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Cognitive Impairment in Parkinson's Disease:

Understanding the problem and unlocking the solution to freezing of gait

LEARNING OBJECTIVES

1) Identify at least three relevant cognitive/motor changes that occur in PD and the evidence on objective testing of each impairment.

2) Describe at least two recent evidence findings in clinical interventions to reduce the frequency FOG and the functional limitations from cognitive impairment in PD.

3) Identify at least three of the best clinical measures to detect capacity and responsiveness in dual task cost for persons with FOG in PD.

4) Identify at least two research findings furthering the cognitive / motor interplay in PD.
Outline

- Neurophysiology of cognitive dysfunction and FoG in Parkinson’s Disease.
- Current evidence for treatment of dual task tolerance for PD patients w/without FoG
- Identifying responders and interventions: DT
- Compensatory efforts in safety training for those that are not able to improve w/ DT
- Case studies translating the evidence with practical intervention strategies
PD – statistics and trends

- Incidence
  - 60,000 newly diagnosed cases/year
  - Frequency of PD will increase 4 fold by 2040

- Prevalence
  - 0.3% in general US population
  - Prevalence increases to 4-5% in those >85 years
  - Average age of onset 60 years

- Progression
  - Can be rapid or slow
  - Progression in symptom severity and number of symptoms

Making a diagnosis in PD

Brainstem structure: the substantia nigra – source of dopamine

Clinically detectable after loss of 60-80% of neurons

Presence of eosinophilic intracytoplasmic inclusions

Binding protein: α-synuclein – creating plaques
Making a diagnosis in PD

- Clinical examination to arrive at diagnosis of PD
- Imaging likely normal: CT, MRI
- Autopsy can confirm
- Diagnosis from clinical presentation: “rule-in”
  - Asymmetrical onset and good response to dopamine
  - Clinical indicators
    - Resting tremor
    - Rigidity
    - Loss of postural reflexes
    - Dyskinesia
    - Gait impairment
    - Bradykinesia
    - Flexed posture
    - Frequent falls

Related conditions...NOT PD

- Multiple System Atrophies: MSAs
- Alzheimer’s Disease
- Fronto-temporal Dementia (FTD)
- Lewy-Body Disease
- Parkinsonisms due to stroke, toxicity, trauma
- Cortico-Basal Ganglia Degeneration (CBGD)
- Progressive Supranuclear Palsy
Pathophysiology of Parkinson’s Disease

Structures involved:

Substantia Nigra

Basal Ganglia: Putamen
Globus Pallidus
Striatum

Dorsolateral Prefrontal Cortex

Pathophysiology of variant subtypes (phenotypes)

- Primary dyskinesia
- Primary tremor and rigidity
- Freezing of gait; posture; and festination
- +/- Cognitive changes
Neurophysiology of PD

Primary dyskinesia

- Structures – Globus pallidus
- Incidence – Young onset, estimated <10% (higher with heavy Levodopa use)
- Presentation – Whole body, progressive Increases with stress, fatigue, distractions
Primary tremor and rigidity

- Ventral intermedius n. (VIM) of the thalamus
- Subthalamic n. (STN) between BG and SN
- Incidence 80%
- Presentation

Freezing of gait; posture; and festination

- Structures – Putamen (automaticity)
- Incidence
- Presentation
Neurophysiology of PD

[Diagrams showing neuroanatomical structures and pathways related to Parkinson's Disease (PD)].

10/20/2016
The Dopamine Pathways

Dopamine is the neurotransmitter used by the reward pathway (also called the mesolimbic pathway, which is closely associated with the mesocortical pathway). But there are two other important pathways in the brain that utilize dopamine: the nigrostriatal pathway and the tuberoinfundibular pathway. Generally, drugs that affect dopamine levels in the brain affect all three of these dopamine pathways.

