Cognitive Impairment and Thought Disturbances in Parkinson's Disease

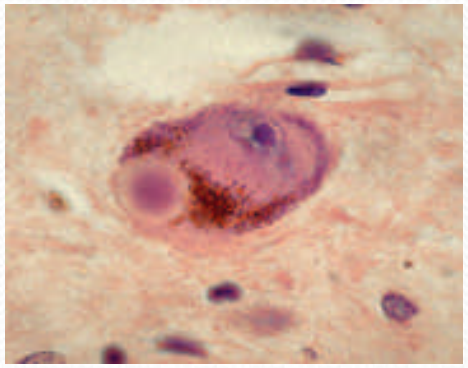
Gail A. Kang, M.D.
San Francisco PADRECC
November 13, 2008

Cognitive Impairment

- Increasing recognition of cognitive problems being present in Parkinson's disease
- Can be more disabling than motoric deficits
- Behavioral features often accompany cognitive impairment
  - Hallucinations and delusions
  - Lack of motivation
  - Personality/mood changes
  - Excessive daytime sleepiness

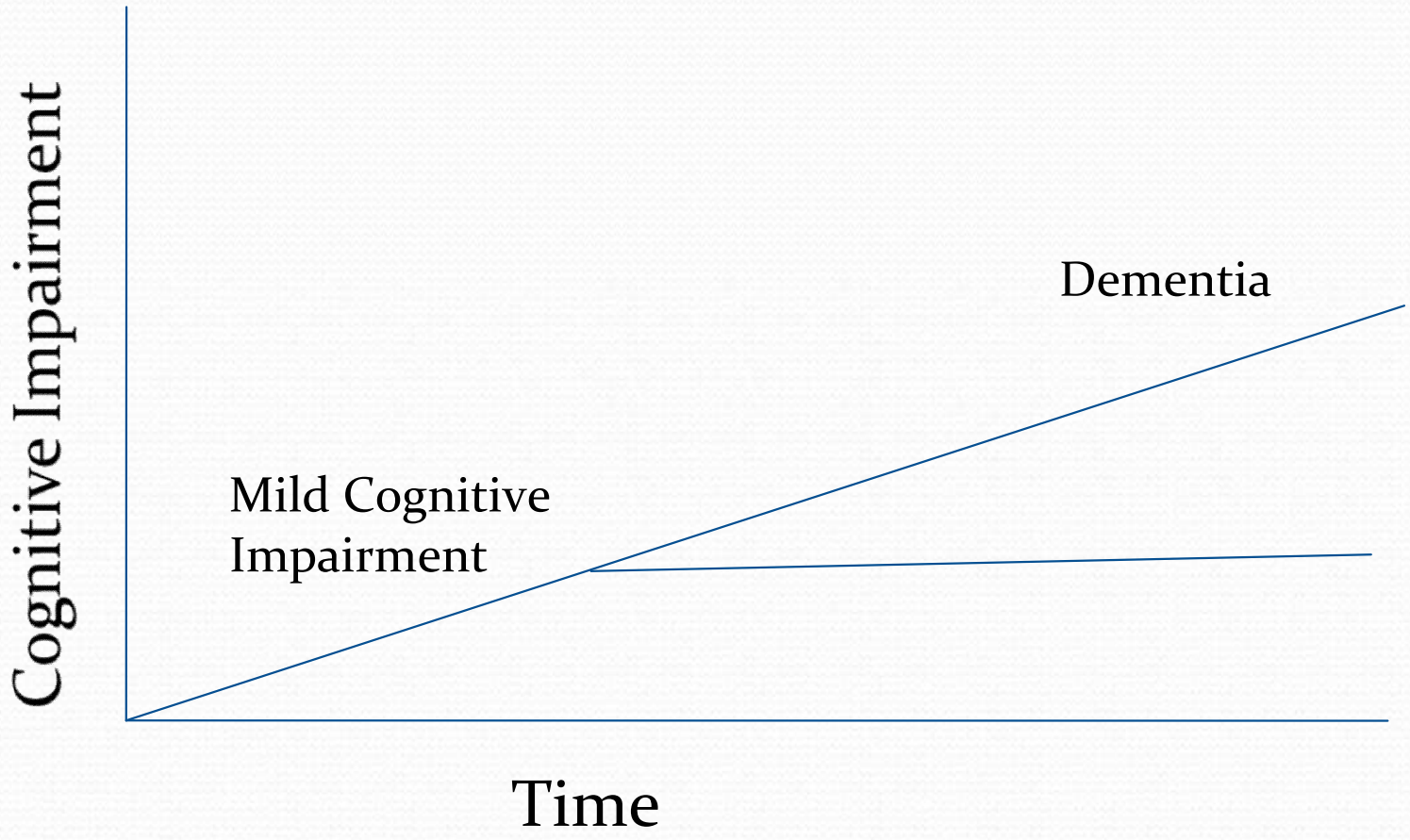
What causes cognitive impairment in Parkinson's disease?

