

Neuropsychology and behavior in Alzheimer's and Parkinson's disease patients

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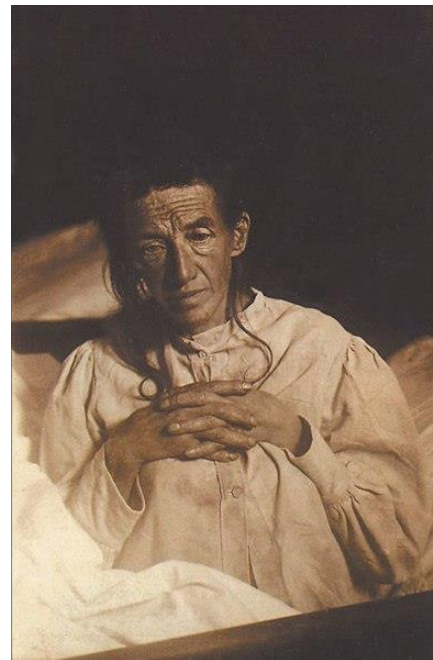
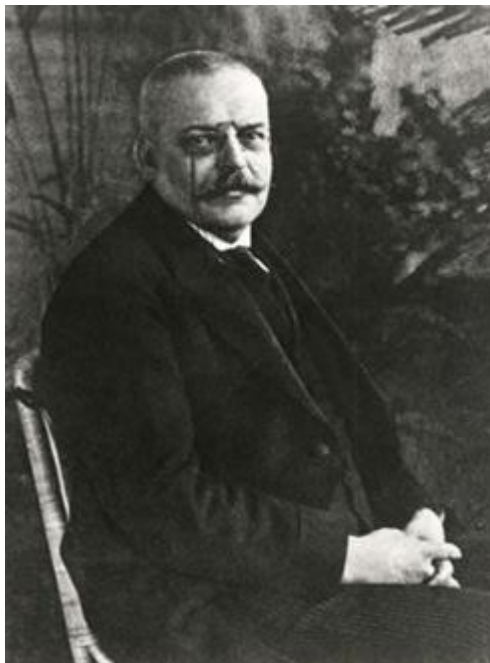


No Financial Disclosures



ALZHEIMER'S DISEASE (AD)

- First documented in 1906 by Alois Alzheimer, a psychiatrist and neuroanatomist, in Germany.
- “A peculiar severe disease process of the cerebral cortex”
- He described a 50 year old woman (Auguste Deter) he had been following due to paranoia, progressive sleep and memory disturbance, aggression, and confusion until her death five years later.



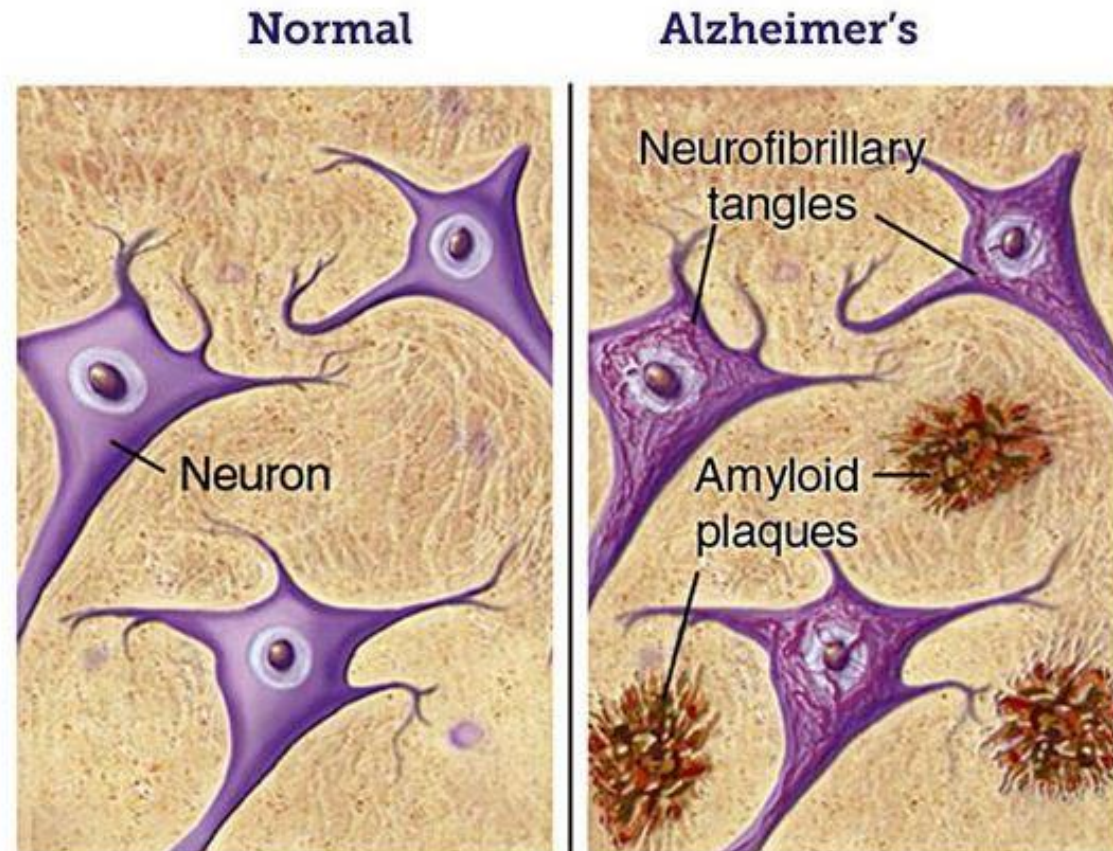
ALZHEIMER'S DISEASE (AD)

- Progressive neurodegenerative condition.
- Most common form of dementia in older adults (>65) (70%).
- 10% of individuals aged 65 or older have AD.
- Dense amnesic syndrome:
 - Memory is first and worst.
- Cognitive difficulties are significant enough to disrupt instrumental daily living skills (IADLs)
 - shopping, housekeeping, accounting, food preparation/meds, telephone/transportation.

