# "...I have tremor"

## Nervous System- Case 3

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# Learning Objectives:

This PBL Package targets the following objectives:

- Describe structures and function of the basal ganglia and its role in control of fine movements.
- Describe roles of neurotransmitters (particularly dopamine) in the normal function of basal ganglia and control of fine movements.
- Discuss the pathology and pathogenesis of Parkinson Disease.
- Use basic sciences to interpret clinical symptoms and signs of an patient with Parkinson Disease.
- Discuss the biochemical and molecular mechanisms underlying the development of Parkinson Disease.
- Discuss the pharmacology of drugs used in treatment of Parkinson disease and the mechanisms by which they work.

# Trigger

Mr. Saad Qahtany a 65-year-old retired security officer comes with his son to a local general practitioner. He has tremor of his right arm and hand. He also feels stiffness in his shoulder region. His son says that "over the last six months we noticed that my father has become slow in his movements".

# Discussion Questions:

- Are there any difficult words you do not understand?
- List the key information about Mr Saad.
- Identify Saad' s presenting problems.
- For each problem, generate a list of possible causes (hypotheses).
- What further information would you like to know from history and examination to refine your hypotheses?

# Trigger (Problem)

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## New Terms/Difficult words

- *Tremor*
- *Stiffness*

# Problems/Hypotheses

Tremor

- Overstimulation of muscular receptors
- Overstimulation of the nerve supply
- Overproduction of chemical transmitters (e.g., thyroxin)
- Anxiety/sympathetic stimulation
- Drug induced

Stiffness

- Muscle problem.
- Higher levels above the muscle (impairment of control of muscle tone).
- Joint problems.

# Problems/Hypotheses

## Slowness of body movements

- Problem with central control and coordination of movements
- Muscle problems (e.g., myopathy)
- Hypothyroidism (decreased metabolic rate)
- Painful conditions
- Chronic advanced diseases

# Facilitation Questions

**Normally we do not have tremor. What are the conditions/ situations or possible causes that could trigger tremor?**

*- Anxiety/overstimulation of the sympathetic nervous system.*
*- Increased levels of thyroxine in the blood (thyrotoxicosis)*
*- Overstimulation of Beta 2-adrenergic receptors (e.g., overdose of ventolin)*
*- Disturbance of fine movements (e.g., Basal ganglia problems)*
*- Old age.*
*- Other drugs*

**What are the possible mechanisms for tremor?**
*Depending on the cause*

# Facilitation Questions

**what are the possible causes of muscle stiffness?**

*- Upper motor neuron lesions (usually causes muscle stiffness). Usually there is sensory loss as well.*

*- Muscle and joint problems*
*- Proximal myalgia and stiffness of the neck, shoulder girdle and the hip region, usually painful (as in polymyalgia rheumatica).*

*- Muscle spasms (as in tetanus).*
*- Muscle cramps (electrolyte imbalance, plus other mechanisms)*
*- Hyperexcitability of the stretch reflex.*
*- Problems in the basal ganglia*

# Facilitation Questions

**What could possibly cause slowness of movement?**

- *Depression*
- *Hypothyroidism.*
- *Parkinson disease*
- *Muscle/ joint pain.*
- *Advanced heart failure, respiratory failure, liver failure etc.*

**Tutor:** *encourage students to scribe a diagram showing group of cells and possible changes.*

# Further Questions

- Do the tremors occur all the time?
- What do you mean by slow movement?
- Do you have any pain during walking or moving your limbs?
- Do you have any other symptoms?
- Do you have any heart/lung problems?
- Are you on any medications?

# Please Read The History & Clinical Examination

# History

Mr. Saad has a tremor of his right arm and hand for the last 8-9 months. At first it occurred occasionally and mainly in his right hand. But over the last two months increased and involved his arm and hand. It increases when people comment about his tremor and when he is in stressful situations.

The stiffness of the right shoulder region has been for about 5-6 months. There is no pain on rest or with moving his shoulder. Mr. Saad also mentions that it is difficult to turn his body in bed or move from side to side.

Saad also was slow in his movements for about 6 months. Sometimes he feels unsteady. When he goes with his family to a shopping mall he is always behind and slows in his walking. He walks in short steps. Saad remembers that when he used to work as a security officer in a similar mall he used to walk a lot during his duty. He also noticed disturbance in his sleep for the last 4-5 years.

# History

**Past Medical History**

Saad has no history of heart, or lung or blood disease. He was admitted to hospital when he was 12-year-old for appendectomy.

**Family History**

He has six grownup children and 12 grandsons and daughters. Saad' s parents died when they were 85 and 82 years old.

