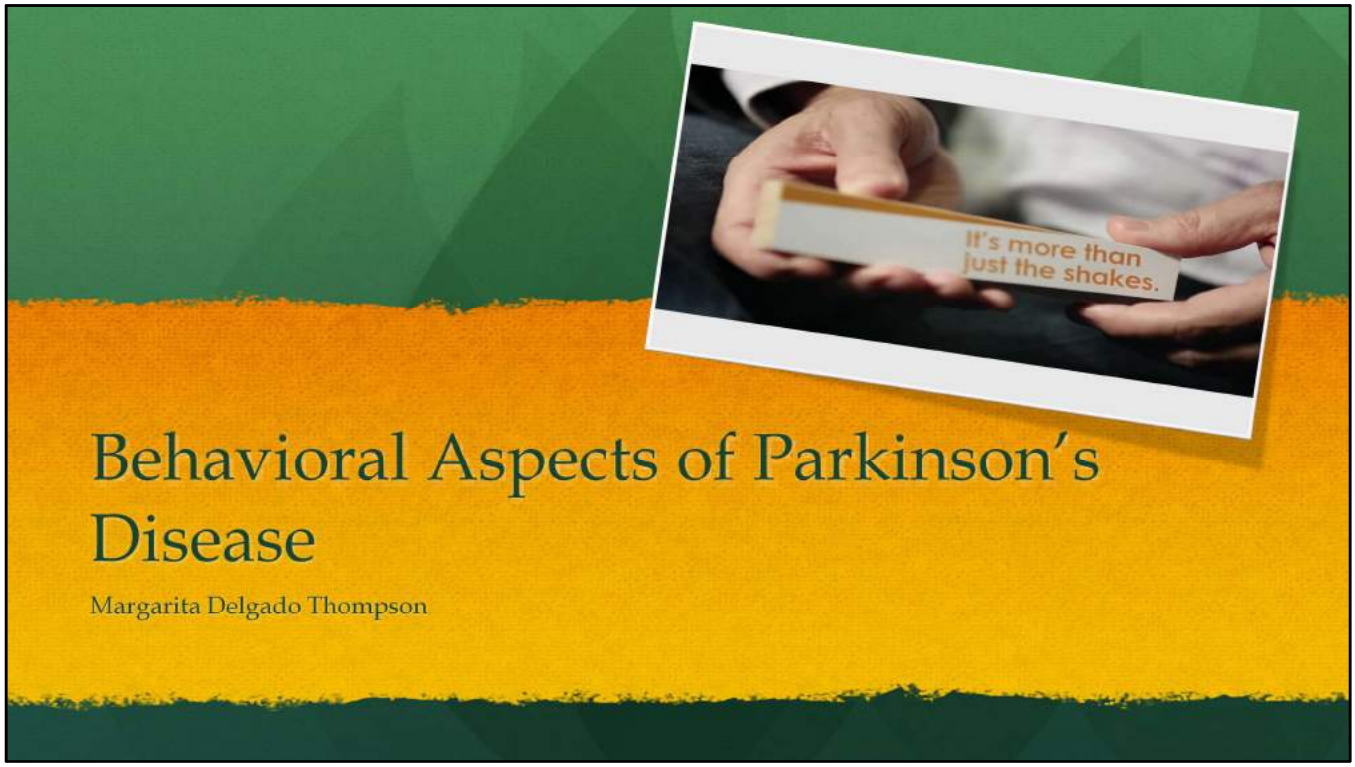
Occupational Therapist

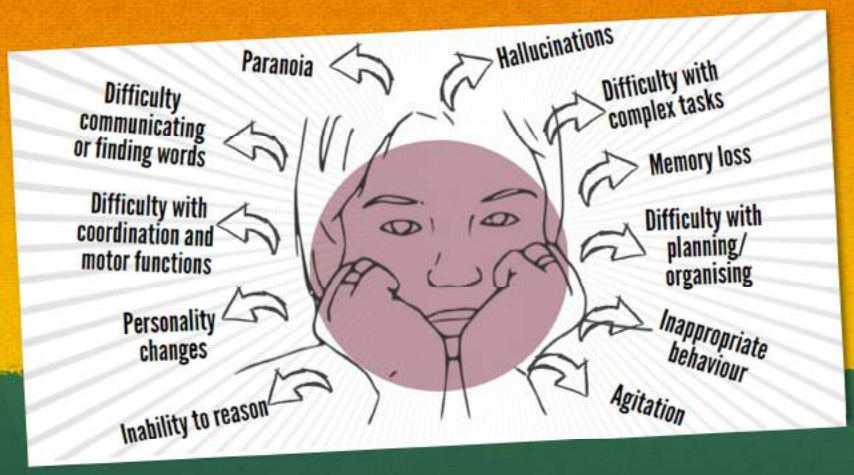
Nurse

Physiotherapist

Psychologist

Social Worker – SUPPORT THE CARER


It's more than
just the shakes.
Behavioral Aspects of Parkinson's Disease
Margarita Delgado Thompson



Cognitive impairment is common in late stage PD

- ~80%
- May develop into dementia

Executive Function

"Trouble completing goal directed tasks"

- Executive function is a description of psychological processes that underlie flexible goal-directed behavior
  - Planning behavior
  - Inhibitory control
  - Attention flexibility
  - Working memory


Using Executive Function
Novel solution required
DRIVE ON LEFT IN AUSTRALIA
Competes against habit
55 km/h
Error Correction

Presented with different stimuli, we have a choice of responses (going to the library, crisis, watching TV). Our responses are baised on the stimulus.

