

# The Mind and Cognition in HIV



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# Introduction



**HIV-associated neurocognitive disorders (HANDs) and mental disorders commonly found in PLWHA.**

**Associated with cognitive deficits across domains.**

**Imaging studies - changes within cortical & subcortical brain regions.**

## **Discuss:**

- **overview of clinical features of HANDs and it's impact on functioning and work**
- **assessment**

# HIV-associated neurocognitive disorders (HAND)



Three categories of disorder:

- Asymptomatic neurocognitive impairment (ANI)
- Mild neurocognitive disorder (MND)
- HIV-associated dementia (HAD)



# Asymptomatic neurocognitive impairment (ANI)



Mildest form.

Mild cognitive impairment in  $\geq 2$  different cognitive domains ( $\geq 1$  SD).

No functional decline.

Very subtle changes in cognitive functioning.

Self-report not sufficient for diagnosis – neuropsychological assessment required.

# Mild neurocognitive disorder



Mild neurocognitive impairment in  $\geq 2$  cognitive domains ( $\geq 1SD$ ) + disturbances in daily functioning.

Neuropsychological assessment required.

# HIV-associated dementia



Most severe HAND.

Marked neurological impairment  $\geq 2$  cognitive domains ( $\geq 2SD$ )  
+ marked disturbance in daily functioning.

Must be rigorously diagnosed, NP assessment required.



Other possible causes must be excluded.

### Secondary opportunistic infections

Toxoplasmosis, progressive multifocal leukoencephalopathy (PML), neurosyphilis, cytomegalovirus (CMV or human herpesvirus 5), encephalitis, brain abscess, cryptococcal meningitis, TB meningitis.

### Tumours

### Vascular disease

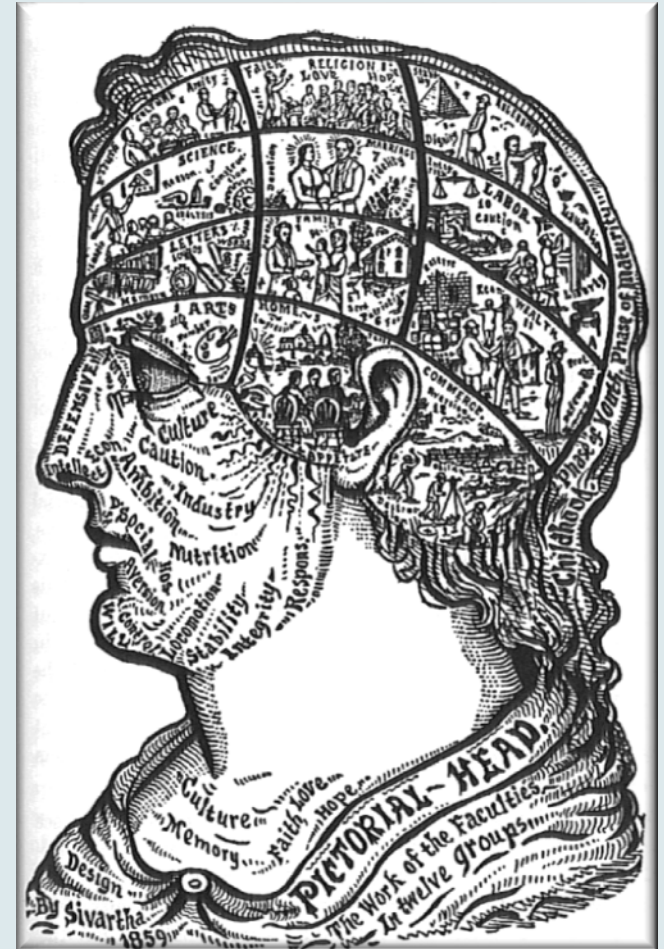
### Drug and substance related disorders

### Primary psychiatric disorders

### Pre-morbid TBI

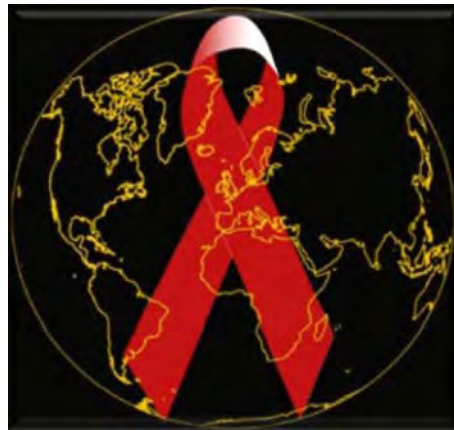
# Cognitive domains

- verbal/language
- attention/working memory
- abstraction/executive
- memory (learning; recall)
- speed of information processing
- sensory-perceptual
- motor skills



# Neuropsychological presentation

The main characteristic of HAND is its patchy and variable nature.



