NEURODEGENERATIVE DISORDERS IN SUB-SAHARAN AFRICA

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What is neurodegeneration?

**Progressive** loss of **structure** or **function** of neurons, including death of neurons.
What are neurodegenerative disorders?

Disorders characterized by gradual, progressive loss of function of part or parts of the nervous system.
Characteristics of NDD

- affect **specific** parts or functional systems of the nervous system
- **selective** involvement of anatomically and physiologically related systems of neurons.
- begin **insidiously**
- **gradual, relentlessly/ceaselessly progressive** course over many years
- typically **irreversible** clinical manifestations
- symptoms usually start in late adulthood
What causes neurodegenerative diseases?

- May be sporadic (commoner) or hereditary (less common)
- Genetic causes (gene mutations / genetic predisposition)
- Environmental toxins
- Oxidative stress
- Aging

Mechanisms: aggregation of abnormal misfolded proteins, cell membrane damage, mitochondrial dysfunction, impaired axonal transport, programmed cell death
Examples of ND disorders

- Progressive dementia: e.g. Alzheimer’s disease (AD), frontotemporal dementia
- Movement disorder: e.g. Parkinson disease (PD), Multiple System Atrophy, Huntington chorea
- Muscle paralysis and atrophy: e.g. Amyotrophic Lateral Sclerosis (ALS)
- Progressive ataxia (incoordination of movement): e.g. Friedreich ataxia, spinocerebellar ataxias
- Progressive neuropathies: e.g. Hereditary sensory neuropathies
- Progressive blindness, ophthalmoplegia, or deafness: e.g. retinitis pigmentosa, mitochondrial diseases
Location of pathology in some ND disorders

- **Prion disease**
  - Location: diffuse cortical
  - Macro: cerebral atrophy
  - Micro: spongiosis, PrP deposits

- **FTD**
  - Location: frontotemporal
  - Macro: cerebral atrophy
  - Micro: tau deposits, Pick bodies

- **AD**
  - Location: temporoparietal
  - Macro: cerebral atrophy
  - Micro: Aβ plaques, tangles

- **LBD**
  - Location: frontotemporal
  - Macro: cerebral atrophy
  - Micro: Lewy bodies

- **PD**
  - Location: midbrain
  - Macro: pallor of substantia nigra
  - Micro: Lewy bodies

- **HD**
  - Location: basal ganglia
  - Macro: neostriatal atrophy
  - Micro: neuronal loss and astrocytosis

- **ALS**
  - Location: motor cortex, brainstem, spinal cord
  - Macro: atrophy of motor neurons and muscles
  - Micro: inclusions (Bunina bodies, Lewy body–like)
How common are ND disorders?

• Predominant in aging populations:
  – No. of older people projected to increase from **420 million** in 2000 to **abt 1 billion** in 2030 (7% to 12%)
  – Developing countries: largest increase in absolute numbers (from 59% to 71% of worldwide aging population)

• Alzheimer's disease is the most common NDD
  – affects >25 million people worldwide
  – global prevalence dementia: 3.9% >60yrs (most have AD)
  – Incidence: about 5 million new cases annually

• Parkinson disease is the second commonest NDD
  – Affects 0.3% of general population globally (1% elderly)
  – Incidence rates vary from 4.5 – 10.7/100,000 per year
  – >6 million affected worldwide

• Significant disease burden: morbidity, mortality, economic and infrastructural expense
How common are ND disorders in SSA?

• Sparse epidemiologic data from community-based studies

• Overall burden unclear, some disease-specific data available

• Kegne et al (2006): Yaoundé, Cameroon (NDD account for 3.9% neurologic consultation at 2 teaching hospitals. Of these, PD (48.8%), dementia (19%), ALS (12%), chorea (20.2%). 73.8% male; age range – 9 to 84 (mean 54.2 years)

• Tekle-Haimanot et al (1990), 1986-1988 door to door survey in 60,820 in rural Ethiopia: prevalence/100,000 for parkinsonism (7), MND (5).
How common are ND disorders in SSA? ii

- Osuntokun *et al* (1982, 1987): western Nigeria: prevalence rate of PD was between 50 - 90 per 100,000 >10 years (59 >39 yrs)

- Dotchin *et al* (2008): rural Tanzania; 161,000 participants; age adjusted PD prevalence of 40 per 100,000

- Dewhurst *et al* (2013): 2232 participants >70 years; Hai district, Tanzania: age-adjusted prevalence of all neurologic disorders – 154.1/1000; prevalence of parkinsonism: 5.9/1000
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<tbody>
<tr>
<td>AD and other dementias</td>
<td>17,108</td>
<td>450 / 5551.2</td>
<td>7,468</td>
</tr>
<tr>
<td>Parkinson disease</td>
<td>2,325</td>
<td>100/973.7</td>
<td>1,086</td>
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Modified from Mathers et al, 2003, WHO GBD 2009
ALZHEIMERS DISEASE

- Most common neurodegenerative disease
- Predominantly a disease of the elderly, with prevalence doubling every 5 years >65 years
- Important social, economic and psychological consequences
- Dementia carries the greatest economic burden of all diseases
- Most data from SSA mainly provide information for all dementias (including vascular dementia, frontotemporal dementia, etc)
AD in Africa

• Overall prevalence of dementia in adults >50 years in Africa: 2.4% = 2.76 million people in 2010
• About 2.10 million of these live in SSA
• Prevalence highest in females ≥80 years (19.7%)
• Little variation between regions
• AD most prevalent (57.1%) of all dementia
• Main risk factors: increasing age, female sex, CVD.