- Lewy body pathology



- Some degree of similar pathology as Alzheimer's disease
- Disruption of dopamine pathways and decrease in acetylcholine

Spectrum of Cognitive Impairment



Parkinson's Disease – Mild Cognitive Impairment (PD-MCI)

- Transitional stage between normal aging and more pronounced cognitive difficulty
- No functional impairment caused by cognitive difficulty
- 20% of Parkinson's disease patients meet criteria for PD-MCI
- Can go unrecognized by clinicians and caregivers
- May represent a "window of time" for optimally beneficial intervention

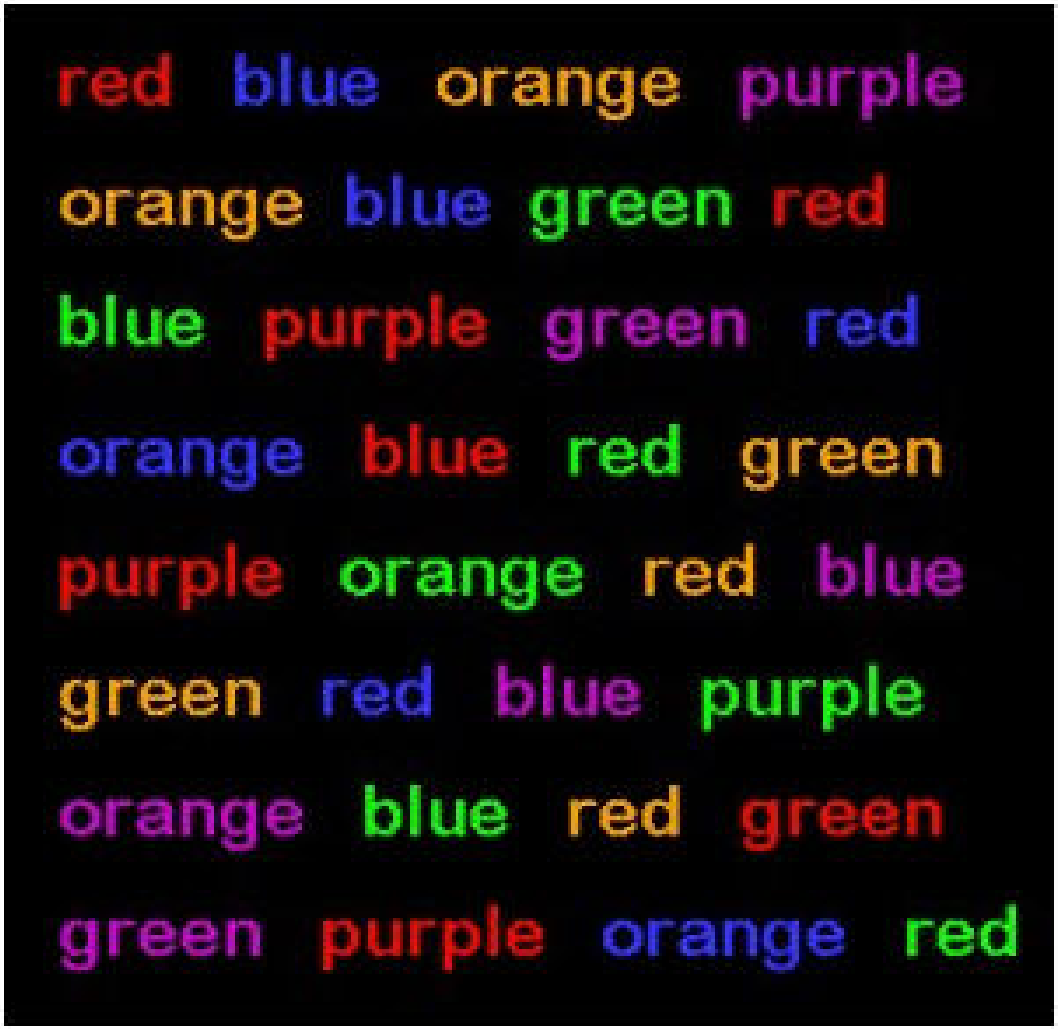
Aspects of cognition most commonly affected in Parkinson's disease

