17TH ANNUAL CONFERENCE OF THE BRITISH HIV ASSOCIATION (BHIVA)

Dr Lucy Garvey
Imperial College Healthcare NHS Trust, London

6-8 April 2011, Bournemouth International Centre

Features of Neurocognitive Performance in over 100 Neurologically-Asymptomatic HIV-Infected Adults Receiving cART

Lucy Garvey, Veena Surendrakumar and Alan Winston
Imperial College, London

Background

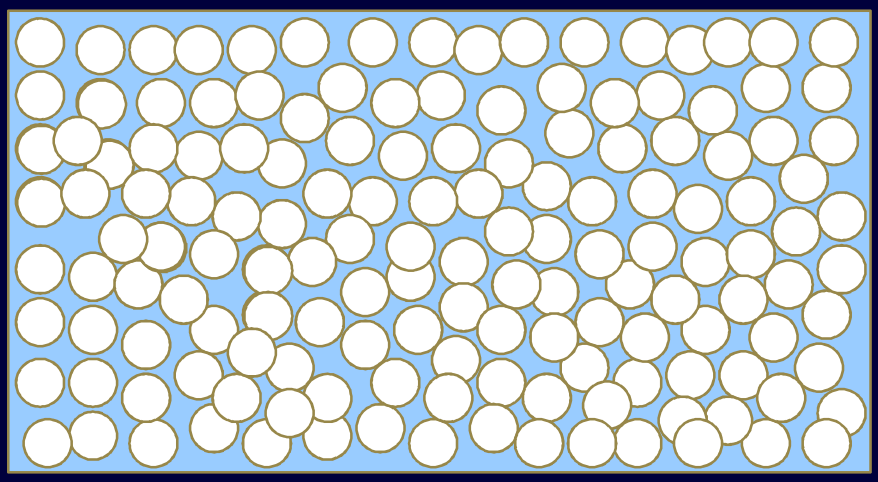
Despite effective cART, HIV-associated neurocognitive disorders (HAND) continue to be reported[1,2]

HAND are associated with difficulties achieving employment, adhering to medication and shorter survival[3-6]

Risk factors for milder forms of HAND are not yet defined

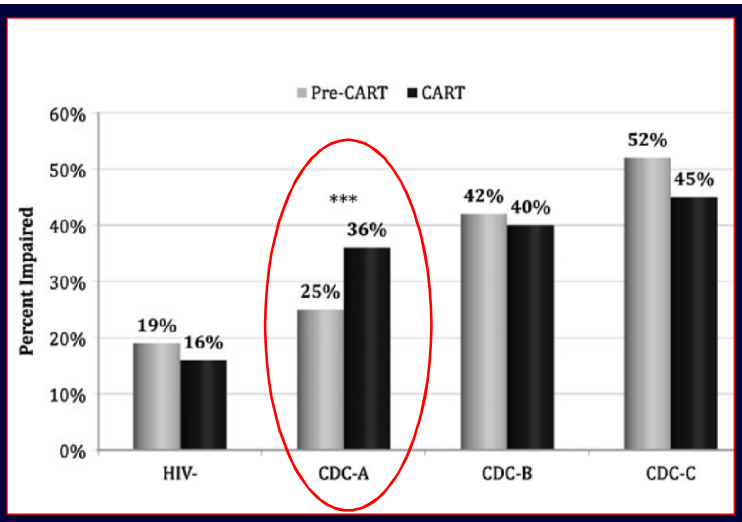
[1] Dore GJ et al. (2003). Aids 17(10):1539-45. [2] McArthur JC et al. Arch Neurol 61(11):1687-96 [3] Vivithanaporn P et al Neurology 75(13):1150-8 [4] Ellis RJ et al. Arch Neurol 54(4): 416-24. [5] Albert SM AIDS & Behaviour 3: 121–128. [6] Tozzi V et al AIDS Res Hum Retroviruses 21(8):706-13

Classification of HAND



Antinori et al Neurology (2007);69;1789-1799

Prevalence of Cognitive Impairment



Heaton RK et al. J Neurovirol (2011): 17 (1) 3-16

Aims

To examine the neurocognitive performance (NcP) scores in a cohort of HIV-infected, neurologically-asymptomatic subjects receiving cART