AD in Sub-Saharan Africa

- Specific data from longitudinal study on dementia from the Ibadan-Indianapolis Dementia Study (started in 1992).
- The IIDS provides incidence, prevalence, risk factor and mortality data for AD in SSA.
- Longest epidemiologic study of AD and dementia in Africa
### Incidence of dementia in SSA

Ibadan-Indianapolis Dementia Study 1992 - 1998

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<tr>
<th>Disorder</th>
<th>Ibadan, Nigeria</th>
<th>Indianapolis, USA</th>
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<tbody>
<tr>
<td>Dementia</td>
<td>1.35% (1.13 – 1.56)</td>
<td>3.24% (2.11 – 4.38)</td>
</tr>
<tr>
<td>Alzheimer’s disease</td>
<td>1.15% (0.96 – 1.35)</td>
<td>2.52% (1.60 – 3.66)</td>
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Based on 5 year follow up

Annual Incidence Rates of Alzheimer's Disease

- Aevarsson and Skoog, 1996
- Bachman, et al, 1993
- Brayne, et al, 1993
- Hagnell, et al, 1992
- Hebert, et al, 1995
- Yoshitake, et al, 1995
- African Americans
- Ballabgarh Indians
- Monogahela Cohort

age in years

annual incidence rate (%)
AD in SSA (contd)

- Higher incidence in older women (> 80 years)
- Increased risk for mortality (IIDS: Yoruba relative ratio=2.83, African Americans relative ratio=2.05).
- Genetic risk factor: Possession of e4 allele of APOE not associated with increased risk for AD in Yoruba (SSA) (in contrast to African Americans (e3/e4: odds ratio 2.32; e4/e4 odds ratio 7.19; compared with the e3/e3 genotype).
PARKINSON DISEASE IN SSA

- PD is the second most common neurodegenerative disease worldwide.

- Prevalence of PD worldwide has been estimated to be 0.3% in the general population and 1% in people over 60 years of age.

- Range of reported country rates: 7 – 329 per 100,000

- SSA (per 100,000): Nigeria 50 - 90, Tanzania 20 - 40, Ethiopia 7.
Distribution of epidemiologic and genetic studies of PD in sub Saharan Africa in 2006. Additional clinical series, genetics studies and prevalence data between 2006 and 2013.
Clinical profile of PD at presentation in Nigerians (1996 to 2006)

<table>
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<tr>
<th>Clinical characteristic (N=98)</th>
<th>Mean (SD)</th>
<th>Median</th>
<th>Range</th>
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<tbody>
<tr>
<td>Age at onset of PD in men, yrs</td>
<td>60.3 (10.4)</td>
<td>62.0</td>
<td>37 - 77</td>
</tr>
<tr>
<td>Age at onset of PD in women, yrs</td>
<td>65.2 (7.9)</td>
<td>68.0</td>
<td>41 - 74</td>
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<tr>
<td>Interval from onset to diagnosis, mo</td>
<td>24.6 (26.1)</td>
<td>12.0</td>
<td>4 - 156</td>
</tr>
<tr>
<td>Hoehn &amp; Yahr scale</td>
<td>2.3 (0.8)</td>
<td>2.0</td>
<td>1 - 4</td>
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* Hallmark: late presentation;

Modified from Okubadejo et al. BMC Neurology 2010
Genetics of PD in SSA

- Data available from Ghana, Nigeria, South Africa and Zambia
- Bardien et al (2010). South Africa – 205 PD. LRRK2 mutation frequency 2% (n=4)
- Yonova-Doing E et al (2012). Zambia – 39 PD. Screened for mutations in LRRK2, SNCA, Parkin, PINK1, and DJ-1. No LRRK2, SNCA, PINK1 or DJ1 mutations found. 2 parkin mutations
MND IN AFRICA / SSA

Radhakrishnan K et al (1986): Benghazi, Libya
• Incidence (1980 – 1985): 0.87 per 100,000 per year
• Prevalence: 3.42/100,000
• Male to female ratio: 2.3 to 1
• Highest incidence at age 50 – 59 both sexes
• Median age at diagnosis: 51 years
• Median time from onset to death: 30 months
• Subtypes (of 23 patients): ALS – 17, PMA – 4, PBP – 2

Sene et al (2004): Hospital-based survey in Dakar, Senegal; ALS only
• 33 patients from 1993 – 2000
• Ages: 16 – 77 years
• Parental consanguinity in 15.2%
• Most lost to follow up

Prevalence of MND in SSA (Tekle-Haimanot, rural Ethiopia): 5 per 100,000
PROJECTIONS

• Based on estimates of persons affected by AD
  – 2.1 million in SSA with AD as at 2010
  – PD prevalence about \( \frac{1}{4} \) AD: 525,000 with PD
  – MND prevalence about \( \frac{1}{8} \) PD: 66,000 MND
  – Other NDD (prevalence unknown): ???

• Number of persons with NDD in SSA may be close to 3 million, and rising!
SUMMARY

• The current and projected burden of NDD in Africa, particularly AD and PD is high

• Additional epidemiologic data are required to further clarify the burden and provide a stronger impetus to drive development of manpower and infrastructural support

• Lack of access to professional care, late presentation, and limited access to treatment are plaguing and urgent issues

• Short-term and long-term strategies to address the burden and gaps are required.