

# NEUROCOGNITIVE DISORDERS CONT...

Mogesie N

BSc, MSc

# Other causes of neuro-cognitive disorders

## 1. Creutzfeldt-Jakob disease (CJD)

- ❧ A rare brain disorder that affects about 1 in every million people worldwide each year
- ❧ CJD belongs to a family of diseases known as the transmissible spongiform encephalopathies (TSEs)
- ❧ Spongiform refers to the fact that the brain becomes filled with microscopic swellings that give the appearance of holes, like a sponge

## ☞Cont....

- ☞CJD and other TSEs are believed to be caused by infectious proteins called prions that become misfolded
- ☞Scientists believe that the presence of misfolded prions can trigger normal proteins to misfold as well, causing a chain reaction
- ☞These abnormal prion proteins tend to clump together, which is believed to be related to the brain damage
- ☞Symptoms usually begin after age 60, and most people die within a year of onset

## **Inherited forms of CJD include:**

### *Fatal familial insomnia:*

- ⌘ This prion disease causes a part of the brain involved in sleep to slowly degenerate
- ⌘ People with the disease have trouble sleeping and may show signs of poor reflexes and hallucinations

### *Gerstmann-Straussler-Scheinker disease*

- ⌘ Symptoms include a loss of coordination (ataxia) and neurocognitive disorder that begin when people are 50 to 60 years old

## 2. Huntington's disease

- ❧ This hereditary disorder is caused by a faulty gene for a protein called huntingtin
- ❧ Symptoms begin around age 30 or 40 years and include abnormal and uncontrollable movements called chorea, as well as gait changes and lack of coordination
- ❧ As the disease progresses, these cognitive problems worsen, and motor difficulties lead to complete loss of ability for self-care

### 3. Parkinson's disease

- ❧ The disturbance occurs in the setting of established Parkinson's disease
- ❧ There is insidious onset and gradual progression of impairment
- ❧ The Parkinson's disease clearly precedes the onset of the neuro-cognitive disorder

# CONT...

- ✧ The essential feature of major or mild NCD due to Parkinson's disease is cognitive decline following the onset of Parkinson's disease
- ✧ The NCD is viewed as *probably due to Parkinson's disease* when there is no evidence of another disorder that might be contributing to the cognitive decline *and when the Parkinson's disease clearly precedes onset of the NCD*

CONT...

- ❧ *The NCD is considered possibly due to Parkinson's disease either when there is no evidence of another disorder that might be contributing to the cognitive decline or when the Parkinson's disease precedes onset of the NCD, but not both*
- ❧ *Frequently present features include apathy, depressed mood, anxious mood, hallucinations, delusions, personality changes, rapid eye movement sleep behavior disorder, and excessive daytime sleepiness*

# CONT..

- ⌘ Among individuals with Parkinson's disease, as many as 75% will develop a major NCD sometime in the course of their disease
- ⌘ The prevalence of mild NCD in Parkinson's disease has been estimated at 27%
- ⌘ Onset of Parkinson's disease is typically between the sixth and ninth decades of life, with most expression in the early 60s
- ⌘ Mild NCD often develops relatively early in the course of Parkinson's disease, whereas major impairment typically does not occur until late

## 4. Secondary neurocognitive disorders

- ✧ These NCDs occur in people with disorders that damage brain tissue
- ✧ Such disorders may include
  - Multiple sclerosis;
  - Meningitis; encephalitis; and
  - Wilson's disease: a disease in which excessive amounts of copper build up to cause brain damage

# Cont...

✧ In rare cases, people with brain tumors may develop NCD because of damage to their brain circuits or a buildup of pressure inside the skull

# Head Injury

## 1. Chronic traumatic encephalopathy

- ✓ Initially known as dementia pugilistica, is caused by repeated traumatic brain injury (TBI), such as in boxers or in people who suffered multiple concussions while playing a contact sport
- ✓ This form of dementia also is characterized by brain atrophy and widespread deposits of tau aggregates

## 2. Subdural hematoma

- ✓ Bleeding between the brain's surface and its outer covering (the dura), is common in the elderly after a fall
- ✧ Subdural hematomas can cause NCD-like symptoms and changes in mental function
- ✧ With treatment, some symptoms can be reversed

## Reversible NCDs

∞ Many conditions that cause NCD can be reversed with the appropriate treatment

∞ Examples

1. Cerebral vasculitis, an inflammation and necrosis (tissue death) of blood vessel walls, can cause a form of dementia that may resolve when the person is treated with immune suppressants

2. Some studies have shown that people with depression are at increased risk of developing dementia



Cont....