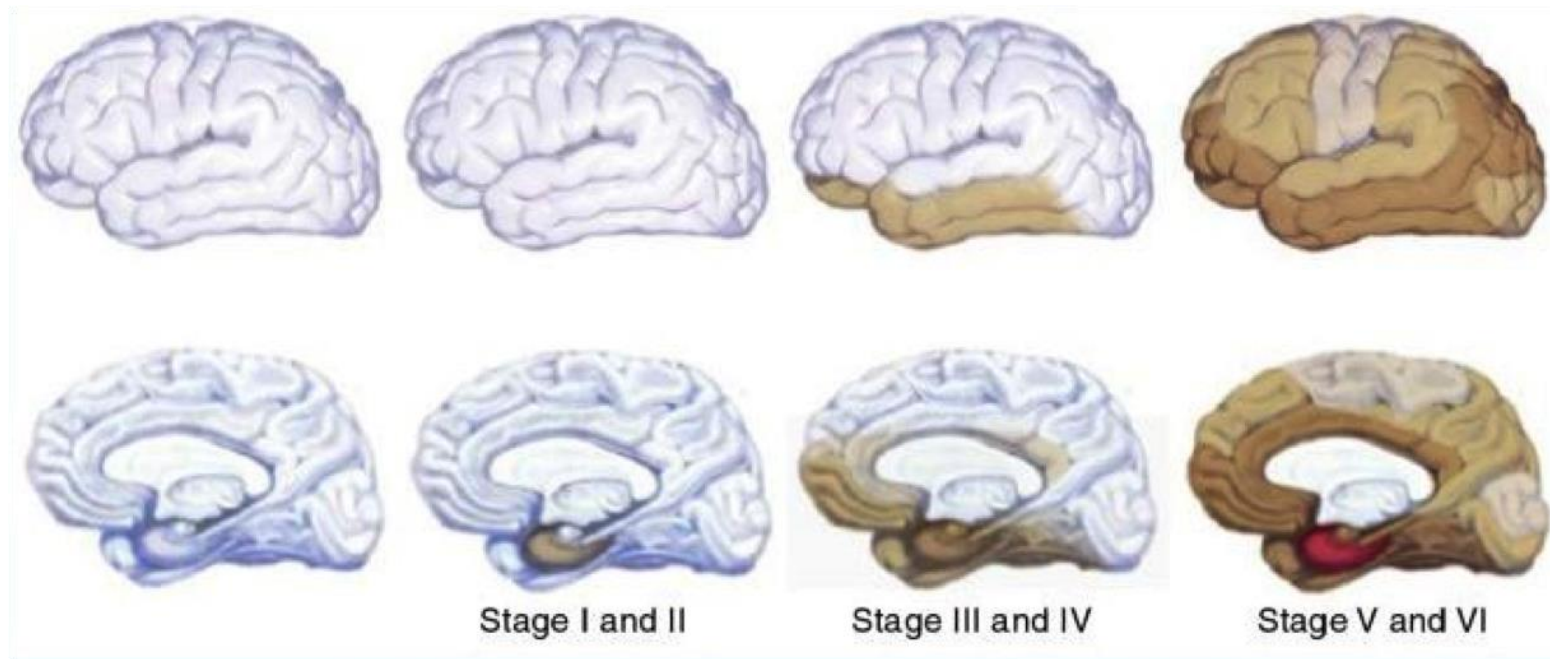
NEUROPATHOLOGY OF ALZHEIMER'S DISEASE

Beta Amyloid Plaques and Neurofibrillary Tangles are the Hallmarks of AD

Normal vs. Alzheimer's Diseased Brain



BRAAK STAGING IN ALZHEIMER'S DISEASE



- Based on the progression of NFT, amyloid plaques progress differently
- Stages I and II: involvement is confined mainly to the transentorhinal region of the brain
- Stages III and IV: more extensive involvement of medial temporal lobes including hippocampus as well as frontal lobes.
- Stages V and VI: extensive neocortical involvement.

BRAAK STAGING IN ALZHEIMER'S DISEASE



Amyloid Plaque Stages



Stage A



Stage B



Stage C

Isocortex

Entorhential Region/
Hippocampus

Tau Braak Stages



Braak I-II



Braak III-IV



Braak V-VI

30 years →

48 years →

■ Mild
■ Moderate
■ Severe

There is some evidence from PET imaging that amyloid plaques may precede NFTs



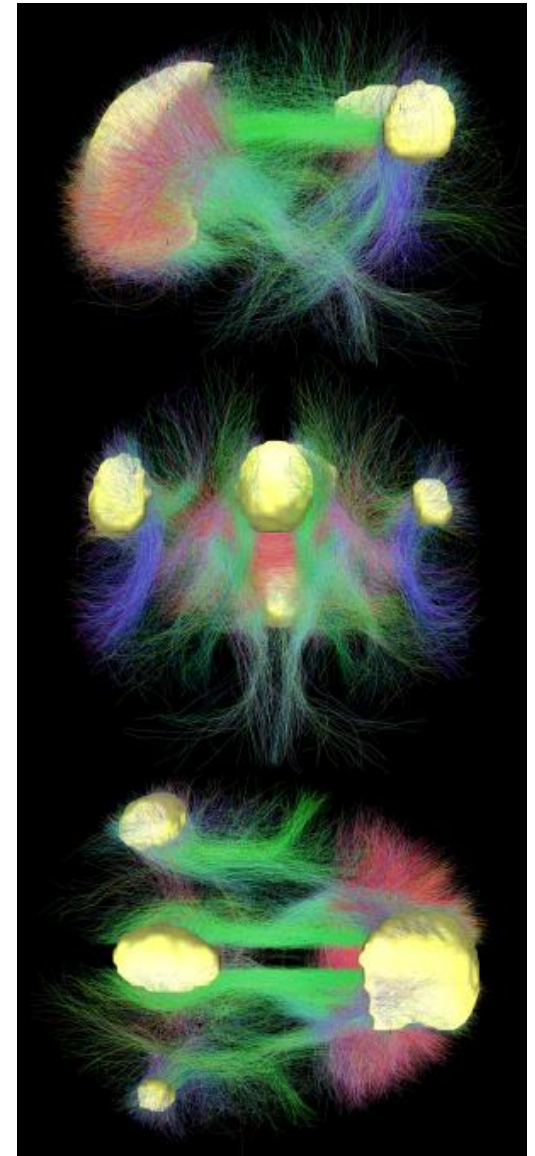
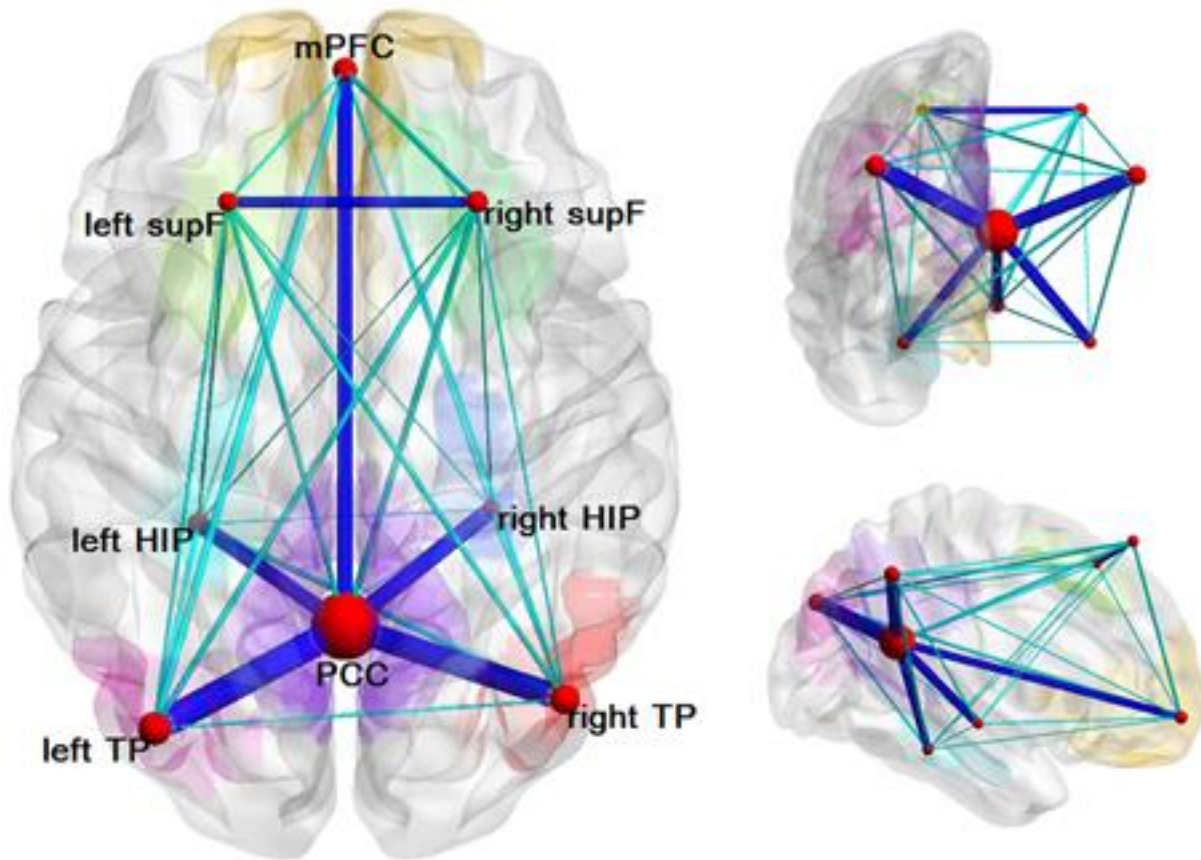
DEFAULT MODE NETWORK



- Default mode network regions appear to be particularly vulnerable to amyloid plaques and NFTs.
- Progressive declines in cognition and changes and behavior in AD track well with the pathophysiological process.