# Verbal/language




Children severely affected.

Adults - frank dementia or localized lesion.

# Attention



having attention deficit  
problems is not too bad.  
i have learned to work  
around the

whoosssshhhhh tornados are  
wickedddd  umm

# Attention



Ability to pay attention prerequisite for registering and remembering information.

Memory complaints may reflect attention-related forgetfulness.

Example: Forgetting whether one locked the door after leaving the house, forgetting where one parked the car.

HIV: Frequent complaint (Selnes, 2007).

# Working memory



Working memory - ability to keep something in mind while you are busy with another task.

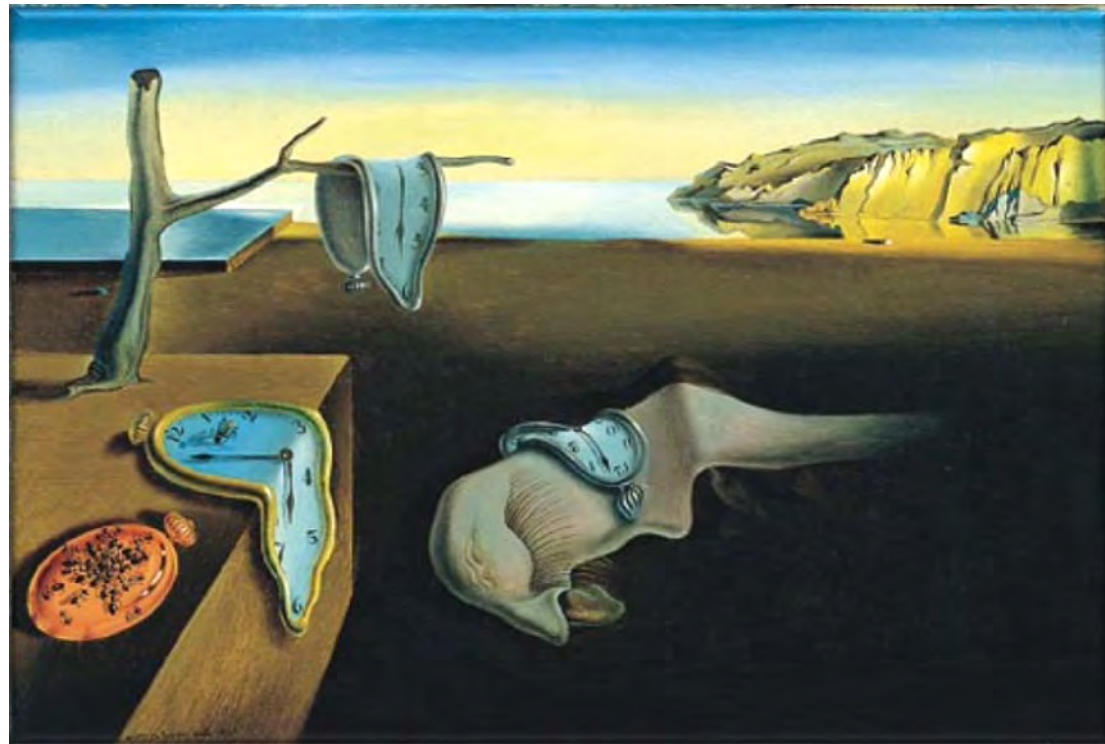
Maintaining and manipulating information in working memory.

Worse with complex information.



Real world scenario: Failing to keep instructions in mind.

# The persistence of memory: semantic and episodic



Information from WM to intermediate store = learning.

Ability to remember people, things, places, events, other ideas.

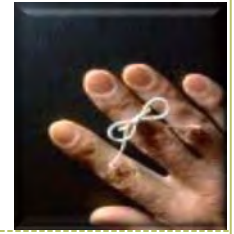
Implicit/procedural memory is the learning of procedures or skills, e.g. riding a bike.

### **HIV:**

- Explicit learning/episodic memory impairment commonly found.
- 50% at varying disease stages.
- Real World: Difficulties with ease of recollecting recently acquired information.
- NP testing, worse on verbal and non-verbal material.
- No evidence of semantic memory breakdown.
- Pattern of memory disturbance - ↓ efficient learning of new information but typically retained.

# ...prospective memory

'remember to remember'



Formation, maintenance, retrieval, execution of future intention.

Independent living & daily tasks.

Self initiated cue monitoring & retrieval.

Demands on retrospective memory (RM) and executive functions.

Highly depended on frontal systems.

## HIV:

- Present on subjective complaints and testing – 30 -60%.
- Pts perceive difficulties inaccurately.
- Over or under reporting.
- Real world scenario: fetch child from school; take meds.