3. Metabolic disorders of the NS, such as mitochondrial disorders, leukodystrophies, and lysosomal storage diseases, can lead to NCD

4. Metabolic problems and endocrine abnormalities such as thyroid problems, low blood sugar levels and low or high levels of sodium or calcium

Cont....

4. Normal pressure hydrocephalus is an abnormal buildup of cerebrospinal fluid in the brain

✿ Elderly individuals with the condition usually have trouble with walking and bladder control before onset of NCD

✿ Normal pressure hydrocephalus can be treated or even reversed by implanting a shunt system to divert fluid from the brain



CONT....

5. Nutritional deficiencies of vitamin B<sub>1</sub> (thiamine), caused by chronic alcoholism, and vitamin B<sub>12</sub> deficiencies can be reversed with treatment

6. Side effects of medications or drug combinations may cause NCDs that arise quickly or develop slowly over time

## Environmental Factors

- ✧ Environmental factors may play a role in the development of certain types of NCD
- ✧ Examples of environmental factors include:

### 1. Anoxia

- ✧ Anoxia and hypoxia can lead to the loss of neurons and diffuse brain injury
- ✧ This type of NCD commonly occurs in people who survive cardiac arrest

## 2. Poisoning

- ✧ Exposure to lead, mercury, other heavy metals, or poisonous substances can lead to symptoms of NCD
- ✧ These symptoms may or may not resolve after treatment, depending on how severely the brain is damaged