**Medication and Allergy**

Nil

**Smoking:**

Nil

**Social History**

He is living with his wife and one of his sons who is married and has three children.

# Clinical Examination

Saad has decreased facial expression. He speaks in a low tone voice. Although he rests his right arm on his body while sitting, his right arm and hand show tremor. There is no evidence of hypothyroidism (low thyroid functions). Both ears are normal. His vital signs are summarized in the table below:

| Vital Signs | Patient | Normal range |
|---|---|---|
| Blood pressure | 130/80 | 100/60- 135/80 mmHg |
| Pulse rate | 70 | 60-100/min |
| Respiratory rate | 18 | 12-16/min |
| Temperature | 36.7 | 36.6-37.2 °C |

# Continue-Clinical Examination

## Nervous System Examination

Gait:

When asked for walking, Mr. Saad stands in a slow movement. On standing his body is leaning forward. He walks in slow and short steps. No evidence of cerebellar disease.

Cranial nerves:

All cranial nerves are normal.

Motor Power Examination:

On passive flexion of the right elbow there is a cogwheel like resistance. Normal on the left side.

Sensory Examination:

Normal for both sides.

## Musculoskeletal System

No evidence of myopathy (muscle disease).

Normal bones and joints.

## Cardiovascular and Respiratory Examinations:

Normal

# Discussion Questions

- Are there words that you do not understand?
- Summarize key information that you have obtained from this progress.
- Identify Saad' s new problems. Provide hypotheses for each problem.
- Use the new information obtained to refine your hypothesis.
- What Should the doctor do at this stage?

# New Terms

**(Tutor: encourage students to use their medical dictionary to find out more about these words )**

- Facial expression
- Hypothyroidism
- Cogwheel like resistance
- Myopathy
- Resting tremor.

**Tutor:** Encourage students to use a medical dictionary resource to discuss the meaning of each of these words/phrases.

# Further findings

- Loss of facial expression
- Low tone voice (soft speech)
- Resting tremor
- Cogwheel rigidity
- Forward flexed posture
- Slowness of movement
- Unsteady (?problem with balance)
- Walking in short steps

# Problems/Hypotheses

Tremor

- Overstimulation of muscular receptors +
- Overstimulation of the nerve supply +
- Overproduction of chemical transmitters +/+
- Anxiety/symphatethic stimulation -
- Drug induced -

Stiffness

- Muscle problem -
- Higher levels above the muscle (impairment of control of muscle tone) +/++
- Joint problems -

# Problems/Hypotheses

Slowness of body movements

- Problem with central control and coordination of movements ++/+++
- Muscle problems (systematic problems like myopathy) -
- Hypothyroidism (decreased metabolic rate) -
- Painful conditions (muscle/tendon tear) -
- Chronic advanced diseases (cardiac/respiratory failure) -

# Hypotheses: Ranking

Most likely:

Saad has a problem in his central nervous system at a level higher than the brainstem, most likely affecting his **Basal ganglia** (tremor, rigidity, slowness of movement and facial expression loss)

No evidence of cerebellar disease.

No evidence of thyroid disease.

Less likely:

- Muscle problem -
- Neuromuscular junction problem -
- Peripheral problem -
- Spinal cord problem -
- Brainstem problem –
- Cerebellar problem -
- Cerebral cortex –
- Problem with internal ear/8$^{th}$ cranial nerve ? -

# Progress 1

The general practitioner refers Mr. saad to a neurology consultant. The consultant explains the nature of the disease to Saad and commences him on Levodopa coupled with a peripheral decarboxylase inhibitor (PDI) tablets. He advices him to use this medication and arranges for him to revisit in five weeks.

# Discussion Questions

- Are there any difficult words that you do not understand?
- On the basis of new information from the clinical examination refine your final hypothesis.
- Why the consultant started him on Levodopa coupled with a peripheral decarboxylase inhibitor (PDI)?
- How this medication can help Saad?
- Work out as a team to identify your "learning issues"

## Difficult words

- Levodopa
- Peripheral decarboxylase inhibitor (PDI).

