Progressive Supranuclear Palsy (PSP)

- Prototypical subcortical dementia
  - 1-6 per 100,000
  - Median age of onset: 65 years
  - Median survival: 6 years
  - Commonly misdiagnosed as PD
    - Treatment ineffective

Progressive Supranuclear Palsy (PSP)

- Cell loss and neurofibrillary changes in multiple regions of the basal ganglia, brainstem, and cerebellum
  - Subthalamic nucleus (motor/visual disturbance)
  - Substantia nigra (motor deficits)
  - Superior colliculus (visual disturbance)
  - Striatum (cognitive deficits)

PSP: Motor Symptoms

- Gait impairment (slowed, wide based)
- Dysarthria
- Bradykinesia
- Rigidity and/or resting tremor
- Swallowing difficulties
- Postural Instability with falling down (backwards)
- Downward gaze abnormalities
PSP: Dementia Syndrome

- Forgetfulness
- Bradyphrenia
- Personality changes
- Apathy or depression
- Pseudobulbar palsy
- Executive system deficits (pronounced)

Albert, Feldman, & Willis (1974)

PSP: Cognitive Symptoms

- Prefrontal/Executive (disproportionately impaired)
- Perseveration
- Grasping reflex
- Utilization behavior
- Poor orientation
- Slowed or impaired reasoning (> PD)
- Apathy
- Inertia

PSP: Cognitive Symptoms

- Language
  - Processing and comprehension relatively spared
  - Slowed speech
  - Dysarthria
- Memory
  - Mildly impaired, complain of forgetfulness
  - Retrieval deficit
PSP: Treatment

- No effective treatments exist for PSP
- Dopaminergic agents help *some* patients, but most are not

https://www.psp.org/materials/ne_dvd_final.html
PSP VS. PD

- PD
  - Atrophy of SN
  - Mild/moderate executive dysfunction
  - Symptoms initially responsive to drug therapies

- PSP
  - Atrophy of several subcortical areas
  - Severe executive dysfunction
  - Poor response to drug therapies
  - Downward gaze palsy

Creutzfeldt-Jakob Disease

- Subacute Spongiform Encephalopathy
- Prion disease
  - disease-causing cellular proteins
  - Forms plaques
  - Forms sponge-like "holes" in brain
- 1 per 1 million
- Most contract it in their 50’s-60’s
- Extremely rapid progression

Variant Creutzfeldt-Jakob Disease

- Human variant of "mad cow disease"
- Younger onset (mean age: 29 vs 60)
- Psychiatric and sensory problems early on
  - Depression, apathy
  - Lower limb paraesthesias (e.g., foot pain)
- Classic EEG finding is absent
Creutzfeldt-Jakob Disease

CJD: Motor symptoms
- Myoclonus (involuntary twitching/jerking)
- Extreme startle reflex
- Cerebellar dysfunction
  - Ataxia
- Extrapyramidal dysfunction
  - Akinesia or Akasthesia
CJD: Cognitive symptoms

- Episodic unresponsiveness
- Disorientation
- Interference effects (attention, memory)
- Verbal and motor perseveration (profound)
- Delayed verbal memory impairment
- Word finding problems
- Visuospatial deficits and apraxia

CJD: Treatment

- Incurable
- Mean time to death: 4 months!
- Neuropsych testing rarely occurs
  - Disease too rare
  - Patient’s untestable by diagnosis

Mixed Dementia

Dementia syndromes with cortical and subcortical features
Mixed Dementia: Types

- Dementia with Lewy Bodies
- Frontotemporal Dementia
- Corticobasal ganglionic degeneration

Dementia with Lewy Bodies (DLB)

- Dementia
- Prominent hallucinations and delusions
- Fluctuations in alertness
- Gait/balance disorder
- Parkinsonism
- 20-30% of degenerative dementias
- ? Second in occurrence behind AD

Dementia with Lewy Bodies

- Lewy Bodies
  - Spherical inclusions found in cytoplasm
  - Common in brainstem of PD
- Found in:
  - Hippocampus
  - Amygdala
  - Cingulate
  - Neocortex
Dementia with Lewy Bodies