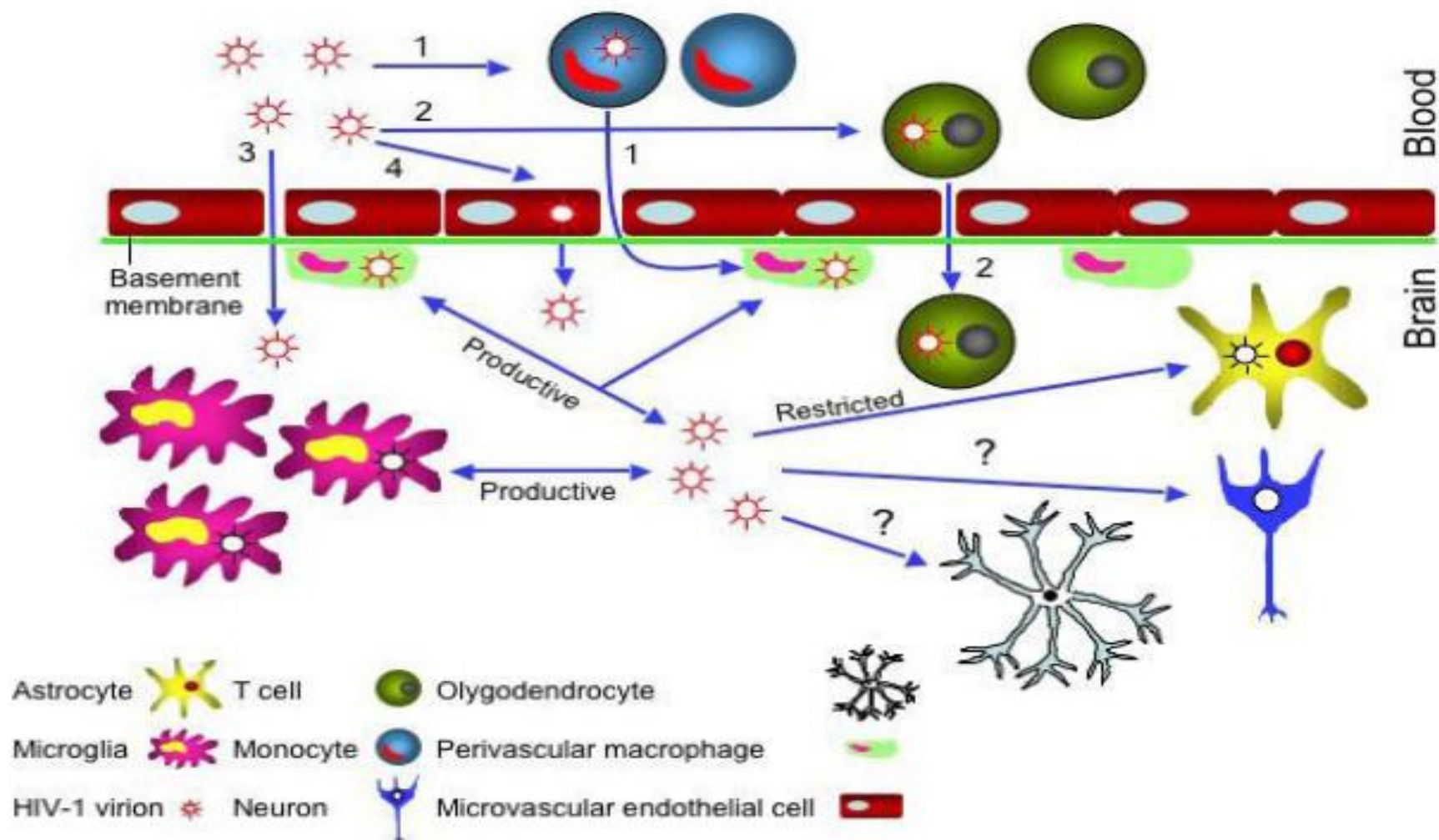
### 3. Substance abuse

- ☞ People who have abused substances such as alcohol and recreational drugs sometimes display signs of NCD even after the substance abuse has stopped
- ☞ This condition is known as substance-induced persisting NCD

