Visual, Auditory, and Somatosensory Impairment in Neurodegenerative Disorders

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Disclosures

• Speaking, consulting, advisory board activities from Biogen, Genzyme, Novartis, Genentech, Bristol Myers Squibb, and EMD Serono
Objective

- Brief review of anatomy of visual, auditory and somatosensory systems
- Discuss how these three systems are impacted by the neurodegenerative diseases of MS, PD, and AD.

Visual System

- Visual Acuity and Contrast Sensitivity
  - Eye Disorders – Cataracts, Retinal Detachment, Glaucoma
  - Optic Nerve – inflammation
- Visual Cortex
  - Visual spatial cognition
  - Hallucinations
- Oculomotor Control
  - Double Vision
  - Saccadic and smooth pursuit dysfunction
### Visual Spatial Impairment in Neurodegenerative Disorders

<table>
<thead>
<tr>
<th>Condition</th>
<th>Bottom-up / top-down</th>
<th>Dorsal / ventral</th>
<th>Allocentric / egocentric</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alzheimer's disease</td>
<td>Bottom-up, most patients, although some patients show top-down</td>
<td>Both are often affected</td>
<td>Allocentric</td>
</tr>
<tr>
<td>Posterior cortical atrophy</td>
<td>Bottom-up, all patients</td>
<td>Dorsal more than ventral, although both are affected with disease progression</td>
<td>Patients cannot use either frame of reference well due to severe bottom-up impairments</td>
</tr>
<tr>
<td>Parkinson's disease</td>
<td>Top-down</td>
<td>Dorsal</td>
<td>Allocentric</td>
</tr>
<tr>
<td>Lewy body dementia</td>
<td>Both, nearly all patients</td>
<td>Both, nearly all patients</td>
<td>Unknown, likely both in most patients</td>
</tr>
<tr>
<td>Corticobasal syndrome</td>
<td>Variable, top-down likely more common but in some patients bottom-up can be prominent, as discussed in text</td>
<td>When visual spatial processing is affected, dorsal impairments are usually more severe</td>
<td>Unknown, likely egocentric</td>
</tr>
<tr>
<td>Progressive supranuclear palsy</td>
<td>Top-down</td>
<td>Attentional impairment is common</td>
<td>Unknown, likely egocentric</td>
</tr>
<tr>
<td>Behavioral variant frontotemporal dementia</td>
<td>Top-down, most patients, although in early stages no visual spatial impairment may be evident</td>
<td>Not impaired</td>
<td>Unknown, may vary with pathologic subtypes</td>
</tr>
<tr>
<td>Semantic dementia and Progressive nonfluent aphasia</td>
<td>Not impaired</td>
<td>Neither impaired early, although SD may affect ventral stream processing with disease progression</td>
<td>Not impaired</td>
</tr>
</tbody>
</table>


### Optical Coherence Tomography - OCT

- Non-invasive study using near infrared light waves to provide cross-sectional images of retina
- Identify neuroaxonal injury, surrogate for neurodegenerative diseases
- AD, PD, HD, MSA, SCA, spastic paraparesis, MS, etc
  - Retinal nerve fiber layer – axonal loss
  - Ganglion cell-inner plexiform layer – neuronal damage

Oberwahrenbrock et al, 2015
Acute Optic Neuritis

RNFL and GCIP thinning in MS subtypes
AD and Vision Loss

- Postmortem studies in AD showed substantial loss of retinal ganglion cell
- Amyloid-beta deposits occur in retina of patients with AD
- RNFL and GC-IP thinning in patients with AD, associated with brain atrophy on MRI
- In a study of 3289 individuals (mean age 68.9, 57% women).
  - 1.2% had dementia
  - 37% higher risk of dementia in those with thinner GC-IPL
  - Thinner RNFL at baseline associated with 44% higher risk of dementia, and 43% higher risk of AD

Mutlu et al, 2018

RNFL thinning associated with future cognitive decline

- UK Biobank prospective study
- 32,038 participants, mean age 56.0, 53.6% women
- Exclude eye disease, vision loss, history of ocular or neurological disease, or diabetes
- Thinnest RNFL quintile 11% more likely to fail 1 cognitive test at baseline
- Follow up cognitive testing in 1251 participants, 3 years later
- Those with 2 thinnest quintiles were twice as likely to have at least 1 worse test score at follow-up

Ko et al, 2018
Retinal changes in PD

- Retinal cells have high concentration of dopamine
- Deposition of alpha-synuclein in retinal ganglion cells in clinicopathology studies
- Thinning of RNFL and GCIP layer observed
- No significant correlation to disease severity or duration

Mailankody et al, 2019

Auditory System

Jafari et al, 2020
Hearing Loss and Dementia

Sherard Audiology, Johnson et al, 2021

Auditory Dysfunction in PD

- Hearing dysfunction more prevalent in early onset PD than late onset PD
- Elderly with hearing loss have higher incidence of PD
- Nonmotor feature of PD
  - Dopamine system contributes to temporal processing of auditory information
  - Dopamine modulates GABA/glutamate effects on auditory processing
  - Alpha synuclein dysfunction
    - Alpha synuclein is expressed in cochlea, early hearing loss in alpha-synuclein deficient mice

Jafari et al, 2020
Hearing Loss and MS

- Systemic Review
- 47 articles
  - 29 case reports
- 1533 patients
- 25% had SNHL
  - S-SNHL 69% (17% overall)
  - P-SNHL 31% (8% overall)

Di Stadio et al, 2018

Somatosensory System

- 2 ascending tracts
  - Fine touch, proprioception - DCML
  - Pain and temperature - ALS
- Alterations
  - Gait and balance
    - Fall risk
  - Pain and paresthesia
- Peripheral nerves

https://open.oregonstate.education/aandp
Somatosensory Impairment in MS

- 82 people with MS
- 66.7% had proprioceptive impairments
- 60.8% had tactile impairments
- 44.9% had vibration impairments
- Somatosensory impairments associated with worse balance

Jamali et al, 2017

Somatosensory impairment in AD

- Somatosensory temporal discrimination threshold (STDT)
- 63 patients: 28 mild-moderate AD, 116 MCI, 19 subjective cognitive deficit. 45 age-matched healthy controls
- Higher values for pts with AD and MCI than subjective cognitive subjects or healthy controls
- Values were not correlated with disease severity
- Possible dysfunction of dopaminergic pathways

D'Antonio et al, 2019
Somatosensory impairment in PD

- Disorders of perception
  - Pain – present in 30-83% patients, increased sensitivity to pain
  - Impaired position sense and limb motion
- Disorders of sensorimotor integration
  - Different activation patterns for tactile discrimination
  - Increased STDT scores
  - Trouble integrating two or more sources (vision and proprioception, object shape and texture)

![Diagram of normal and altered tactile processing](Conte et al, 2013)

Conclusion

- Visual impairment common in neurodegenerative diseases
  - Direct inflammation of optic nerve or deposition of abnormal proteins in retina
  - Impairments in eye movements
  - Cortical visual information processing
  - OCT surrogate marker – more data in MS and AD
- Auditory impairments
  - Auditory information processing
- Somatosensory impairments
  - Direct disruption of ascending tracts
  - Somatosensory information processing