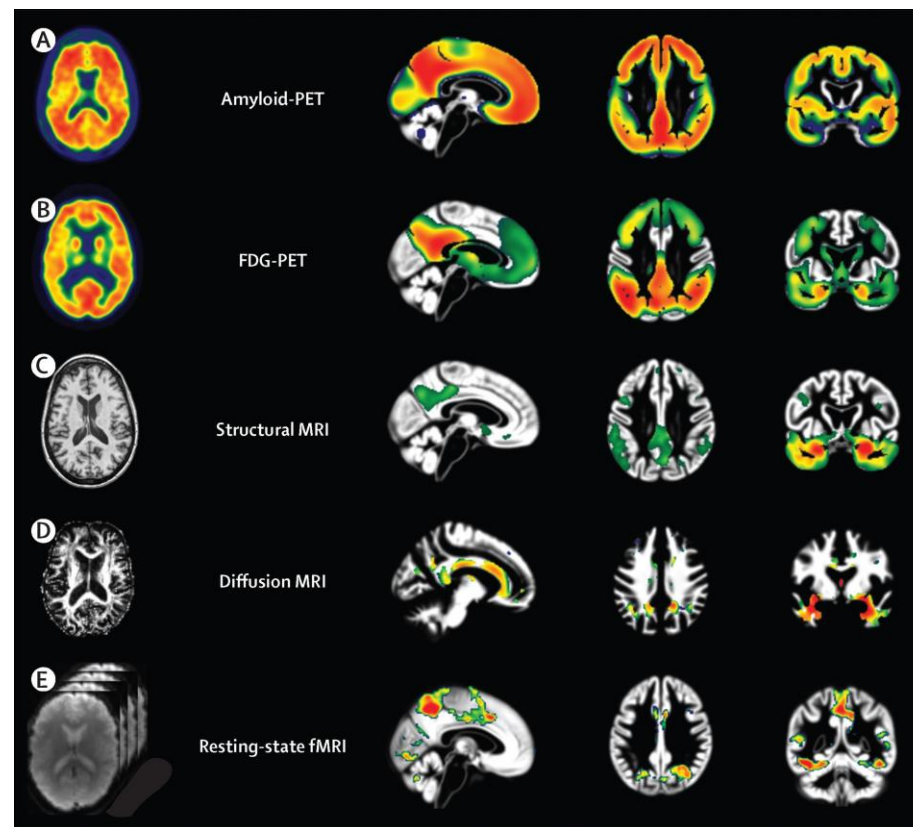


DEFAULT MODE NETWORK



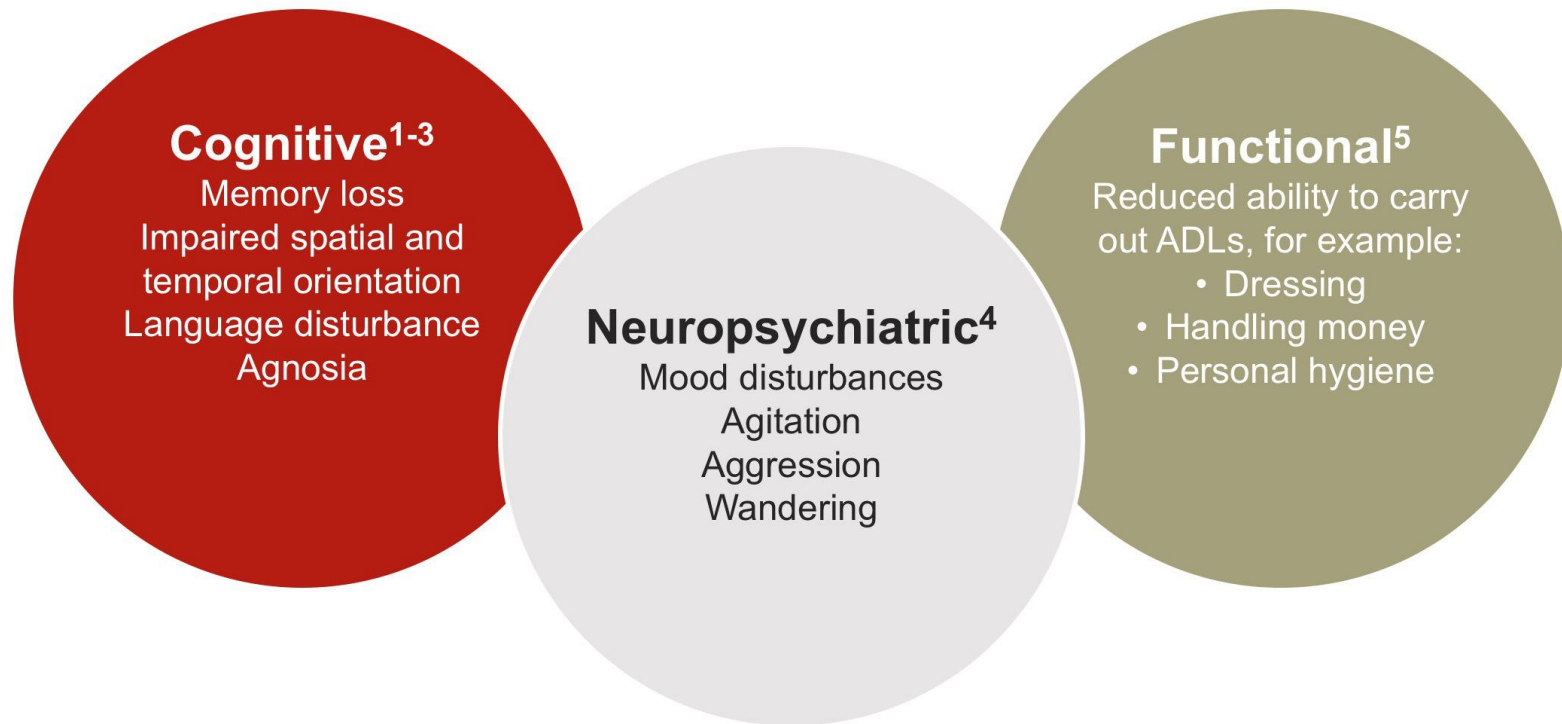
IN-VIVO NEUROIMAGING IN ALZHEIMER'S DISEASE

- A long preclinical phase where brain changes begin in middle age, many years before cognitive decline can be detected.
- Plaques and tangles target DMN regions as well as other areas that are involved in different cognitive functions and behavior as the disease progresses.