- **Nigrostriatal pathway**
  - Substantia nigra to striatum
  - Motor cortex
  - Deep stimulation in this pathway can result in Parkinson's disease

- **Mesolimbic and Mesocortical pathways**
  - Ventral Tegmental Area to Nucleus Accumbens, Amygdala & Hippocampus, and Prefrontal Cortex
  - Motivation and emotional response
  - Reward and desire
  - Addiction
  - Can cause hallucinations and schizophrenia if not functioning properly

- **Tuberoinfundibular pathway**
  - Hypothalamus to Pituitary gland
  - Hormonal regulation
  - Maternal behavior (nurturing)
  - Pregnancy
  - Sensory processes

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**Figure 1:** An illustration of brain regions and their functions related to dopamine pathways.

- **LIR DLPGC:** Attention, impulsive behavior, risk-taking, working memory, planning, decision
- **LIR M1:** Motor abilities
- **R IPC:** Selective attention, inhibition
- **R TIP:** Working memory
- **pre-SMA:** Inhibition

**Figure 2:** A detailed map of brain regions indicating the effects of dopamine on various cognitive functions.
Cognitive Changes

- **Structures** – SN, caudate and the DLPFC

- **Incidence** – 30% of PD population

- **Presentation** – Higher in those with flat affect, hearing loss, retropulsion, and higher fall rates

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Neurophysiology of cognitive dysfunction and FoG in PD

- Substantia Nigra

- Basal Ganglia nuclei

- Dorsolateral Prefrontal Cortex (DLPFC)

- Pedunculopontine nucleus connectivity
Alternative Neural substrate site: Dorsolateral prefrontal cortex (DLPFC)

**DLPFC** is critical in:

- **Motor planning:** Action selection  
  (Rowe et al, 2000)

- Cognitive processes associated with learning during practice  
  (Cross et al, 2007)

- **Motor memory consolidation**  
  (Shadmehr and Holcomb, 1997)

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Explanations for the dual role of M1 and DLPFC in motor memory consolidation

1. **Cognitive Processing difference**
2. **Goal vs. Movement representation**
Freezing of Gait (FoG): A diagnostic symptom?
Which of these conditions routinely exhibit FoG?
• Multiple System Atrophies: MSAs
• Alzheimer’s Disease
• Fronto-temporal Dementia (FTD)
• Lewy-Body Disease
• Parkinsonisms due to stroke, toxicity, trauma
• Cortico-Basal Ganglia Degeneration (CBGD)
• Progressive Supranuclear Palsy

Freezing of Gait (FoG) correlations
MOST common with:
• Adult-onset PD
• Festinating presentation
• Cognitive impairment

LESS common with:
• Dyskinetic presentation
• YOPD
• Parkinsonisms
The Function of FoG

Beyond the neurophysiology...to the function

• Visual distractions
• Cognitive and psychological distractions
• Temporal distractions
• Sequencing distractions

The Function of FoG: Visual distractions
The Function of FoG: Cognitive and psychological distractions

The Function of FoG: Temporal distractions
The Function of FoG: Sequencing distractions

Evidence supporting DT training in people without PD

Dual task training physiology:

- Models of attention
- Dual task testing parameters
Evidence supporting DT training in people without PD

- Dual task training physiology:
  - Retraining automaticity
  - Procedural memory centers
  - Reducing frontal lobe resources

- Models of attention

- Dual task testing parameters
Sohlberg and Mateer Model

• Focused
• Sustained
• Selective
• Alternating
• Divided

Sustained Attention

*Sustained attention* (vigilance or concentration):

• The ability to maintain a consistent behavioral response during continuous and repetitive activity.
Focused Attention

Focused attention:

The ability to respond discretely to specific visual, auditory or tactile stimuli

Selective Attention

Selective attention:

The ability to maintain a behavioral or cognitive set in the face of distracting or competing stimuli. Therefore, it incorporates the notion of "freedom from distractibility."
Alternating Attention

Alternating attention:

The ability of mental flexibility that allows individuals to shift their focus of attention and move between tasks having different cognitive requirements.