The responses compete, and the strongest one is the one that we act on.

In this case if bake-off is on, we would choose to watch TV. However if there is an exam the next day, we need to pass the exam to become a doctor. So the goal exerts its influence and biases the pathway that will most lead to this goal

In order to do this we need:
1. maintain the goal in mind
2. Control systems to be able to inhibit stimulus driven behavior

The patient was troubled by her inability to prepare her family's evening meal. The patient could remember the ingredients for the dishes but she could not organise her actions into a proper sequence. She might assemble all of the ingredients but become flustered and switch her preparation from one dish to other, or mix up which items belonged together

Tests of Executive Function

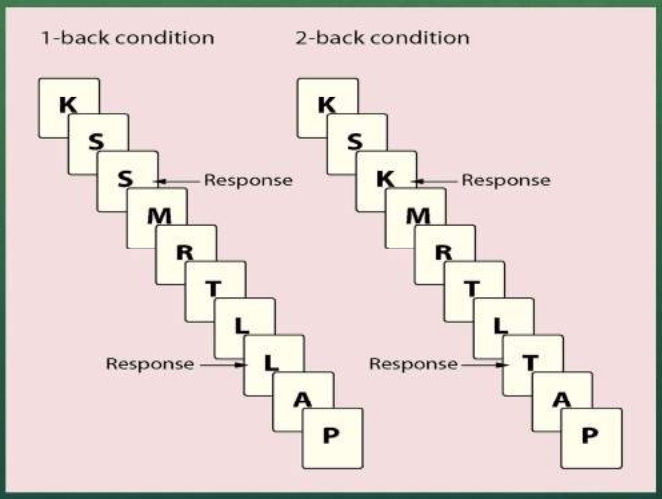
Wisconsin Card Sorting Test

- Strategic planning
- Organized searching
- Environmental feedback
- Goal oriented behavior
- Controlling impulsive behavior

4
1
3

N-Back Task

- Accesses working memory

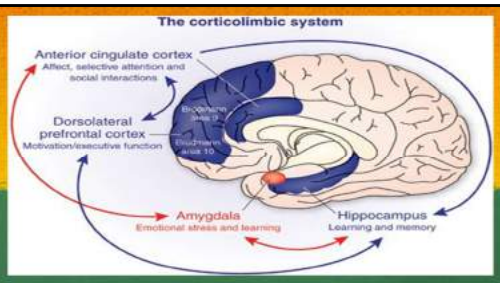


In addition there are tests that test individual sections of Executive Function

Temporal/RecencyMemory

Which object was shown last?

Stroop Test



Blue
Red
Orange
Blue
Green
Blue
Green
Orange
Red
Green
Red

Task of Interference

Accesses attention – identifies important piece of information and ignores irrelevant information