- Executive Function
- Attention
- Recent memory
- Visuospatial Skills

Executive Function

- Range of abilities
- Forming a plan to solve problems
- Ability to perform abstract reasoning
- Shifting of mental effort easily
- Initiation of appropriate actions, inhibiting inappropriate actions

Example of Executive Function Task



Attention

- Ability to focus or concentrate on information presented
- Essential process in learning and remembering information

Recent Memory

- Three step process:
  - 1) Paying attention to information presented so that the information can be encoded accurately into our brains
  - 2) Storing the information
  - 3) Retrieving the information effectively and efficiently

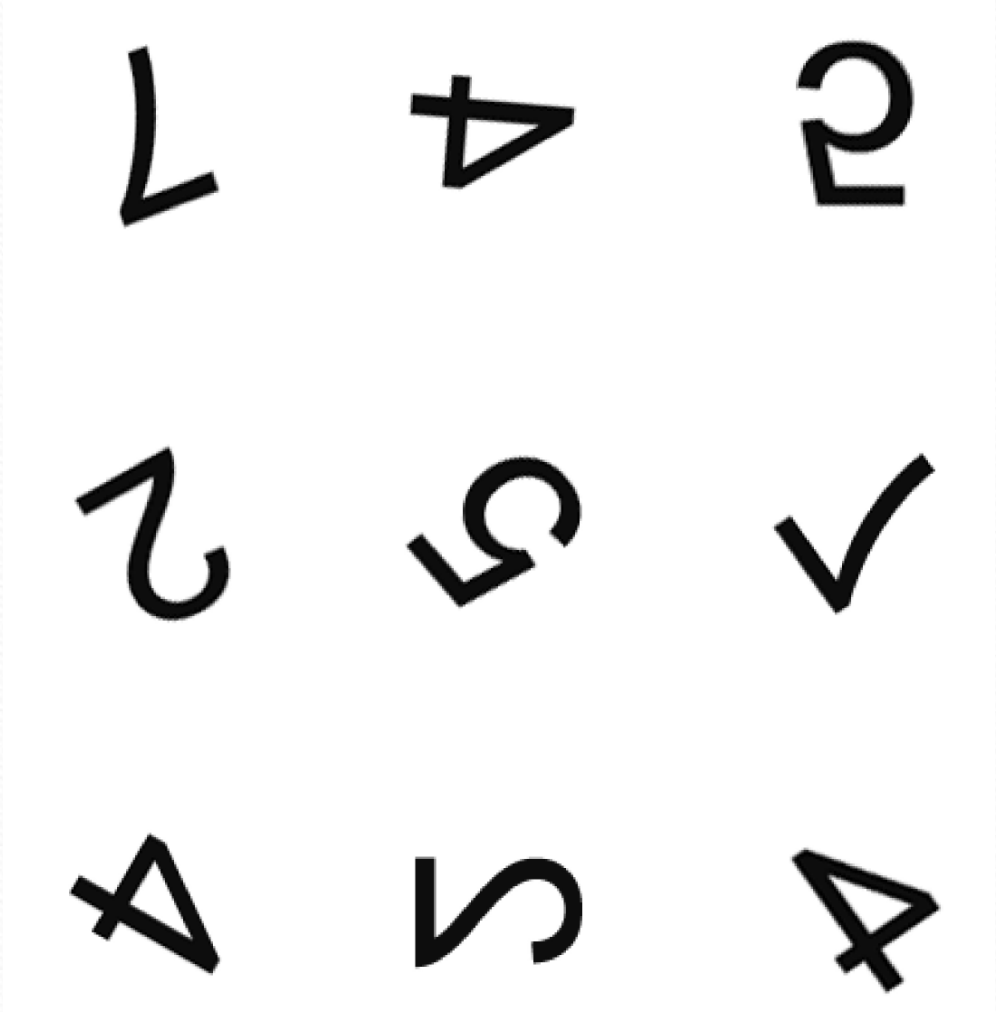
Visuospatial Skills

- Visually perceive objects and understand the spatial relationship among objects

- Every day examples:
  - Going from one room to another at home
  - Navigating way in new city
  - Doing puzzles

  - Mental Rotation

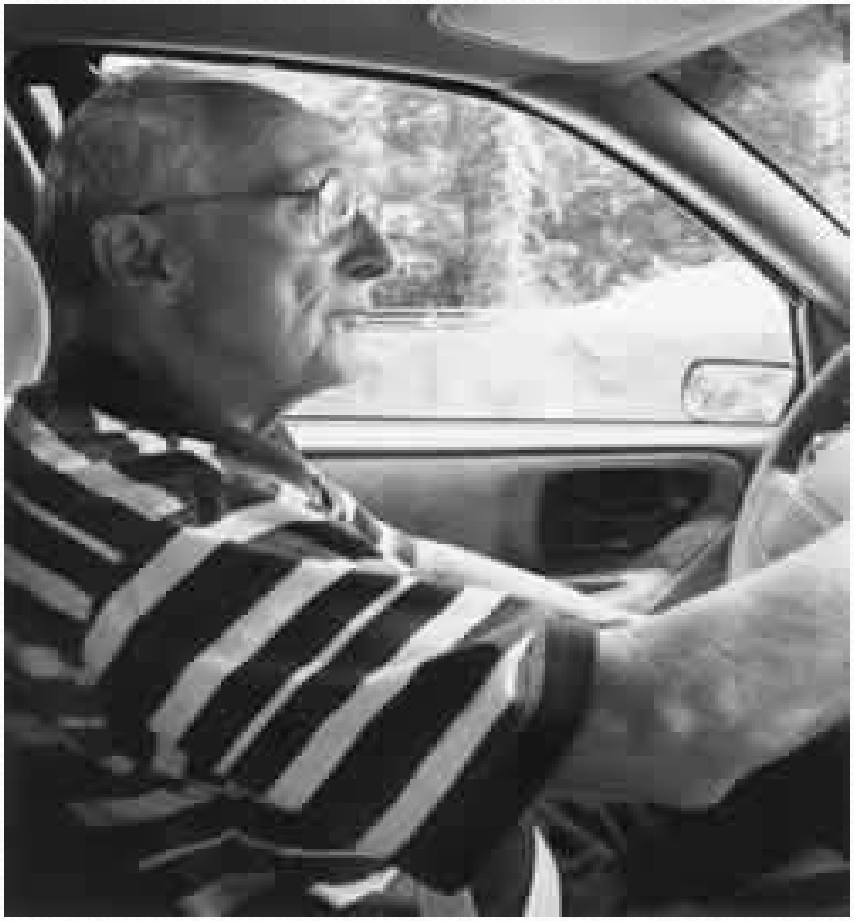
Visuospatial Skills



Situations which may be challenging due to cognitive impairment

- Problem-solving
- Performing complex tasks with multiple steps
- Remembering to take medications
- Following a conversation
- Grocery shopping
- Recreational activities