# Psychomotor & motor abilities



**Slowed movement; slowed information processing.**

**Motor tasks, e.g. Finger Tapping Test, or tests involving speed and fine motor coordination (Grooved Pegboard).**

**Slowed completion of GP related to HIV disease stage.**

**Declines linked to future progression to HAD (ND Hand).**





Real world scenario: clumsy hands, assembly line work, counting tablets.

# Executive functions and abstracting ability



Complex goal-orientated behaviour, adaptation to environmental changes and demands.

Ability to plan and anticipate outcomes (cognitive flexibility), direct attentional sources to meet demands of non-routine events.

Central to most HIV neurocognitive impairment profiles.

Associated with impairments in everyday functioning.

Deficits: abstraction (concreteness), novel problem solving, set shifting, cognitive slowing, disinhibition, poor cognitive & social planning and the ability to plan ahead and order meaningful events chronologically.

Real world scenario: Make sound financial decisions. Clean an untidy kitchen e.g. Ms D.



Get to your destination - **on time!**

# Visuoperception



Ability to detect, understand, manipulate, integrate visual stimuli.

Largely unaffected - subtle deficits – little research.

Visual attention abnormalities.

Mental rotation 3D objects.

Increased risk of negative consequences in daily life – driving.



Real world scenario: Important to assess professional drivers.

# Mental Illness in South Africa



## Freeman (2007) – Prevalence among HIV/AIDS Patients

- Any Disorder 43.7%
- Major Depression 11.1%
- Mild Depression 29.9% (Total 41%)
- PTSD 4.9%
- Alcohol Abuse and/or Dependence 15.3%
- Drug Abuse and/or Dependence 2.2%

## SASH Study – National Lifetime Prevalence

- Any Disorder 30.3%
- Mood Disorders 9.8%
- PTSD 2.3%
- Alcohol Abuse and/or Dependence 14%
- Drug Abuse and/or Dependence 4.5%

Slide from Dr Andersen

# Depression and Functional Abilities



HIV associated with impairments in medication adherence, driving, employment, finance management, cooking, shopping (Heaton et al., 1999).

Heavy reliance on self report measures.

## **Be aware:**

Higher levels of depression among those who over report problems with medicine management, driving, cognition.

Genuine cognitive dysfunction predictive of under-reporting of functional deficits (April et al., 2010).

Neurocognitive impairment and incident major depressive episodes are two independent processes (Cysique et al., 2007).

# Driving



**Deficits in rapid orienting of visual attention and reductions in early visual processing capacity.**

**HIV+ with NP impairments = decreased driving skills when assessed using PC-based driving simulators.**

**↓ executive functioning, attention, speed of information processing, and motor abilities most closely associated with poor driving abilities. Divided attention most prominent (Marcotte, 2004/2006).**

## **Useful Field of View Test:**

Declines in visual attention not solely result of advancing disease nor high levels of general cognitive impairment, suggesting a process occurring at least partially independent of disease progression as well as cognitive deficit which is not entirely captured by common NP tests.

Real life implications = more accidents (Marcotte, 2006) ■

# Neurocognitive Impairment and HIV Risk factors



Barrier to effective HAART use and HIV management.

Poor medication adherence and HIV risk-taking behaviour exacerbate HIV symptoms.

HIV risk factors (mental illness/substance abuse) trigger neurocognitive impairments/poor adherence → HIV associated neurological dysfunction.

**To reduce transmission and progression of HIV we must understand the complex and reciprocal relationship between neurocognitive impairment and HIV risk factors.**

# Sexual risk behaviour



Impact of susceptibility factors for cognitive dysfunction (e.g. substance abuse/mental illness) on sexual risk taking behaviours:

- Major mental disorder ↑ sexual risk taking behaviour.
- Comorbid substance use further associated with increased risk (Teplin et al., 2005).

Nature of cognitive impairment caused by HIV = ↑ risk-taking behaviour.

- **Impaired executive function** inhibits rational decision-making preventing consideration of future outcomes in favour of current rewards → prevents individuals from making safe sexual choices.
- **Slowed information processing/reaction time** prevent timely, appropriate consideration of risk variables during decision making.
- **Dysfunctional impulse control**, which can result from HIV/substance use/mental illness on fronto-striatal circuit prevents execution of safe sexual practices (Anand et al., 2010).

# NP assessment

Digit Symbol Coding: 20 (M = 50.88)

↓ motor speed and cognitive slowing; perseveration.



# Screening



Many different tests available. Batteries extensive and time-consuming - need rapid screening tool.

The Mini Mental State Examination (MMSE):

- Well known, limited usefulness - mainly detects cortical (Alzheimer's disease) instead of subcortical dysfunction.