ALZHEIMER'S DISEASE: SYMPTOMS

Examples of symptoms of Alzheimer's disease



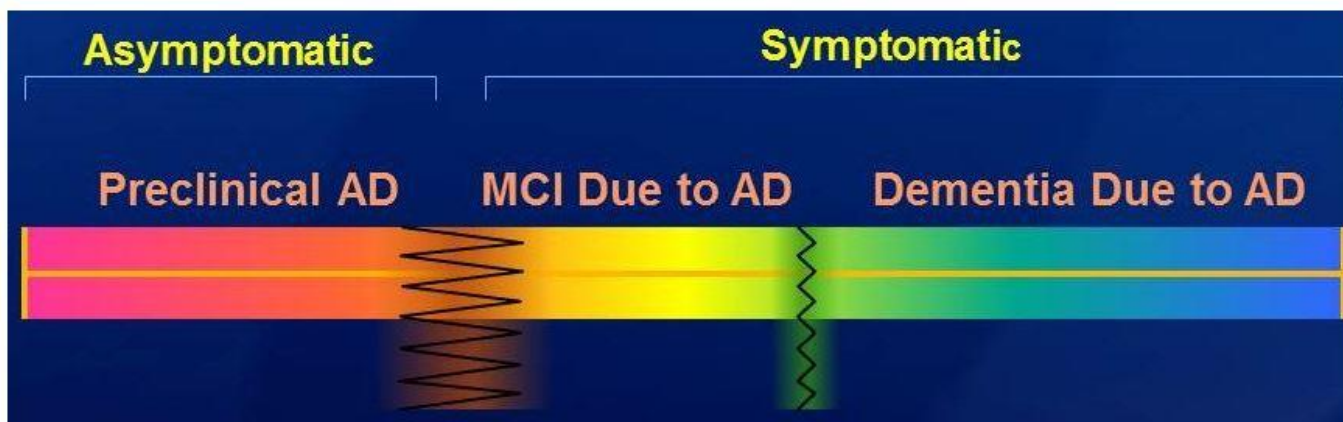
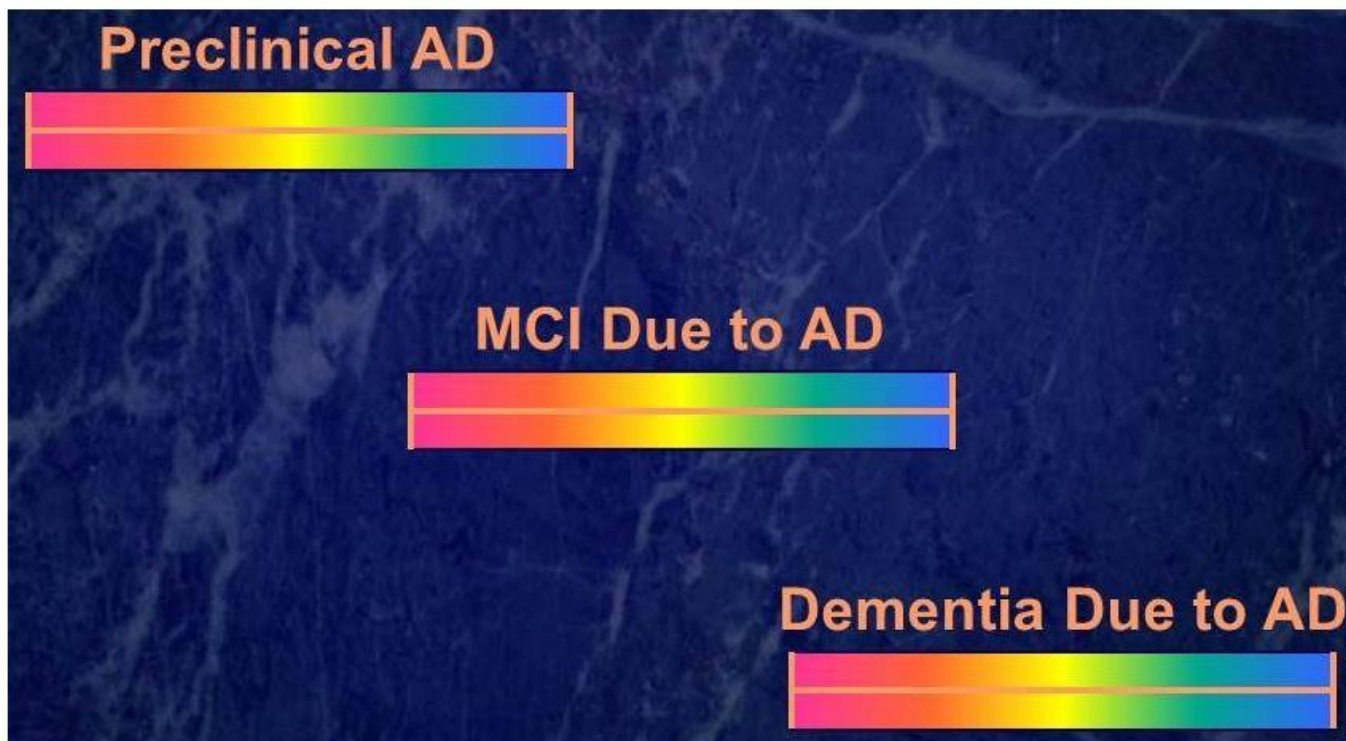
ADL=activity of daily living

1. Joubert et al. In: Gauthier (ed);2007; 2. Rainville et al. In: Gauthier (ed);2007
3. Alzheimer's Association. Alzheimers Dement 2016;12(4):459-509;
4. G elinas et al. In: Gauthier (ed);2007; 5. Teng & Cummings. In: Gauthier (ed);2007