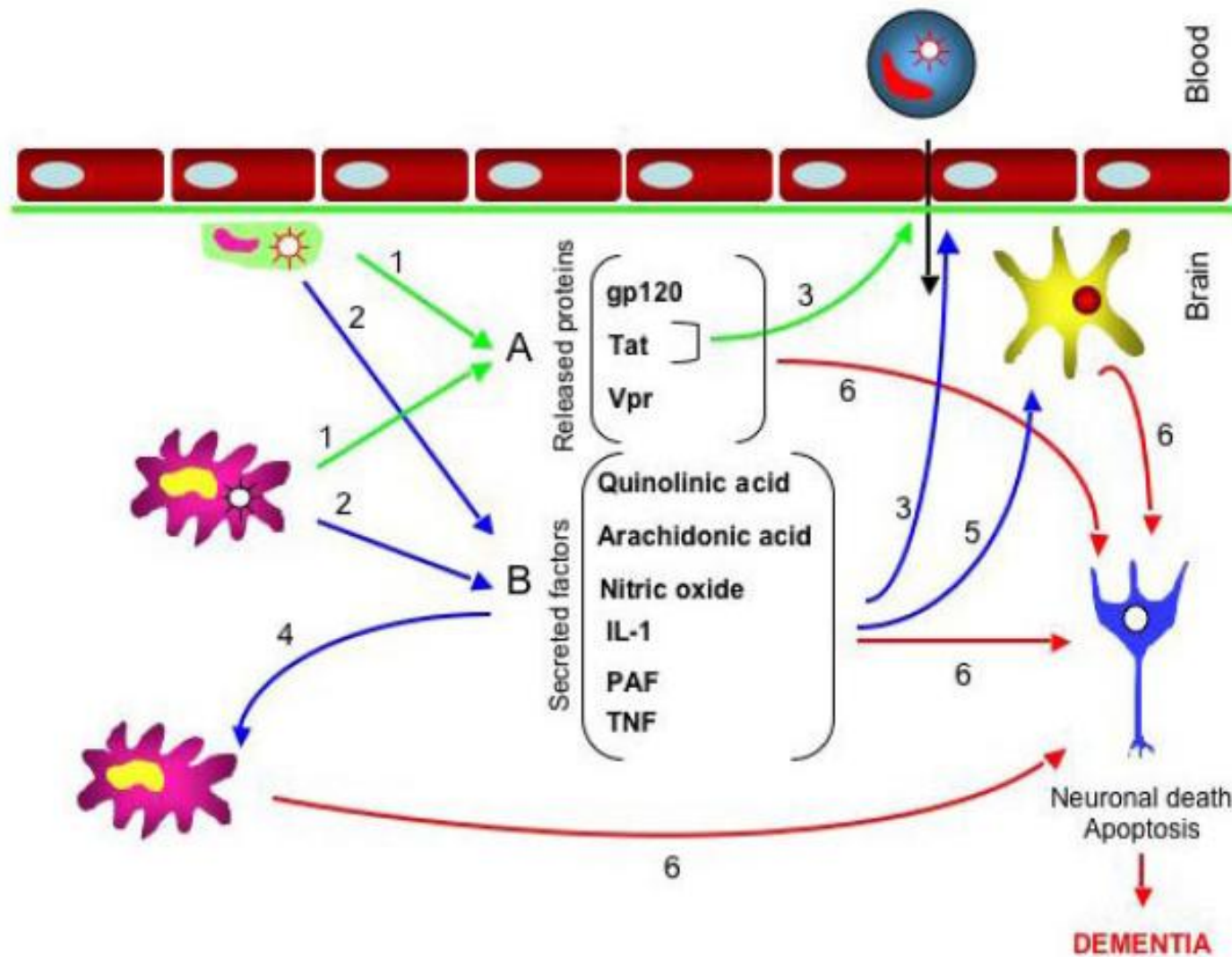
## **Infectious Disease**

### **NCD due to HIV**

- ❧ NCD due to HIV can occur in people who are positive for the human immunodeficiency virus, the virus that causes AIDS
- ❧ HIV damages the brain's white matter and leads to a type of NCD associated with memory problems, social withdrawal, and trouble concentrating
- ❧ People with NCD due to HIV may develop movement problems as well

**Figure 1**

**HIV-1 neuroinvasion.** 1) According to the "Trojan Horse hypothesis" entry of HIV-1 into the brain takes place by the migration of infected monocytes which differentiate into perivascular macrophage. 2) The passage of infected CD4<sup>+</sup> T cells can be another source of infection in the brain. Other probable causes of CNS infection might be: 3) the direct entrance of the virus or 4) entrance of HIV-1 by transcytosis of brain microvascular endothelial cells. Once the virus is in the brain it infects productively macrophages and microglia. Astrocyte infection is known to be restricted. The infection of oligodendrocytes and specially neurons is questionable.



**Figure 2**

**Mechanism of neuropathogenesis.** Two components of this mechanism are: A) the direct effect of the HIV-1 infection, including HIV-1 proteins and B) the indirect consequence of infection comprising the secretion of cytokines and neurotoxins. The infected macrophages and microglia participate actively in the neurodegeneration by: 1) shedding viral proteins and 2) releasing significant amount of cytokines and neurotoxins into the CNS. 3) Tat and TNF- $\alpha$  contribute to the disruption of the blood brain barrier, which in turn become more permeable to infected monocytes and cytokines present in the periphery. The secreted pro-inflammatory cytokines activates 4) microglia and 5) astrocytes which in turn secrete neurotoxins, moreover the alteration of astrocytes function results in an increase in the level of neurotoxicity in the brain. 6) Multifactorial neuronal injury: neurotoxins released from several sources, as the direct and indirect consequences of HIV-1 infection, lead to neuronal injury.

# Modified HIV dementia scale

| Maximum Score | Score | Activity/Test  |
|---------------|-------|--|
| n/a           | n/a   | <b>Memory/Registration:</b> State four words for the patient to recall (dog, hat, green, peach), pausing 1 second between each each. Then ask the patient to restate all four.   |
| 6             | ( )   | <b>Psychomotor Speed:</b> Ask the patient to write the alphabet in upper case letters horizontally across the page; record time: _____ seconds.<br><br>≤ 21 sec = 6<br>21.1 - 24 sec = 5<br>24.1 - 27 sec = 4<br>27.1 - 30 sec = 3<br>30.1 - 33 sec = 2<br>33.1 - 36 sec = 1<br>> 36 sec = 0                                       |
| 4             | ( )   | <b>Memory Recall:</b> Ask the patient to restate the four words from Memory/Registration above. Give one point for each correct response. For words not recalled, prompt with a "semantic" clue, as follows: animal (dog); piece of clothing (hat), color (green), fruit (peach). Give 1/2 point for each correct after prompting. |
| 2             | ( )   | <b>Construction:</b> Copy the cube below; record time: _____ seconds. (<25 sec = 2; 25 - 35 sec = 1; >35 sec = 0)<br>line drawing of a cube  |

