Parkinsonism

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Objectives

- To review the concept of parkinsonism
- To explain the importance of identifying the syndrome
- To review neuroleptic parkinsonism, its effects, and gaps in our knowledge
- To review other causes of parkinsonism than neurodegenerative disorders and antipsychotics
Parkinsonism: Definition

- “Looks like Parkinson’s disease”
- An akinetic, rigid syndrome associated with slowness, stooped posture, reduced stride, reduced armswing
- AKA “Parkinson syndrome”
Parkinson Syndrome
UK Brain Bank definition

- Bradykinesia + at least one of:
  - Rest tremor
  - Rigidity
  - Postural instability

- No exclusionary features
Other common features

- Executive dysfunction
- Speech changes
- Micrographia and other visuo-spatial abn
- Autonomic dysfunction
- Depression and other behavioral changes
UK Brain Bank Criteria for PD
3 or more of following

- Unilat onset
- Rest tremor
- Progressive
- Persistent asymmetry
- 70-100% response to L-D
- Severe LID
- L-D response > 5 years
- Clinical course > 10 years
Parkinson’s disease

- Defined by motor features
  - Tremor at rest
  - Brady and akinesia
  - Rigidity
  - Posture, gait and balance changes

- Exclusionary: dementia; eye movement abnormalities; corticospinal tract signs; other things that don’t fit (“atypical” features)
“Classic” idiopathic PD
Causes of parkinsonism

- Normal aging
- Parkinson’s disease
- Other neurodegenerative disorders (PSP, MSA, CBD)
- Inherited disorders (Huntington’s, Wilson’s disease, SCA)
- Psychiatric disorders
- Drugs
- Vascular disease
- Essential tremor
- NPH?
Dopamine

- Reducing dopamine transmission induces parkinsonism
  - Blocking receptors
  - Reducing synthesis
  - Reducing re-uptake
  - Reducing packaging into vesicles
  - Destroying cells that produce dopamine
  - Destroying cells stimulated by dopamine
Recognizing parkinsonism

- Not recognized in half of cases seen in teaching hospital medical ward
- Not recognized in Nursing Home used for geriatric fellowship training
- Often missed by neurology residents
- ? Taught in psychiatry training programs
PD Unrecognized
Rare case 1
Resolved-no treatment
Wilson’s disease
Obsessional slowness
Psychiatric disorder
Medications

- Dopamine receptor blocking drugs
- Dopamine depleting drugs (tetrabenazine; reserpine; metyrosine)
- Lithium
- Valproic acid
- Cinnarizine, flunarizine (South America)
Neuroleptic parkinsonism

- Clinical overlap with idiopathic PD
- Statistical differences from IPD
  - Less tremor
  - More symmetry
- Cannot be clinically distinguished from PD
- DaT scan *probably* reliable (not an approved use)
Neuroleptic/parkinsonism effects

- Stigma
- Increased risk of falls
- Neuroleptics (atypical and typical): increased mortality
- Legal
Non-verbal cues in the self-presentation of parkinsonian patients.

Pitcairn TK, Clemie S, Gray JM, Pentland B.

Source

Department of Psychology, University of Edinburgh, UK.

Abstract

Parkinson's disease (PD) patients are seen as cold, withdrawn, unintelligent and moody, and appear to relate poorly to the interviewer (Pentland, Pitcairn, & Gray & Riddle, 1987). The cues responsible for this are shown to be related not only to the type of limb and body movements made, but also particularly to the facial expressions. The expressions seen are not only reduced in frequency but are also qualitatively different, particularly in the smiles which are seen to be 'false' smiles. The implications of this for a treatment regime are discussed in relation to the neurology of the disease. It would seem that non-verbal training methods may not produce the required effects because of the shift in neural pathway used from that which normally controls spontaneous expressive movements (via the basal ganglia) to that used in voluntary movements.
Practitioners (N = 284) in the United States and Taiwan judged 12 Caucasian American and 12 Asian Taiwanese women and men patients in video clips from interviews. Half of each patient group had a moderate degree of facial masking and the other half had near-normal expressivity. Practitioners in both countries judged patients with higher masking to be more depressed and less sociable, less socially supportive, and less cognitively competent than patients with lower masking.
Neuroleptic parkinsonism

- Mechanism presumably related to D2 blockade (not so clear)
- Uncertain time to onset
- Uncertain time/% resolution with continued use
- Highly variable sensitivities
- Highly uncertain duration
- Low quality evidence for treatment
Cumulative % = number with NIP/total cumulative # with NIP
Simpson Angus Scale (modified)

- Gait
- Arm dropping
- Shoulder shaking
- Elbow rigidity
- Wrist rigidity
- Leg pendulousness
- Head dropping
- Glabella tap
- Tremor
- Salivation
How long does NIP persist?

- While on neuroleptic
  - “of 402 patients receiving placebos [in addition to neuroleptic]...82% seemed to get along quite well w/o antiparkinson med” (Klett CJ et al. Arch Gen Psychi 1972)

- While off neuroleptic
  - Weeks, to months, to years
  - Forever?
Atypicals and Parkinsonism

- What does “atypical” mean?
- Why don’t the drug trials inform us about EPS side effects including parkinsonism?
- The Simpson Angus Scale
Fifth and sixth best selling drugs in US: Abilify and Seroquel

In 2007 21.3% of Psychiatrist visits for anxiety resulted in Rx for an antipsychotic

Number of Antipsychotic Rx in U.S.

2001: 28 million
2011: 54 million

Advertising 2007 $1.3 Billion  2011 $2.4 B

98% of 2011 advertising for Abilify/Seroquel
NIP (unrecognized)

CONSENT

[Handwritten text]

Risperidone 2mg BID
4/24/07

[Handwritten text]

Date

[Handwritten text]
Aripiprazole 15mg + Lithium 300 mg; DaT negative

108718
2/28/14
Biological variability of NIP
β-CIT Imaging in Subjects with Parkinsonism on Neuroleptics
Parkinsonism not always related to dopamine

- Essential tremor
- Vascular parkinsonism
- Aging
- Psychiatric/psychogenic
Normal MRI & DaT
ET-Park (DaT -)

137359

12/4/41

9/13/12
ET with parkinson features (162100)
Sustention & action tremor; no bradykinesia or rigidity
Vascular Park;DaT -

153887

6/28/13
Lithium: normal DaT

023560
2/27/13
L. 900 mg QHS
NIP + TD

Reserpine 1 mg, 2 mg
1032do
10/8/12
OD TID
89 YO referred for tremor
Consequences

- Increased risk of falls
- Fatigue, depression, “executive” dysfunction; communication; reduced work; reduced quality of life
- Stigma
Does recognizing parkinsonism matter?

- See next slide
Parkinson’s disease-untreated
PD treated
Take home points

- Look for parkinsonism, esp in fallers
- Try to diagnose cause of parkinsonism
- Be aware of antipsychotic drug side effects
- Check for anti-emetic use
- NIP lasts weeks to months after discontinuation
- Institute fall precautions
- Parkinsonism is stigmatizing
- Identifying a syndrome leads to better diagnoses and then better treatment.