# Facilitating Questions

**Can the doctor use Dopamine instead of levodopa?**

*No. Dopamine does not cross the blood-brain barrier.*

**Why did the doctor give him peripheral decarboxylase inhibitor (PDI) as well?**

*Levodopa is decarboxylated to dopamine in the brain and in the periphery. The formation of dopaimine in the blood causes many of the Levodopa's adverse effects . If Levodopa is given alone, most of levodopa will be decarboxylated to dopaime, resulting in side effects such as nausea and vomiting and small amounts of Levodopa will reach the brain. Therefore PDI is given with Levodopa to reduce the incidence of nausea and vomiting and inhibit the peripheral decarboxylation.*

**Tutors:** *Encourage students to use resources to find out answers.*

**What are the anatomical structures forming the basal ganglia?**

**What are the functions of the basal ganglia?**

**Explain how disturbances in the basal ganglia functions could result in tremor and slowness of movement?**

**Tutor:** *These issues are new to the students. They might add them to their learning issues.*

# Facilitating Questions

**Do you know a Nobel prize winner whose work has contributed to a better understanding of the physiology underlying this problem or helped in the development of a medication for such disorder?**

**Tutors:** *Encourage students to add this to their learning issue.*

# Hypotheses: Ranking

Most likely:

Saad has a problem in his central nervous system at a level higher than the brainstem, most likely affecting his **Basal ganglia** (tremor, rigidity, slowness of movement and facial expression loss)

No evidence of cerebellar disease.

No evidence of thyroid disease.

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- Brainstem problem –
- Cerebellar problem -
- Cerebral cortex –
- Problem with internal ear/8$^{th}$ cranial nerve ? -

# Learning Issues

# Learning Issues

- Structures and functions of the basal ganglia.
- Role of basal ganglia in controlling fine movements.
- Neurotransmitters (particularly dopamine) responsible for the normal function of basal ganglia and control of fine movements.
- Pathology of Parkinson Disease.
- Interpretation of patient' s clinical symptoms and signs.
- Biochemical and molecular mechanisms underlying the development of Parkinson Disease.
- Pharmacology of drugs used in treatment of Parkinson disease.

# Tutorial Two

# Discussion Questions

***After the students spent about 60 minutes addressing their learning issues. You might spent 10-15 minutes on these questions:***

## Discussion Questions:

- What do you think the cause of Saad' s problem is? What are the pathological changes underlying this problem?
- In what way can L-DOPA of help?
- What investigations would you like to order for Saad at this stage?

# Nobel Laureates

# Discussion Questions

## Nobel Laureates

Do you know a Nobel prize winner whose work has helped in understanding a physiological principle related to this case or helped in the develop of a medication for this disorder? Discuss how his/her work helped in advancement of our knowledge in this area.

Students may spend 10 minutes discussing this issue. Those interested could submit a written submission to my on my email
sazer@ksu.edu.sa

# Please Read Progress 1

# Progress 1

Five weeks later, Mr. Saad comes to see the neurology consultant. He feels much better. His arm and hand tremor are much less than used to be.

At the end of the consultation the neurologist, who is also a Professor of Neurology at King Saud University discusses with Mr Saad a research project he has been working on. He explains to him, "...this research is a joint project with three international universities. He asks Mr. Saad if he is willing to be part of the research. He explains to him and his son the value of the research for possible new discovers that could help in treating patients with similar condition. He also explains to them what is needed for the research project. He answers Saad' s questions. The consultant also shows them that the research has been approved by King Saud University Human Research Committee. Saad agrees to join the research project as a volunteer. He signs the consent forms required and receives copies of papers explaining the research outline in a simple language and what is required from Saad.

# Discussion Questions

- Are there words that you do not understand?

- On the basis of the new information, what is your final hypothesis?

- Why do we need research?