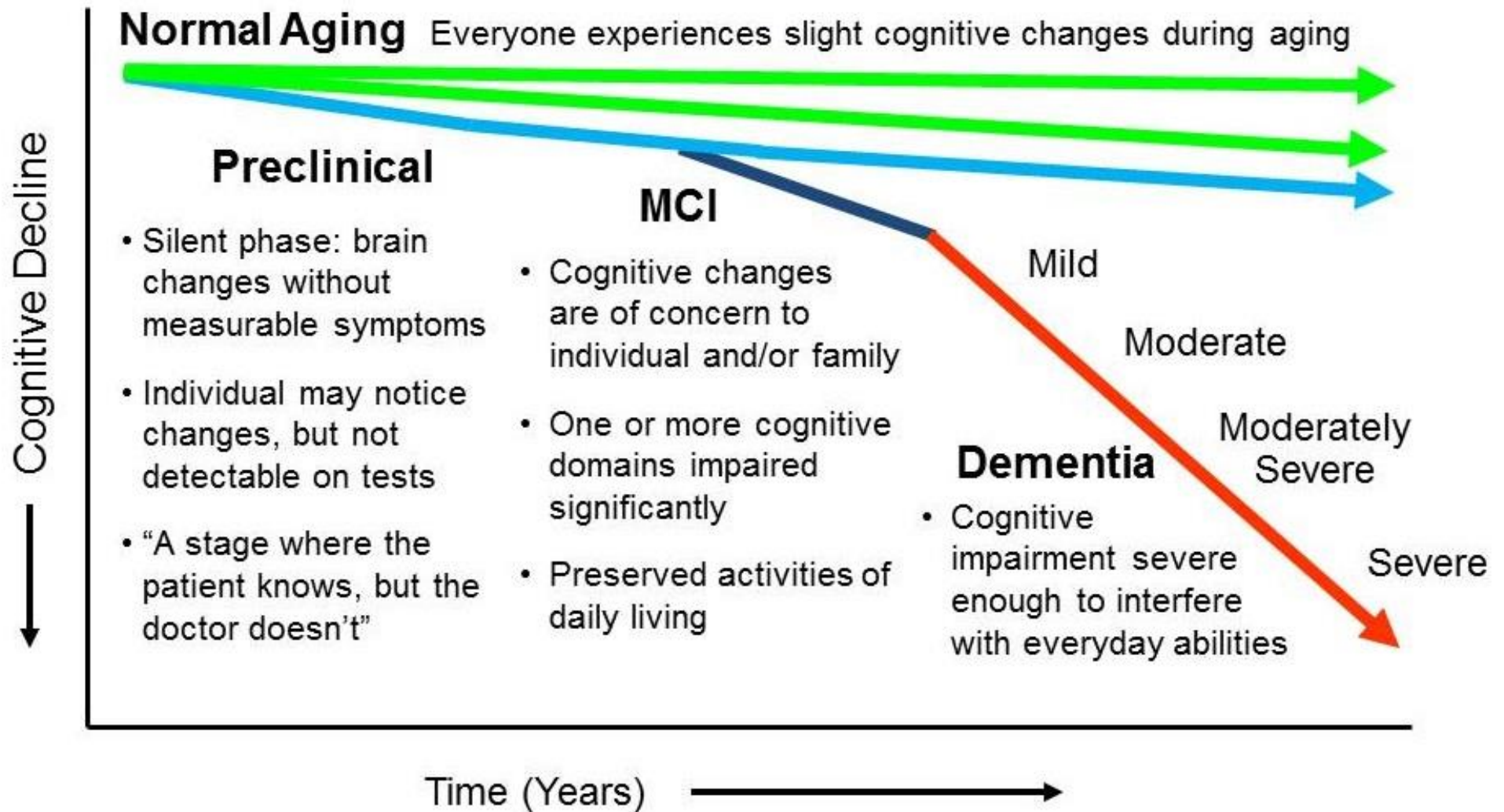
MILD COGNITIVE IMPAIRMENT

- Amnestic Mild Cognitive Impairment (aMCI)
 - Prodromal phase of AD.
 - Impairments in learning and remembering new information that are not significant enough to disrupt IADLs.
- ***Continuum Perspective: Every patient with AD goes through an aMCI phase, but not every patient with aMCI goes on to develop AD.***
 - aMCI: annual conversion rate to AD of 10-15%
 - A small percentage of individuals with aMCI, remain aMCI for years without converting to AD, others revert back to normal.
 - Time course of decline is variable.
- aMCI is too late in the disease process to prevent decline to AD.

A CONTINUUM PERSPECTIVE



A CONTINUUM PERSPECTIVE



NEUROPSYCHOLOGY OF ALZHEIMER'S DISEASE



- Neuropsychological assessment has been an important component in the diagnosis and staging of AD severity for over 40 years.
 - Has been used to identify the earliest cognitive and behavioral symptoms of AD.
- Assessment of the ability to form and retain new information is a critical component for the differential diagnosis of AD.



NEUROPSYCHOLOGY OF ALZHEIMER'S DISEASE



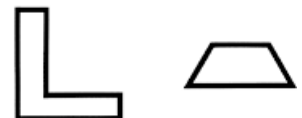
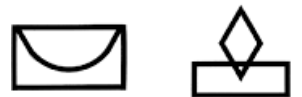
- Episodic memory: Memory for every day events (such as times, location geography, associated emotions, and other contextual information)
- The severity of deficits in episodic memory correlate with extent of atrophy in entorhinal cortex and hippocampus.
- Often tested in the clinic using word lists, stories, and geometric shapes.



NEUROPSYCHOLOGY OF ALZHEIMER'S DISEASE



- “I am going to read to you a list of words, listen carefully and when I’m through I want you to tell me all of the words you can” (“boat, spinach, lamp.....”)
 - Repeat the list several times and test free recall
 - Test delayed memory for the list (20-30 minutes later)
 - Recognition memory
 - “I am going to read some more words, some were on the list and others were not.....”
- “I am going to read to you short story.....”
 - “Anna Thompson, employed a cook in a school cafeteria.....”
- “I am going to show you a page with some figures for 10 seconds....”



NEUROPSYCHOLOGY OF ALZHEIMER'S DISEASE



- Typical memory profile in AD involves:
 - Flat learning curve
 - Rapid forgetting of any information that was learned
 - Minimal benefit from recognition cues
 - Lots of false positive and intrusion errors.
 - They might not even remember having been read a story or word list!
 - Poor orientation and knowledge of current events.
- Recall of a word list after a 10-minute delay has been shown to accurately differentiate early AD patients from healthy elderly controls with 90% accuracy.



NEUROPSYCHOLOGY OF ALZHEIMER'S DISEASE

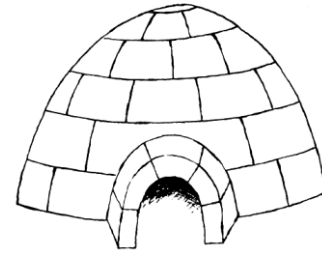


- Language and semantic knowledge are often the next domain negatively impacted in AD.
- A deterioration in the structure and content of semantic memory that supports language.
 - general knowledge of facts, concepts, and the meanings of words
- Typically, occur when plaques and tangles encroach upon temporal, frontal, and parietal association cortices.



NEUROPSYCHOLOGY OF ALZHEIMER'S DISEASE

- Picture/object naming: what is this called?
- Verbal fluency
 - Semantic fluency: number of animals generated in 60s.
 - Phonemic fluency: number of words that begin with a specific letter in 60s.
- Verbal abstract reasoning:
 - “tell me how badge and crown are alike”
- Vocabulary: “what does plagiarize mean?”
- Reading progressively more difficult words on a page.



NEUROPSYCHOLOGY OF ALZHEIMER'S DISEASE

- Semantic fluency is often worse than phonemic fluency.
- Verbal abstract reasoning can be negatively affected in AD.
- Oral word reading relatively unaffected for most of the disease process.



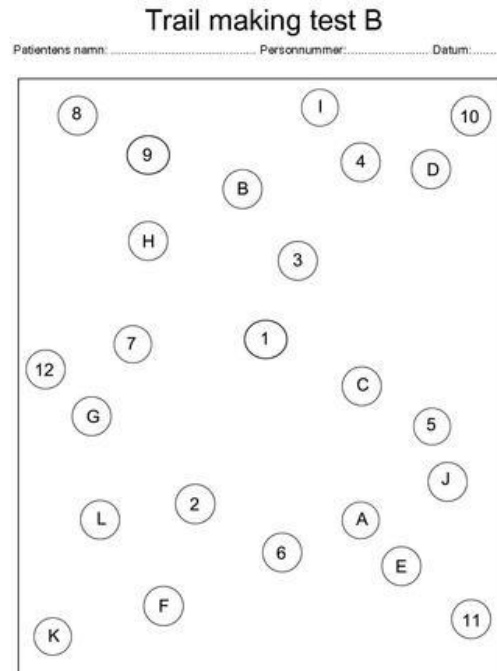
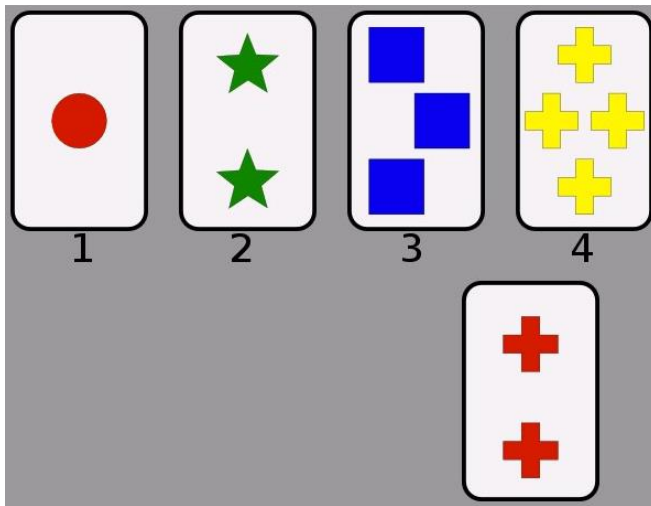
NEUROPSYCHOLOGY OF ALZHEIMER'S DISEASE