Maximum score: 12 points; a score of <7.5 points suggests possible HAD (note, this test is not specific)

Adapted from McArthur JC. *Minor cognitive motor disorder: Does it really exist?* Hopkins HIV Rep. Nov 1996;8(4):8.

## Diagnosis of NCDs

- ✧ First assess whether the individual has an underlying treatable condition such as depression, abnormal thyroid function, drug-induced encephalopathy, normal pressure hydrocephalus, or vitamin B<sub>12</sub> deficiency
- ✧ In many cases, the specific type of NCD that a person has may not be confirmed until after the person has died and the brain is examined

## **An assessment generally includes:**

### **➤ Patient history**

∞ Typical questions about a person's medical and family history might include asking about whether NCD runs in the family, how and when symptoms began, and if the person is taking certain medications that might cause or exacerbate symptoms

## ➤ **Physical exam**

⌘ Measuring blood pressure and other vital signs may help physicians detect conditions that might cause or occur with NCDs. Such conditions may be treatable

## ➤ **Neurological evaluations**

⌘ Assessing balance, sensory function, reflexes, vision, eye movements, and other functions helps identify signs of conditions that may affect the diagnosis or are treatable with drugs

## The following procedures also may be used when diagnosing NCD:

✓ **EEG**

✓ **Brain scans (CT or MRI)**

✧ These tests can identify strokes, tumors, and other problems that can cause NCD

✧ Scans also identify changes in the brain's structure and function

## ➤ Cognitive and neuropsychological tests

- ✧ These tests measure memory, language skills, math skills, and other abilities related to mental functioning
- ✧ For example, people with AD often show impairment in problem-solving, memory, and the ability to perform once-automatic tasks

## ➤ **Laboratory tests**

∞ Measuring levels of sodium and other electrolytes in the blood, a complete blood count, a blood sugar test, urine analysis, a check of vitamin B<sub>12</sub> levels, cerebrospinal fluid analysis, drug and alcohol tests, and an analysis of thyroid function

## ➤ **Psychiatric evaluation**

∞ This will help determine if depression or another mental health condition is causing or contributing to a person's symptoms


# Treatment


✧ Some NCDs are treatable

✧ However, therapies to stop or slow common neurodegenerative diseases such as AD have largely been unsuccessful, though some drugs are available to manage certain symptoms

# Cont...

- ✧ Most drugs for NCD are used to treat symptoms in AD
- ✧ One class of drugs, called cholinesterase inhibitors, includes donepezil, rivastigmine, and galantamine
- ✧ These drugs can temporarily improve or stabilize memory and thinking skills in some people by increasing the activity of the cholinergic brain network

- 
- ❧ The drug memantine is in another class of medications called NMDA receptor antagonists, which prevents declines in learning and memory
  - ❧ NMDA receptor antagonists work by regulating the activity of the neurotransmitter glutamate
  - ❧ When glutamate activity levels are excessive, neurons may die

- 
- ❧ Memantine may be combined with a cholinesterase inhibitor for added benefits
  - ❧ These drugs are sometimes used to treat other NCDs as well
  - ❧ None of these drugs can stop or reverse the course of the disease

## **General measures of treatment:**

- ❧ Supportive medical care
- ❧ Emotional support for pts & their families
- ❧ Pharmacological Rx for specific sms, including disruptive behavior

## **Psychosocial therapies**

- ❧ The deterioration of mental faculties has significant psychological meaning for pts

✓ Pt's identities begin to fade

→emotional reaction: depression, anxiety, catastrophic  
terror

∞ Nature & course of their illness are clearly explained

∞ Assistance in grieving & accepting the extent of their  
disability

∞ Help pts find ways to deal with defective ego functions

✓ Keeping calendars for orientation problems



**Thank You**