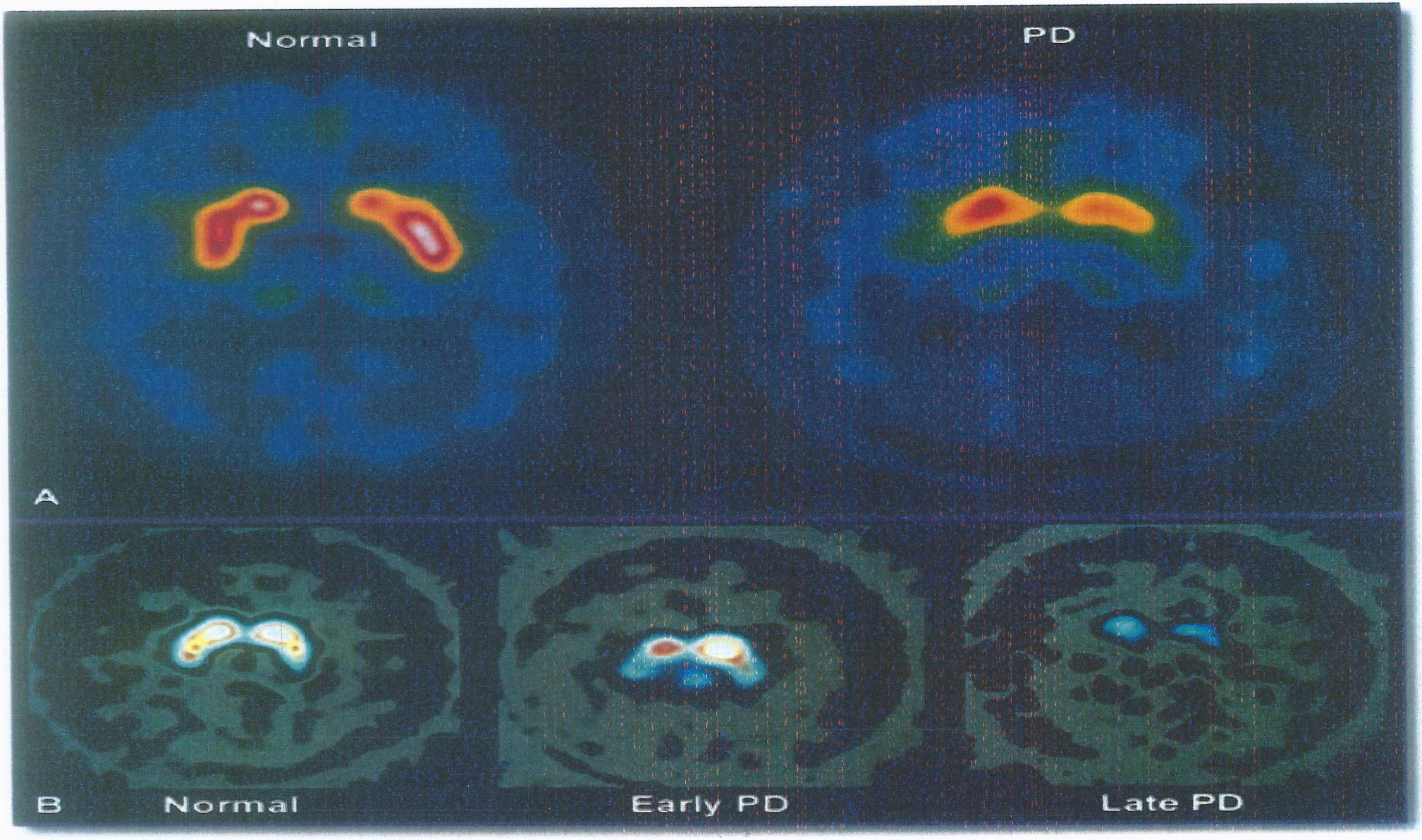
- Why a research project has to be approved by the university human research committee?

# Progress 2

The images below are from the research project conducted on patients with Parkinson Disease. Normally such investigations are not needed for the diagnosis of Parkinson disease (PD). As with the case of Mr Saad, Parkinson disease is diagnosed through history and clinical examination findings. Such research projects could help in understand the progression of the disease, the mechanisms by which medications work, and the role of therapy in delaying disease progression.

The images show a reduction in the uptake of 18F DOPA, and β-CIT Spect uptake by the putamen of patients with Parkinson disease (PD) compared to normal control (Normal). The uptake correlates with the disease progression. Saad' s images confirm that he has an early PD.

# [$^{18}$F]DOPA PET AND β-CIT SPECT IMAGES IN NORMAL AND IN A PATIENT WITH PARKINSON DISEASE (PD)



# Report

**REPORT:**

- **IMAGES A: [$^{18}$F]DOPA PET UPTAKE IN THE PUTAMEN IS REDUCED IN PATIENTS WITH PD COMPARED WITH NORMAL CONTROLS.**

- **IMAGES B: REDUCTION IN β-CIT SPECT UPTAKE IN THE PUTAMEN CORRELATES WITH THE SEVERITY OF PD**

# Discussion Questions

- Are there words that you do not understand?
- Summarize key information that you have obtained from this progress.
- Construct a mechanism summarizing your final hypothesis with regard to the site of the lesion, the mechanisms underlying Saad' s problems. Provide supportive evidence from history, clinical examination and investigation results.

# Facilitation Questions

**Why do we need a consent from the patient?**

- *Legal purposes.*
- *Patient's and doctor's rights.*
- *Evidence that patient's permission has been given.*
- *Evidence that the advantages and risks of a procedure have been discussed with the patient.*

**What are the scientific basis behind these investigations?**

*Assessment of the functional status of the different parts of the basal ganglia.*

**What are the uses of such research projects?**

- *Assessment of the functional status of basal ganglia.*
- *Possibly testing the mechanisms of new drugs working on the basal ganglia.*
- *Studying the impact of new drugs on PD progress, and long term effects.*

# Please Read the Closure

# Case Closure

Over the next 5-6 months Mr Saad shows some improvement. He much less tremor and his walking is more stable. He is also able to do work that needs fine movements such as unbutton his shirt or tie his shoe laces. He regularly see his doctor every 4-5 months.