A brief overview of the neurodegenerative diseases of the brain

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April 23, 2019
We will explore three questions today:

1) What are the neurodegenerative diseases of the brain?
2) What do these diseases have in common?
3) How do they differ?
To answer these questions we must first understand that different diseases of the body produce different **signs** and **symptoms**.

A **sign** is an **objective** manifestation of a disease, whereas a **symptom** is an **subjective** manifestation of a disease.

The group of **signs** and **symptoms** produced by a specific disease process is called a **clinical syndrome**.
Disease process

Clinical syndrome

**Symptoms of lung infection:**
- body aches
- low energy
- shortness of breath
- chills

**Signs of lung infection:**
- fever
- cough
- wheezing
- difficulty breathing

"Pneumonia"
Whereas different regions of the lungs do the same thing, different regions of the brain do very different things.
A very brief history of...

CEREBRAL LOCALIZATION *

*The (mostly) precise science of predicting which region/s of the brain are damaged or malfunctioning based on a careful examination of a patient’s signs and symptoms (i.e. the clinical syndrome).

Early 1800's

1848

Late 1800's

1900

Late 1900's

Currently

Prinz J. Gall

P. Gage was “no longer gaga”

Paul Broca

Korkinman Brodman

“Principles of Behavioral and Cognitive Neurology”

Modular and Distributed model
Franz J. Gall

Early 1800's

P. Gage was "no longer gage"

1848
P. Gage was “no longer gage”

1848
Paul Broca

“...I had thought that if there were ever a phrenological science, it would be the phrenology of [the cortex], and not the phrenology bumps [on the head].”

*Father of anatomo-clinical correlations

Late 1800’s
"Principles of Behavioral and Cognitive Neurology"

Late 1900’s

Modular and Distributive model

Currently
Modular and Distributive model

Cognitive Neuroscience. 2012;3(3-4):247-8
THE BASICS OF CEREBRAL LOCALIZATION

**PARIETAL LOBE**
- sensation
- language
- spatial navigation
- interpretative

**FRONTAL LOBE**
- movement
- reasoning
- personality
- multitasking
- language

**OCCIPITAL LOBE**
- "elementary" visual processing

**TEMPORAL LOBE**
- language
- behavior
- vision
- hearing
- memory

**CEREBELLUM**
- balance
- coordination

**BRAIN STEM**
- neurotransmitters
- sleep
- movement
Different brain diseases "attack" different brain substrates and different brain regions:

Cerebrovascular diseases (primarily arteries)
Demyelinating diseases (primarily myelin)
Infectious diseases (various substrates)
Neurodegenerative diseases (primarily neurons)
But beyond Alzheimer's disease, there are many other neurodegenerative diseases of the brain:

- Frontotemporal lobar degeneration
- Lewy body disease
- Parkinson's disease
- Corticobasal degeneration
- Huntington disease
- Progressive supranuclear palsy
- Creutzfeldt-Jackob disease
- etc.
HEALTHY BRAIN

BRAIN WITH A NEURODEGENERATIVE DISEASE
Each neurodegenerative disease of the brain is caused by the progressive accumulation of a specific *pathognomonic* protein inclusion, or proteinopathy. Over time, this accumulation becomes toxic to the brain, leading to irreversible degeneration (death) of neurons and atrophy.
Neurodegenerative disease

- Neuronal pathology
- Neuronal death
- Glial proliferation

Clinical syndrome
Amyloid beta
amyloid plaques

TAU
neurofibrillary tangles

AD

clinical syndromes

Memory syndrome → Typical AD
Language syndrome → Logopenic variant of AD
Visual syndrome → Posterior variant of AD
Behavioral syndrome → Frontal variant of AD
Frontotemporal lobar degeneration (FTLD)

- MAPT
  - Pick disease
  - Corticobasal degeneration
  - Progressive supranuclear palsy
- GRN, C9orf72, VCP
  - Type A, B, C, D
- FTLD - TAU
- FTLD - TDP
- FTLD - FUS
- FTLD - UPS

Frontotemporal dementia
Frontotemporal dementia

- Behavioral
  - Behavioral-variant frontotemporal dementia (bvFTD)

- Language
  - Primary progressive aphasia (PPA), non-fluent variant
  - PPA, semantic variant

- Motor
  - Parkinsonian syndromes
  - Motor neuron disease syndromes
WHAT ABOUT DEMENTIA?
Almost all neurodegenerative diseases of the brain begin insidiously and progress relentlessly over the span of years.