- Executive Function: a set of cognitive processes that are necessary for the cognitive control of behavior:
 - Attentional control
 - Inhibitory control
 - Working memory
 - Cognitive flexibility
 - Multitasking
 - Reasoning
 - Problem solving
 - Planning/Organization
 - Set-Switching
- Executive dysfunction is often evident as early as the MCI stage.
- Declines in executive function correlate with declines in IADLs in AD



NEUROPSYCHOLOGY OF ALZHEIMER'S DISEASE



“Switch between telling me different types of fruits and furniture” for 60s

- BLUE** **GREEN** **YELLOW**
- PINK** **RED** **ORANGE**
- GREY** **BLACK** **PURPLE**
- TAN** **WHITE** **BROWN**



NEUROPSYCHOLOGY OF ALZHEIMER'S DISEASE

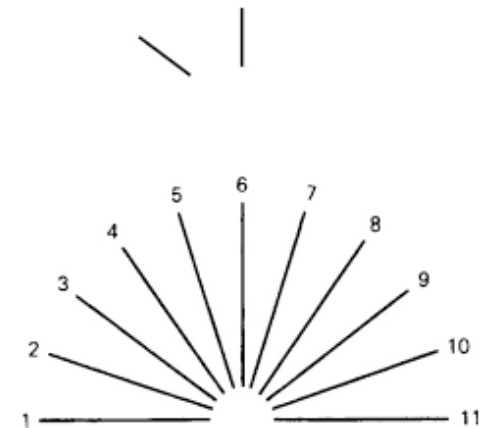
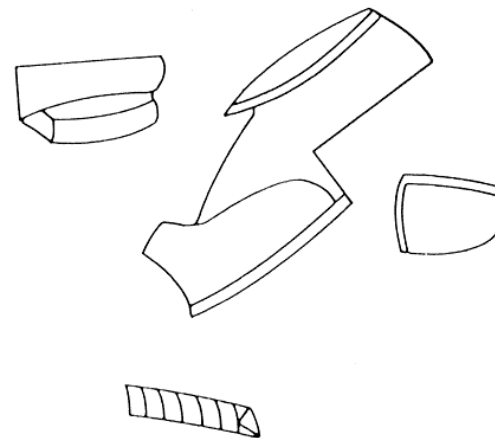
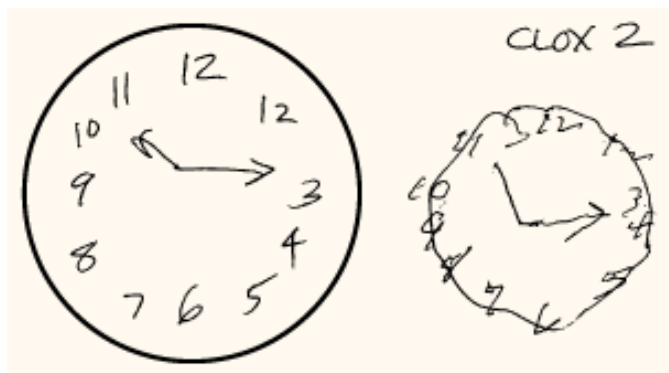
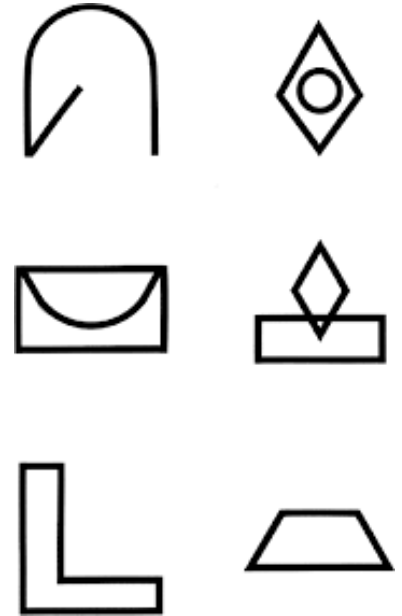
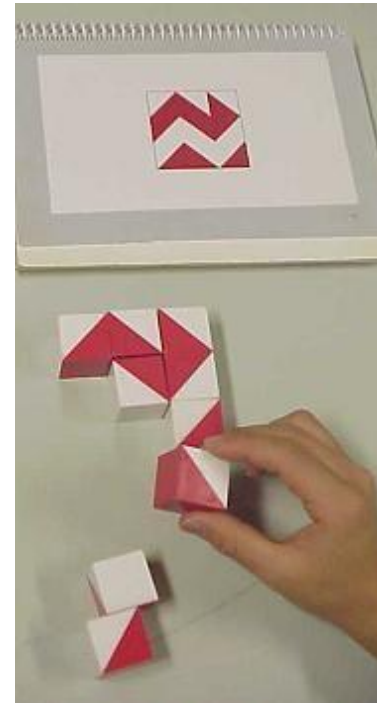
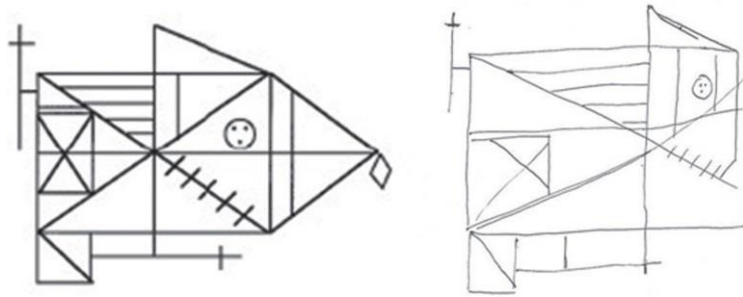


- Deficits in visuospatial skills are also evident at some point in the course of the disease.
- Visuoconstructional and visuoperceptual abilities
- Visual orientation deficits



VISUOSPATIAL SKILLS

- Clock Drawings (spontaneous, copies)
- Simple and Complex Figure Copy
- Judging Line Angles
- Visual Organization skills
- Spatial Reasoning



NEUROPSYCHOLOGY OF ALZHEIMER'S DISEASE



- What I have presented so far is the typical course of cognitive changes in AD.
- There are rare variants:
 - Posterior Cortical Atrophy (PCA), visuospatial variant of AD.
 - Language variant of AD.
 - Frontal variant of AD.