Divided/Switching Attention

Divided attention:

• The ability to respond simultaneously to multiple tasks or multiple task demands.
Broadbent’s Filter Model of Attention

Networks of attention
Attention

Personalize your treatment planning and recall:

Affected by motivation
Arousal
Fatigue
Task/environmental

Dual task training strategies:

• Prioritization
• Habituation
• Automatization
Dual task training strategies:

Prioritization

Subtle or overt
Pre-cued alerting the patient to prioritize
Gradually fading the cue/reminder
Expect emerging self-monitoring/vigilance

*Requires cognition OR caregiver cueing

Dual task training strategies:

Habituation

Gradually increasing environmental and task complexities while recovering motor control
Dual task training strategies:

Automatization – an ordered progression:

1) Repetitions to build familiarity + implicit memory
2) Integration to include a variety of environments
3) Dual task test for baseline
4) Warned distraction loading
5) Subtle and more complex distraction dosage/load
6) Dual task test for comparison

Declarative + Procedural together

• Learning style - baseline and imposed

• Declarative subsidizing procedural

• Which comes first?
Procedural Memories...

• Automaticity is lost in this form of PD

• Overlearned tasks (procedural memories) are built through repetition and ALSO stored in:
  - Cerebellum
  - Supplementary Motor Area (SMA)
  - Premotor Cortex
Types of learning

Explicit Learning:

– declarative, conscious verbalizable knowledge of facts and events supported by declarative memory
– memory for words, scenes, faces, stories
– assessed by conventional tests of recall and recognition

Implicit Learning:

AKA: nondeclarative, procedural, abstract knowledge without verbalizable or conscious awareness

– supported by procedural memory
– changes in performance as a result of experience
– skill learning, habit formation, classical conditioning, priming
Procedural memories gone explicit

Dual task testing parameters
Research and clinical paradigms

- TUGO platform
  CTUG
  TUG-m

- WART
- Auditory Stroop
- Trails B
Dual task testing parameters
Research and clinical paradigms

- TUGO platform
  - Single task TUG
  - Single task distractor
  - Dual task combination

- Distractors: Cognitive, manual, visual, auditory

Evidence supporting DT training in PD patients without FoG

- Gait

- Turning-specific

- Sit to stand transitions
Evidence supporting DT training and compensation in FoG

See bibliography:

- Niewboewer
- Horak
- Peterson
- King

Compensatory training: Why, What and Who?

- Where learning is impaired in PD
- What is the viability of cerebellar compensation
- Is response to perturbation training the or even a determinant in responsiveness to DT?
- Is cognition the determinant for responsiveness?
- Perhaps awareness, specifically self monitoring is an indicator
Compensatory training: Why, What and Who?

- **Why** and when do we choose compensatory training?

- **What** is compensatory training?
  Visual (through cerebellar) networks?
  Physical
  Caregiver-based
  Auditory
  Environmental

- **Who**: Should ALL persons with PD receive compensatory training – even if they are a DT responder?

Compensatory training: Why, What and Who?

**Who** ARE responders to DT?

- Is response to perturbation training the or even a determinant in responsiveness to DT?
- Is cognition the determinant for responsiveness?
- Perhaps awareness, specifically self monitoring is an indicator
Compensatory efforts: Non-responders

- Strengthening
- Endurance training
- Motor learning
- Adaptive equipment
- Sensory cues
- Caregiver training
- Home safety

Compensatory efforts: Strengthening

- Strength dosage considerations
- Power training
- Functional strengthening
Compensatory efforts: Endurance

• Why endurance training?
• Machine-based
• Functional endurance training
• Home recommendations

Compensatory efforts: Motor Learning

Blocked practice and the role of cues

• Cerebellar
• Functional
• Procedural
Compensatory efforts: Adaptive

- Walkers
- Canes
- Walking poles/trekking poles

Compensatory efforts: Sensory Cues

- Environmental changes
- Visual (VR, other tech, physical, person)
- Auditory (tech, machine, person)
Compensatory efforts: Caregivers

• Limiting distractions

• When to/how to help physically

• When and how to help verbally

Compensatory efforts: Home safety
CASE STUDIES

Translating the evidence with practical intervention strategies

Bibliography

Bibliography