- 15-36% of dementia patients have Lewy Bodies in neocortex and brainstem
- Most also AD changes
- Typically include pure dementia cases with cortical Lewy Bodies and those those with AD+LB under Dementia with Lewy Bodies

DLB: Demographics

- Age of onset comparable to AD
- Males more susceptible (1.5:1) and have worse prognosis
- Duration may be rapid (1-5 years) or typical to AD in other cases
- Mean duration: 6 years
**DLB: Diagnosis**

- Has two of the following core features for probable and one for possible DLB
  - Fluctuating attention/alertness
    - Occurs in 80-90% of DLB, only 20% of AD
  - Visual hallucinations: well formed and detailed
  - Spontaneous motor features of parkinsonism

**Dementia with Lewy Bodies**

- Features supportive of the diagnosis are:
  - Repeated falls
  - Syncope
  - Transient loss of consciousness
  - Neuroleptic sensitivity
  - Systematized delusions
  - Hallucinations in other modalities

**Dementia with Lewy Bodies**

- Imaging:
  - MRI shows DLB patients with hippocampal volume between those of normal controls and AD patients
  - More hypoperfusion in the occipital lobes than AD
DLB: Cognitive Profile
- Fluctuating cognition
- Attentional deficits
- Executive system dysfunction
- Visuospatial deficits
- Memory no impairment to mild impairment
- Hallucinations

DLB: Differential Diagnosis
- AD \(\rightarrow\) early hallucinations, fluctuation in alertness, sensitivity to neuroleptics
- PD \(\rightarrow\) the dementia with PD is subcortical with different symptoms

Cortical vs Subcortical Dementias

<table>
<thead>
<tr>
<th></th>
<th>Cortical</th>
<th>Subcortical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Language</td>
<td>Aphasia</td>
<td>No Aphasia</td>
</tr>
<tr>
<td>Memory</td>
<td>Recall=Recog</td>
<td>Recall&lt;Recog</td>
</tr>
<tr>
<td>Visuospatial</td>
<td>Impaired</td>
<td>Impaired</td>
</tr>
<tr>
<td>Frontal/Exec</td>
<td>Similar imp.</td>
<td>Disproportionally impaired</td>
</tr>
<tr>
<td>Mental Speed</td>
<td>Normal till late</td>
<td>Slowed early</td>
</tr>
</tbody>
</table>
Memory Function in Cortical & Subcortical Dementias

<table>
<thead>
<tr>
<th></th>
<th>Cortical</th>
<th>Subcortical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Free Recall</td>
<td>Impaired</td>
<td>Impaired</td>
</tr>
<tr>
<td>Encoding</td>
<td>Poor</td>
<td>Normal(?)</td>
</tr>
<tr>
<td>Recognition</td>
<td>Impaired</td>
<td>Normal</td>
</tr>
<tr>
<td>Priming</td>
<td>Variable</td>
<td>Present</td>
</tr>
<tr>
<td>Incidental</td>
<td>Absent</td>
<td>Present</td>
</tr>
</tbody>
</table>

Care of the patient with dementia

- Inform and teach caregivers about the nature and progression of the disease.
- Refer to relevant support groups
- Driving issues
- Power of attorney
- Respite and home care programs. Future plans
- Genetic testing?

Care of the patient with dementia

- Maintain high level of activity (exercise programs, daily activities).
- Nutrition. Check for weight loss and nutritional indices (B12, albumin)
- Encourage personal and social functions as much as possible
Common problems in patients with dementia
- Delirium: Fluctuating impairment of attention and orientation, usually of acute onset and due to a medical condition.
  - Reversible
  - 50% of patients with delirium have underlying dementia
  - Presence of delirium precludes cognitive testing for dementia

Common problems in patients with dementia
- Nutrition
  - Malnutrition is common, worsens as disease advances.
- Incontinence
  - Usually a late manifestation. Pharmacological treatment often worsens cognition.
- Sleep Disturbance
  - Very common, avoid medications as much as possible.

Neuropsychologist's Role
- Differential diagnosis
- Assist with treatment approaches
- Patient and Family Education
- Future Plans
- Monitoring Progression and Treatment Rx
  - Changes in living/care arrangements
  - Driving
  - Adjustment to disease