Accesses goal driven behavior – override habitual response

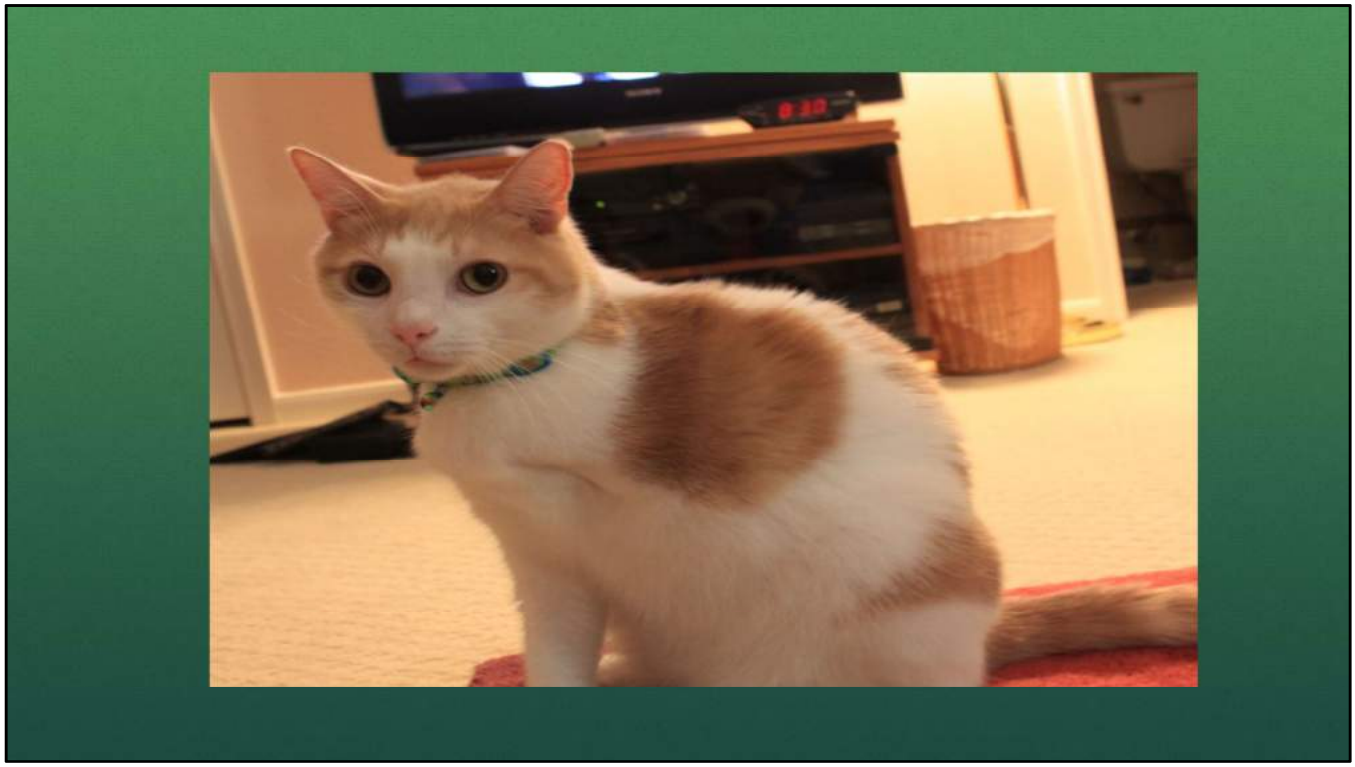
Activates 2 Areas of the Brain

- Dorsolateral prefrontal cortex
  - Activates areas required for the task
  - Ignores irrelevant information
  - Selects information that will fill the goal
- Anterior cingulate cortex
  - Decides what answer to say

Attention

"Increasingly disorganized"

- Attention decides what stimulus the brain focuses on
- Once the stimulus has attention, the brain processes more of the stimulus



- What color rug is Scamp sitting on?
- What is the time on the clock?
- Did you notice he only had three legs?

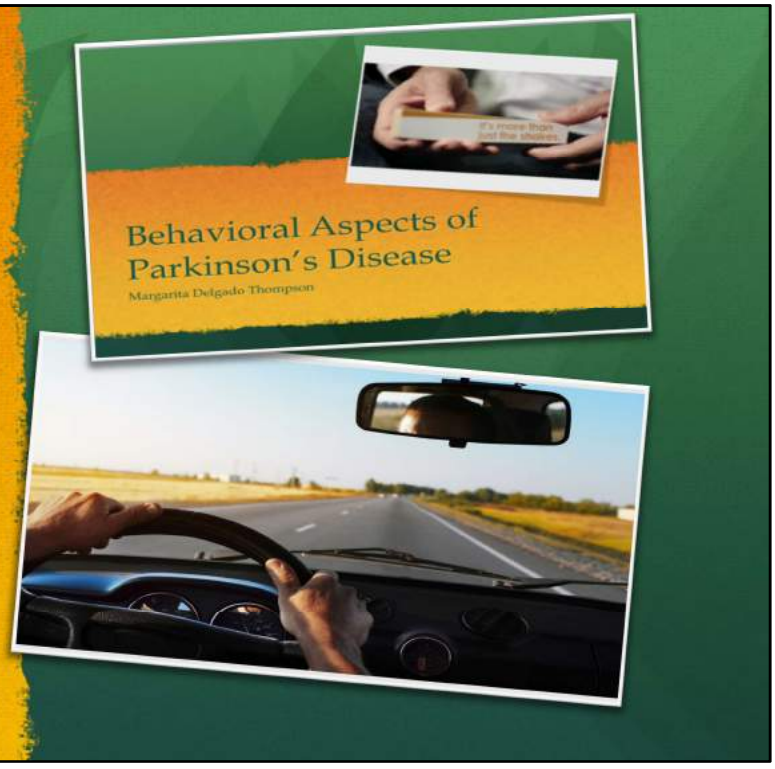
Attention is limited:

- Select only a subset of information
- Can be divided – hard to maintain and limits memory
- Only sustained for a limited period - linked to arousal (how interested you are in the subject)

Top-Down

Active attention

Influenced by what the individual wants to focus on



Bottom-Up

Passive attention
Influenced by stimuli that "catches your attention"

Dementia

Parkinson's Dementia

- A patient who develops dementia after more than a year of having the movement symptoms of Parkinson's

Lewy bodies dementia

- Patient develops symptoms of dementia before or at the same time as developing the movement symptoms of Parkinson's

Depression

1. Decrease in dopamine in brain may cause depression
2. Reaction to the disabling symptoms
   - Isolating
   - Losing activities
3. Family history of depression (independent of PD diagnosis)
4. Other causes of depression EX: thyroid or nutritional deficiencies