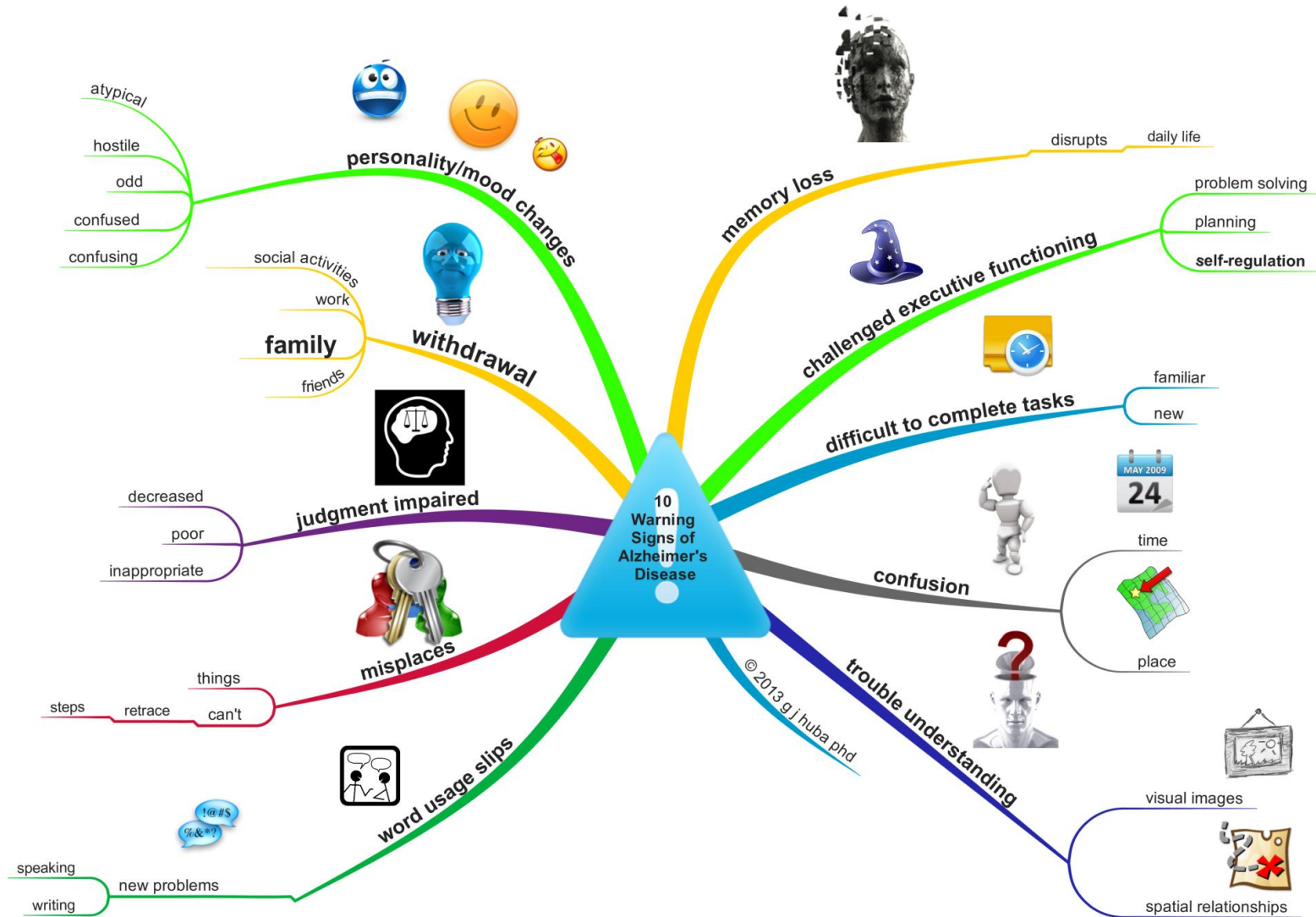
NEUROPSYCHOLOGY OF ALZHEIMER'S DISEASE



- Behavioral and personality changes are also evident early in the disease process.
 - Impaired self-awareness (anosognosia)
 - Increased irritability, temper tantrums.
 - Depression, apathy
 - Paranoia
 - Hiding things or believing other people are hiding things
 - Imagining things that aren't there
 - Pacing, wandering
 - Unusual sexual behavior
 - Hitting others
 - Misunderstanding what he or she sees or hears



NEUROPSYCHOLOGY OF ALZHEIMER'S DISEASE



PARKINSON'S DISEASE (PD)

- Progressive neurodegenerative condition that affects mainly the motor system.
 - Most common symptoms: tremor, rigidity, slowness of movement, and difficulty with walking
- Affects about 2% of individuals over the age of 65.
- The first clear medical description was written in 1817 by James Parkinson in “An Essay on the Shaking Palsy.”
 - “Involuntary tremulous motion, with lessened muscular power, in parts not in action and even when supported; with a propensity to bend the trunk forward, and to pass from a walking to a running pace: the senses and intellects being uninjured.”
- In the mid-1800s, Jean-Martin Charcot refined and expanded on Parkinson's early description
 - Charcot also differentiated PD from multiple sclerosis and other disorders characterized by tremor.