All neurodegenerative diseases lead to disability and death. Although we have symptomatic drug therapies and non-pharmacological therapies and other support strategies available to offer patients and their families, we do not have drug therapies that can cure, stop, or "slow down" these diseases.
2018 ALZHEIMER’S DISEASE FACTS AND FIGURES

ALZHEIMER’S DISEASE IS THE 6TH leading cause of death in the United States

16.1 MILLION AMERICANS provide unpaid care for people with Alzheimer’s or other dementias

These caregivers provided an estimated 18.4 BILLION HOURS of care valued at over $232 BILLION

Between 2000 and 2015 deaths from heart disease have decreased 11% while deaths from Alzheimer’s disease have increased 123%

1 IN 3 seniors dies with Alzheimer’s or another dementia

It kills more than breast cancer and prostate cancer COMBINED

EARLY AND ACCURATE DIAGNOSIS COULD SAVE UP TO $7.9 TRILLION in medical and care costs

IN 2018, Alzheimer’s and other dementias will cost the nation $277 BILLION

BY 2050, these costs could rise as high as $1.1 TRILLION

5.7 MILLION Americans are living with Alzheimer’s

BY 2050, this number is projected to rise to nearly 14 MILLION

EVERY 65 SECONDS someone in the United States develops the disease

alzheimer’s association
THE BRAINS BEHIND SAVING YOURS:
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AD is the most common cause of dementia in the world.
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Economists predict:
Preventing or delaying the onset of Alzheimer's by 5 years would cut Medicare spending for Alzheimer's by half.
Neurological evaluation

The purpose of the interview is to attempt to quantify each patient’s cognitive abilities. The patient has to be asked to solve the challenge words of the four main cognitive domains: memory, language, executive functions, and motor. A global neuropsychological assessment is also administered.

Scores on each task are graded according to norms that take into account the patient’s age and level of education.

Neuropsychological evaluation

Investigations

- Brain imaging: MRI, PET
- Functional neuroimaging
- Other tests: SPECT, EEG, functional testing, etc.

Diagnosis

- Neurological examination
- Neuropsychological testing
- Investigations
- Level of independence
- Clinical diagnosis

Treatment plan and support

- Neurologists
- Neuropsychologists
- Nurses & Social workers
- Disease-specific treatments
- Signs/symptoms-specific treatments
- Level of impairment-specific support
- PCP
- Patient & Family
Neurological evaluation

The Basics of Cerebral Localization

Cognitive changes
- Memory function
- Attention, concentration
- Executive function
- Language function
- Visual-spatial function

Motor changes
- Balance
- Coordination
- Brisk reflexes
- Upper motor neuron signs

Behavior, personality, emotional processing changes
- Attention, concentration
- Mood changes
- Identity changes

Neuropsychological evaluation

History of present illness

Sleep changes
- Difficulty falling asleep
- Excessive daytime sleepiness

"Paper and pen" examination performed by a neuropsychologist.
History of present illness

**Cognitive changes**
- Memory function:
  - short-term episodic memory
  - long-term episodic memory
  - semantic memory
  - working memory
- Language function:
  - expressive language
  - receptive language
- Executive function: difficulty multitasking, concentrating, judgement/problem solving, performing multi-step tasks
- Visuospatial function: difficulty navigating (getting lost), gauging depth/distance, recognizing faces, recognizing objects

**Motor changes**
- Problems initiating movement
- Problems coordinating movement
- Weakness
- Rigidity/stiffness
- Involuntary movements (tremor, muscle jerks, twitching, etc.)
- Changes in gait pattern
- Imbalance and/or unexplained falls
- Asymmetries in movement

**Behavior, personality, emotional processing changes**
- Behavioral disinhibition
  - socially inappropriate behavior
  - impulsiveness
- Apathy or inertia
- Loss of sympathy/empathy
- Compulsive/ritualistic behaviors
- Altered food preferences
- Late-life "psychiatric" changes

**Sleep changes**
- Snoring & apnea
- Dream enactment behaviors

**Autonomic and sensory changes**
- Urinary incontinence
- Constipation
- Positional dizziness
- Diminishing sense of smell
Neurological examination

- mental status
- cranial nerves
- motor system
- sensory system
- coordination
- gait

= 1-3hrs
Neurological evaluation

"Paper and pen" examination performed by a neuropsychologist.

The purpose of this examination is to attempt to quantify each patient's cognitive abilities. The provider administers tasks that challenge each of the four main cognitive domains (memory, language, executive, visuospatial). A global mood/psychiatric assessment is also administered.

Scores on each task are graded according to norms that take into account the patient's age and level of education.

Neuropsychological evaluation

Investigations
"Paper and pen" examination performed by a neuropsychologist.

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Investigations

Blood work:
- Routine labs
- Markers of inflammation
- Genetic testing

Brain imaging: MRI, PET

Cerebrospinal fluid analysis (lumbar puncture): optional

Other tests: PET, sleep study, autonomic function testing, etc.

Diagnosis
Diagnosis

- Neurological evaluation
- Neuropsychological testing
- Investigations
- Level of independence
- Clinical diagnosis

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Treatment plan and support

- Neurologists
- Neuropsychologists
- Nurses & Social Workers
- Disease-specific treatments
- Sign/symptom-specific treatments
- Level of impairment-specific support
- PCP
- Patient & Family

Neuropsychological testing

+ Investigations

Level of independence

Clinical diagnosis
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GLOBAL
BRAIN HEALTH
INSTITUTE