Driving and Parkinson's Disease



Other causes or contributing factors of cognitive impairment

- Illness
- Depression
- Anxiety
- Medication Side Effects
  - Pain medications
  - Medications for urinary problems
  - Parkinson's disease medications
- Thyroid abnormality
- Vitamin B12 deficiency

Medications for cognitive problems in Parkinson's disease

- **Cholinesterase Inhibitors**
  - *Rivastigmine (Exelon)*
    - Improvement in cognition (Emre et al, 2004)
    - Improvement in behavioral symptoms (apathy, sleepiness, hallucinations) (Emre et al., 20004, McKeith et al, 2000)
  - *Donepezil (Aricept)* and *Galantamine (Razadyne or Reminyl)*
    - Small studies have been performed
    - Mild improvement in cognition and behavioral symptoms (Thomas et al, 2005, Ravina et al., 2005, Aarsland 2003)

Side Effects of Cholinesterase Inhibitors

- Most frequent side effects: nausea, abdominal pain, diarrhea
- Rivastigmine has higher rate of causing side effects
- Worsening of tremor reported to occur in 10% of patients; may improve with longer duration of taking medication (Oertel et al, 2008)

Memantine (Namenda)

- NMDA Antagonist
- May provide neuroprotection/delay progression in cognitive decline
- No formal study on its effect on cognitive function in Parkinson's disease

External cues can help patients with cognitive impairment

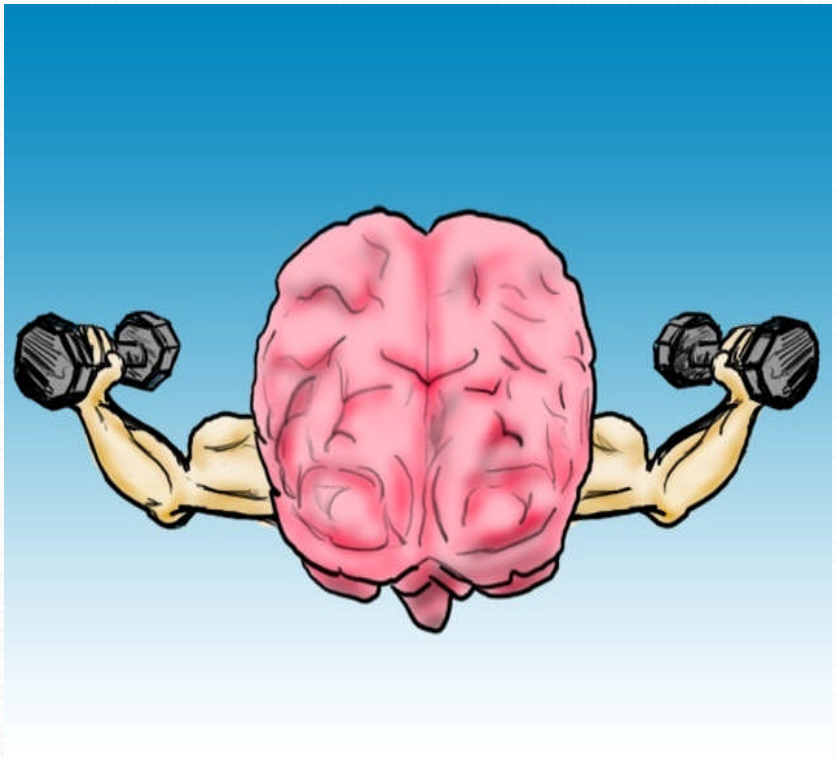
- Medication Timer/cell phone timer
- medication in pill box
- Reminder signs throughout house
- Lists
- Schedule
- Simplification of tasks

Is there a role for cognitive exercise in Parkinson's disease?