The HIV Dementia Scale (HDS):

- Four cognitive domains (verbal memory recall, psychomotor speed, visual construction and response inhibition)
- Useful for detecting milder cognitive deficits?
- Requires literacy and language comprehension – limits usefulness.

International HIV Dementia Scale (IHDS):

- Three cognitive domains (psychomotor speed, motor speed and verbal memory recall).
- Useful for detecting milder cognitive deficits?

Standardized and regularly administered symptom questionnaires.

Don't substitute complete NP evaluation required for HAND diagnosis.

## HIV Cognitive Performance Questionnaire

The following questions will give you an indication if a patient is experiencing symptoms that may be indicative of cognitive impairment secondary to HIV. If the patient is experiencing difficulty in any of the domains a neurocognitive assessment may be necessary.

The scale was designed to create a clinical impression and is not rated. Please use in conjunction with the International HIV Dementia Scale (IHAD).

In the last month, have you...

1. had any difficulty remembering to do something (e.g., what to buy when you go to the shop) or remembering what people say to you?  Y  N
2. become more easily distracted than before? (e.g., having difficulty following a conversation, or to keep your attention on what you are doing when it is noisy)  Y  N
3. noticed that you think or act more slowly than you usually do? (e.g., it takes longer or is more difficult for you to sort out problems around the house, or to follow new instructions)  Y  N
4. noticed that your hands are clumsy? (e.g., you find it more difficult to handle small change/coins, roll cigarettes, sew on buttons, or push the buttons on a cell phone)  Y  N
5. been moving slower than before? (e.g., walking slower)  Y  N
6. been less concerned with your problems?  Y  N

# IHDS



**Memory Registration** – Give four words to recall (**dog, hat, bean red**) – 1 second to say each. Ask patient all 4 words. Repeat if patient doesn't recall all immediately. Say you will ask for recall of the words again a bit later.

**Motor Speed:** Have the patient tap the first two fingers of the non-dominant hand as widely and as quickly as possible. Time: 5 seconds

**4 = 15 in 5 seconds**      **3 = 11-14 in 5 seconds**      **2 = 7-10 in 5 seconds**      **1 = 3-6 in 5 seconds**      **0 = 0-2 in 5 seconds**

**Psychomotor Speed:** Have the patient perform the following movements with the non-dominant hand as quickly as possible: Time: 10 seconds

Clench hand in fist on flat surface

Put hand flat on surface with palm down

Put hand perpendicular to flat surface on the side of the 5<sup>th</sup> digit.

Demonstrate and have patient perform twice for practice.

**4 = 4 sequences in 10 sec**      **3 = 3 sequences in 10 sec**      **2 = 2 sequences in 10 sec**      **1 = 1 sequences in 10 sec**

**0 = unable to perform**

**Memory Recall:** Ask the patient to recall the four words. Prompts with semantic clue : animal (dog); piece of clothing (hat); vegetable (bean); colour (red).

Give 1 point for each word spontaneously recalled.

Give ½ point for each correct answer after prompting.

Maximum – 4 points.

\_\_\_\_\_/4

Total: Sum of the scores on items 1-3. Maximum score = 12 points. A score of  $\leq 10$  should be evaluated further for possible dementia.



# HAART



## WHO?

NOT exclusive to patients with advanced HIV disease and low CD4 count.  
HIV encephalopathy AIDS defining disease.

HAART – improve concentration, speed of mental processing, mental flexibility, fine motor function, visuospatial and constructional abilities, memory - stop or reverse symptoms (Tozzie et al., 1999).

Reducing incidence of severe forms of HAND – neuroactive antiretrovirals may be associated with psychiatric symptoms due to increased blood-brain barrier penetration – impaired concentration and neuropsychiatric complications (Cespedes et al., 2006).

**The earlier the better!**

# Why NP testing?



## Essential for three reasons.

- **First**, HANDs are treatable. CD4 count of 250+ may qualify for early HAART.
- **Second**, benefit from additional treatment, planning and support, due to the risk of poor or erratic adherence.
- **Third**, HAD is an independent risk factor for mortality.

Investigations should include brain imaging.

A recent MRI imaging study done by this department illustrates that organic brain damage is already evident with mild cognitive impairment (Hoare & Joska, 2010).

25% of HIV positive patients from a community sample presented with HAD (Joska, 2010).

# Clinic



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# Summary



Cognitive degeneration and CD4 count does not appear to be related and cognitive impairment may already be evident in HIV+ patients with a CD4 count as high as 350 or more.

HAART administered in the early phases of cognitive decline results in better long term cognitive resilience, medication adherence, daily functioning, and improved longevity.

This makes a strong argument for HAART to be administered at the first signs of cognitive decline as evidenced by neuropsychological testing, as opposed to on account of CD4 count.