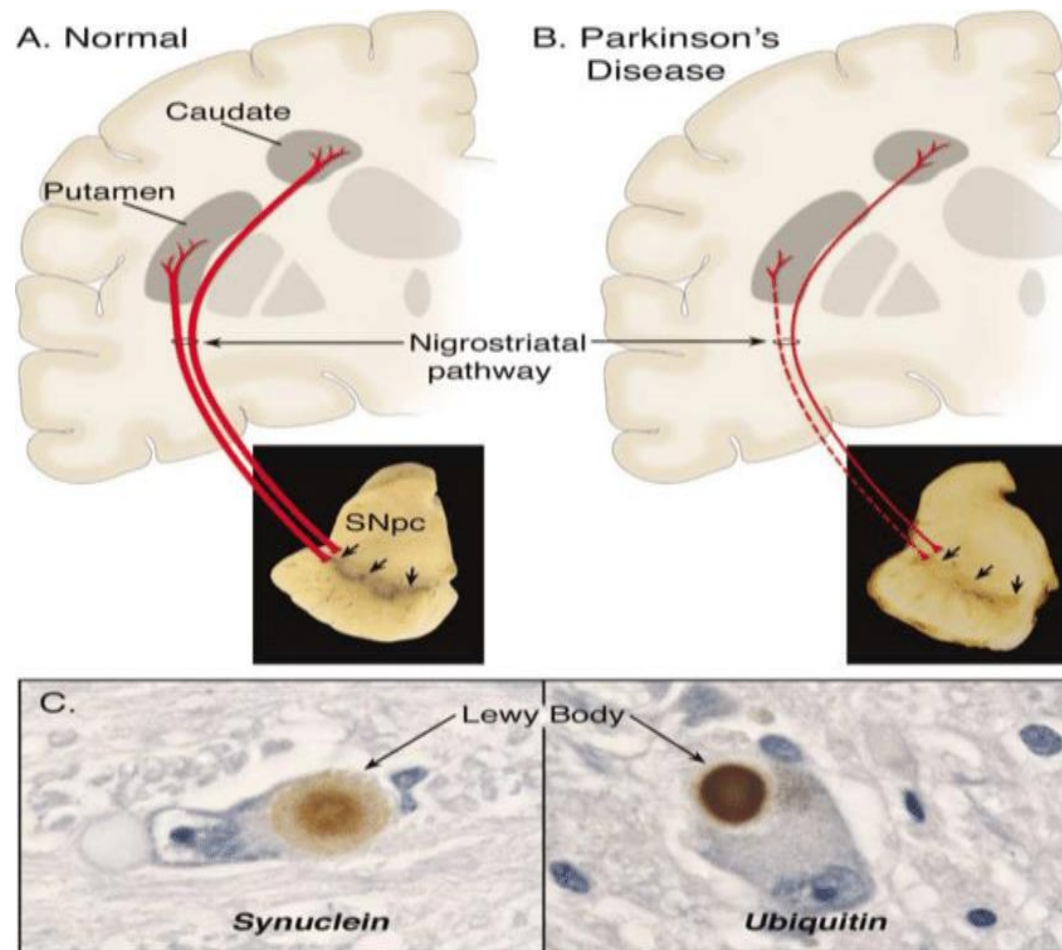
James Parkinson



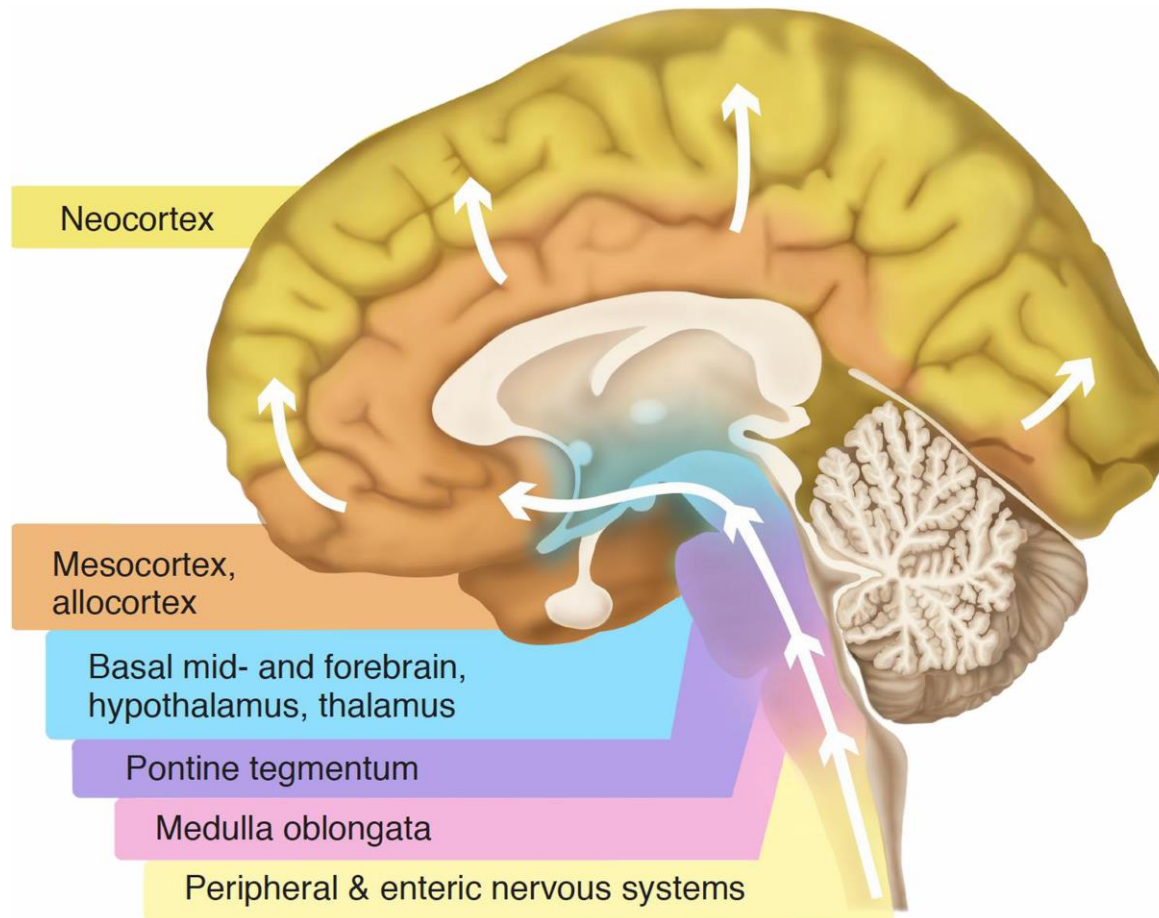
Jean Martin Charcot

NEUROPATHOLOGY OF PARKINSON'S DISEASE

- Neuronal loss in the substantia nigra with dopaminergic denervation of the striatum
- Neurodegeneration accompanied by neuronal inclusions composed of α -synuclein (Lewy bodies) is considered the typical pathologic correlate of PD.



BRAAK STAGING IN PARKINSON'S DISEASE



PARKINSON'S DISEASE (PD)



- Non-motor symptoms such as changes in behavior and cognitive impairment are common in PD.
- 25.8% of PD patients were found to have MCI in one study.
- Estimates suggest that 50-80% of PD patients may experience MCI and dementia over the entire course of their illness.
- The average time from onset of PD to developing dementia is about 10 years in some studies.
- The profile of cognitive impairment in PD can be differentiated from AD.



PARKINSON'S DISEASE (PD)



- Risk factors for cognitive impairment in PD include:
 - Advanced age at diagnosis
 - Duration of disease
 - Greater severity of motor symptoms
 - Presence of autonomic dysfunction
 - Symmetrical disease presentation
 - Poor responsiveness to dopaminergic treatments
 - Postural instability and gait disorder (PIGD)
 - Low baseline cognitive functioning
 - Early development of hallucinations, confusion, and psychosis while on dopaminergic medications.
 - Excessive daytime sleepiness
 - Low CSF beta-amyloid levels
 - White matter hyperintensities on MRI
 - REM Sleep behavior disorder



PARKINSON'S DISEASE (PD)

- The pattern of cognitive deficits in PD is indicative of frontal-subcortical dysfunction.
- Attention: Impairments in both focused and complex attention (choice reaction time, internally cued behavior).
 - Fluctuations in attention are also common.
- Executive function:
 - Planning/organization skills, set-shifting, and concept formation are impaired
 - Perseveration and difficulty maintaining mental set are common.
 - Slowed mental speed (bradyphrenia)

PARKINSON'S DISEASE (PD)

- Visuospatial skills: Impairments on tasks that require visual orientation, perception, and construction.
 - Usually early and disproportionate to the level of overall cognitive impairment.
- Memory:
 - Impaired free recall of recent events or on tasks that require learning new information
 - Flat learning curve
 - Memory typically benefits from recognition cues
 - Information is getting in, otherwise recognition would not be intact (differentiates from AD).
- Language: typically not affected that much.
 - Measures of language fluency (word finding difficulties) may be impaired due to bradyphrenia
 - Semantic language is often preserved (differentiates from AD).

PARKINSON'S DISEASE (PD)

- Behavioral changes and neuropsychiatric symptoms are common in PD but more common in PD-D.
- Apathy: Loss of motivation, interest, and effortful behavior.
- Changes in personality and mood including depressive features and anxiety.
- Hallucinations: Mostly visual, usually complex formed visions of people, animals, or objects.
 - Hallucinations are often not distressing to patient.

PARKINSON'S DISEASE (PD)



- Delusions: Usually paranoid, such as infidelity or believing that unwelcome guests are living in the home.
- Hallucinations and delusions may follow dopaminergic treatment but are more common in PD-D than in PD
- Excessive daytime sleepiness.
- At least one neuropsychiatric symptom is present in more than 90% of PD-D patients.



CASE EXAMPLES:

COGNITIVE DOMAINS	Case 1: Amnesic MCI (AD)	Case 2: Non-Amnesic MCI (PD)	Case 3: Non-amnesic MCI (Vascular)	Case 4: Depression
PREMORBID FUNCTION	Average	Average	Average	Average
MEMORY				
Remote Memory	Normal	Normal	Normal	Normal
Verbal Learning	Impaired	Normal	Normal	Mixed
Verbal Memory	Impaired	Normal	Normal	Mixed
Visual Learning	Impaired	--	Normal	Impaired
Visual Memory	Impaired	--	Normal	Normal
Recognition Memory	Impaired	Normal	Normal	Normal
LANGUAGE				
Picture Naming	Impaired	Normal	Normal	Normal
Phonemic Fluency	Normal	Normal	Impaired	Normal
Semantic Fluency	Impaired	Normal	Normal	Normal
VISUOSPATIAL SKILLS				
Clock Drawing	Normal	--	Normal	Normal
Spatial Reasoning	Normal	Normal	Impaired	Normal
PROCESSING SPEED	Normal	Impaired	Mixed	Normal
ATTENTION/WORKING MEM	Normal	Normal	Normal	Normal
EXECUTIVE FUNCTION				
Problem Solving	Normal	Impaired	Impaired	Impaired
Visual Set-Switching	Normal	--	Impaired	Normal
Verbal Set-Switching	Impaired	--	--	Normal
DEPRESSION	Mild	Moderate	Moderate	Moderate



THANK YOU FOR YOUR ATTENTION!!!!