- Benefit of cognitive rehabilitation in Parkinson's disease patients with Mild Cognitive Impairment (Sinforiani et al., 2004, Sammer et al., 2006)

- Cognitive exercises may be more beneficial if tailored according to the patient's particular weaknesses

- Puzzles, crossword puzzles, handheld devices or computer programs



Physical Exercise and Cognition

- Studies with patients at risk for developing Alzheimer's disease have shown improvement in memory after regular physical exercise for six months (Lautenschager et al., 2008)
- Improved blood flow in brain seen in human studies (Colcome et al., 2004)
- Animal studies have shown increase in nerve cell growth (Uda et al., 2006)

Psychosis in Parkinson's Disease

- Hallucinations and/or Delusions
- Can occur in up to 40% patients
- Tends to occur years after motor symptoms begin
- Patients often do not inform caregivers and/or physicians about presence of these symptoms

Risk Factors for Psychosis in Parkinson's Disease

- Age
- Cognitive decline
- Depression
- Disease duration
- Visual impairment

Hallucinations in Parkinson's Disease

- Visual hallucinations are the most common
  - Presence hallucinations
  - Passage hallucinations
  - Small people
  - Animals
  - Insects
  - Complex hallucinations
- Can be "benign" with insight retention, especially in initial stages
- May remain non-bothersome or can become quite distressing
  - Inability to discern that hallucinations are real or not
- Auditory and tactile hallucinations

Delusions in Parkinson's Disease

- Less frequent in comparison to hallucinations
- Fixed belief that is not true
- Often of paranoid nature
- Common delusions:
  - Medications are being given incorrectly
  - Others are plotting against patient
  - Concerns of losing money
  - Infidelity

Causes of Psychosis in Parkinson's Disease

- Medications are often major contributing factor
  - Parkinson's disease medications
    - Dopamine agonists
    - Levodopa
    - Artane
    - Selegiline
    - Amantadine
  - Pain medications
  - Medications for urinary incontinence

Psychosis can be triggered or worsened by other conditions

- Infection
- Dehydration
- Electrolyte Abnormality
- Fatigue

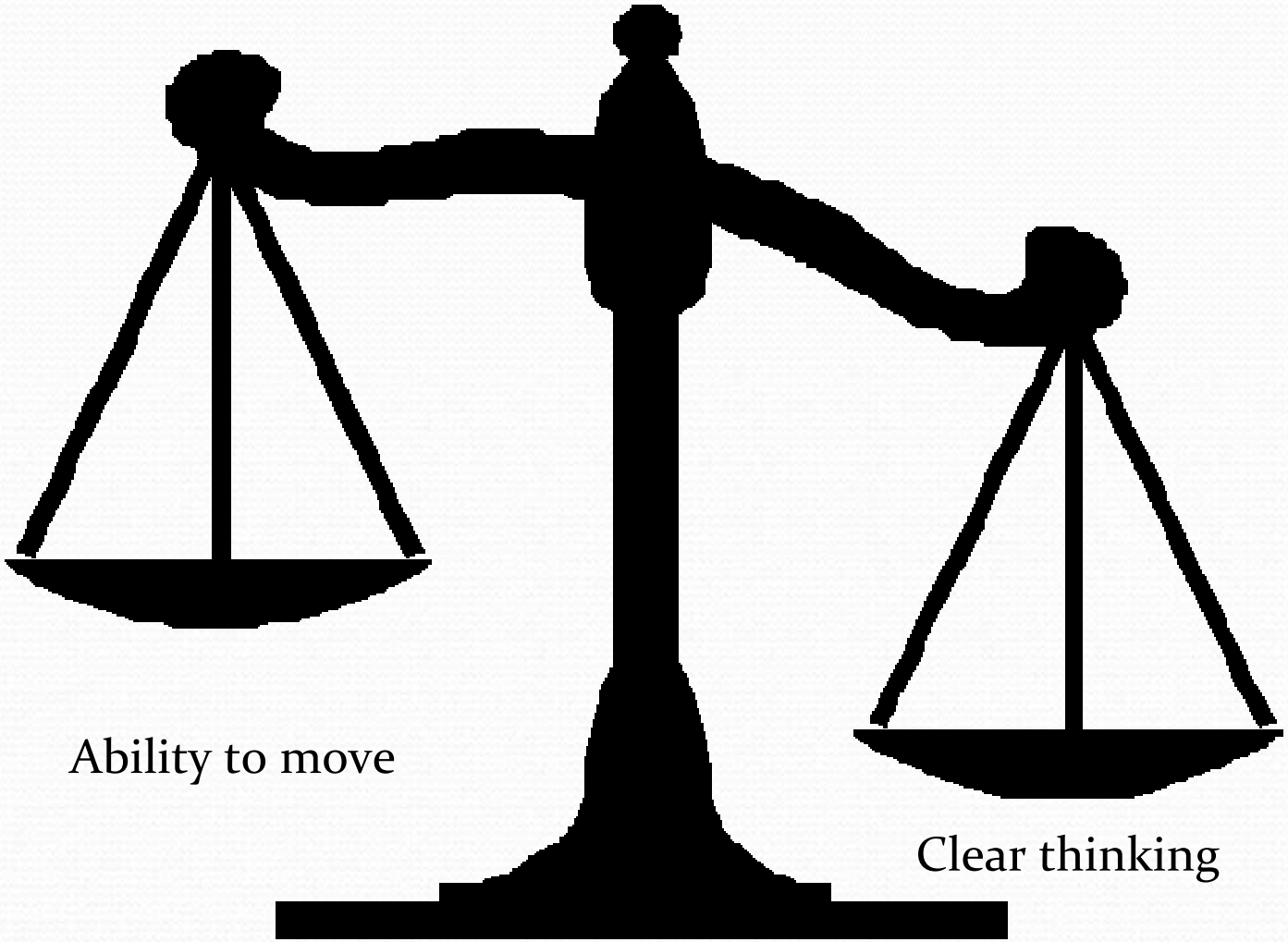
Change of Setting or Routine

- Hospital stay or respite care
- New home
- Re-arrangement of furniture
- Change in schedule
- Time of day

Medication Management in the Treatment of Psychosis in Parkinson's Disease

- Generally follows a step-wise approach:
  - Determine if any non-Parkinson's disease medications can be discontinued
  - If patient's psychosis began after initiating treatment with a certain Parkinson's disease medication with typically milder motoric benefit (i.e. entacapone, selegiline, amantadine), consider discontinuing that medication
  - Decrease or discontinue dopamine agonist
  - Attempt to minimize reduction of levodopa (Sinemet) unless psychosis is severe and unresponsive to other measures

Treatment of Psychosis in Parkinson's Disease



Neuroleptic Medications in Treatment of Psychosis

- Severe hallucinations
  - Neuroleptic medication given concurrently with adjusting Parkinson's disease medications
- "Benign" Hallucinations
  - Take a more step-wise approach
  - If hallucinations continue after making adjustments, consider initiating neuroleptic medication
  - Initiating treatment with neuroleptic at time when patients were experiencing "benign hallucinations" delayed progression of symptoms by two years (Goetz et al., 2008)

Neuroleptic Medications

- Quetiapine (Seroquel)
  - Typical dosage 25-150 mg/day
  - Generally few side effects
  - Small risk of worsening motor function

- Clozapine(Clozaril)
  - Typical dosage 25-36 mg/day
  - Tends to be more effective than other neuroleptic
  - Reports of improvement in motoric function
  - Need for weekly blood draw

Cholinesterase Inhibitors in Treatment of Psychosis in Parkinson's Disease

- No large study has been done
- Based upon clinical reports and small studies appear as if may be quite effective in treatment of psychosis
- Some movement disorders specialists use this type of medication prior to a trial with a neuroleptic