Methods

Cross-sectional study at St Mary's Hospital, London 2009-10

Attending the HIV Outpatient Dept for routine clinical care

Inclusion criteria

HIV-1 infection >6 months

Aged over 18 years

Proficient in English

On stable cART with plasma HIV RNA <50 copies/mL for >3 months

Exclusion criteria

Any current neurological complaint / disease

Untreated syphilis

Hepatitis B co-infection

Current AIDS defining illness

Current interferon and/or ribavarin

Hepatic synthetic function impairment

Any recreational drug use in past month

Alcohol abuse

Methods

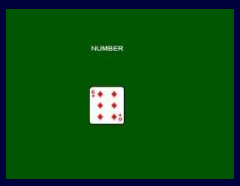
Subjects completed two cerebral function assessments:

1. A computerised cognitive assessment
2. The International HIV Dementia Scale (IHDS)

Computerised cognitive test

Research tool (*Cogstate™*) developed and used to investigate cognitive performance

PPV of 81% when compared to formal neuropsychological assessment in HIV-infected subjects[1]



[1] Cysique LA et al Arch Clin Neuropsychol 21(2): 185-94.

Computerised cognitive test

Composite *Z*-score calculated including cognition speed, performance accuracy and executive function

Neurocognitive impairment (NCI) was diagnosed where task scores were more than 1SD below the mean of age-matched population data* in ≥ 2 domains

**n=879 healthy adults aged 25-70*

The International HIV Dementia Scale (IHDS)

Rapid screening tool

1. Memory recall of 4 words — Scored out of 4

(dog, hat, bean, red)

1 point for every word remembered

2. Tapping — Scored out of 4

No. of finger tapping complete in 5 secs recorded

3. Performing sequence with wrist (non dominant hand) — Scored out of 4

No. of times sequence complete in 10 secs recorded

Sacktor NC et al (2005) Aids 19(13): 1367-74

Methods

Patient demographics and clinical parameters collected:

- -Age, gender, ethnicity, time-elapsed since HIV diagnosis, nadir and current CD4+ cell count, plasma HIV RNA
- -Type of current cART (PI- or NNRTI- based) and CPE score of current cART (2007, 2010 versions)

Associations between composite *Z*-score and clinical parameters were evaluated using linear regression (SPSS v18.0)

Results

			Total
Patient demographics	Number of subjects, *n*		101
	Age (years), *median [IQR]*		53 [43-62]
	Male gender, *n (%)*		89 (88)
	Ethnicity, *n (%)*	*White*	88 (87)
		Black	7 (7)
		Other	6 (6)
HIV disease parameters	Time since HIV diagnosis (years), *median [IQR]*		14 [9, 18]
	Nadir CD4+ count, (cells/uL), *median [IQR]*		185 [83, 260]
	Current CD4+ count (cells/uL), *median [IQR]*		525 [373, 710]
	Chronic HCV coinfection, *n(%)*		25 (25)
Details of current cART	Plasma HIV RNA below 50 copies/mL, *n(%)*		101 (100)
	Current cART, *n(%)*	*NNRTI- based*	54 (53)
		PI-based	47 (47)
	CPE score 2007, *median [IQR]*		1.5 [1.5, 2.5]
	CPE score 2010, *median [IQR]*		7.0 [7.0, 8.5]

Results of NcP assessments - NCI

Overall rate of NCI in cohort = 19/101 (19%)

Individuals with NCI poorer performance in cognitive domains:

- *psychomotor speed*
- *executive function*
- *divided attention*

Association of composite Z-score and clinical parameters

	Univariate analysis		Multivariate analysis	
Clinical parameter	**P value**	**95% CI**	**P value**	**95% CI**
Age, *per 10-year increase*	**<0.001**	**[-1.20, -0.57]**	**<0.001**	**[-1.03, -0.42]**
Male gender	0.27	[-1.20, 0.57]	-	
HCV infection	0.11	[-0.17, 1.74]	-	
Education , *per 10 year increase*	0.10	[-2.00, 0.56]	-	
Years since HIV diagnosis, *per 10-year increase*	0.66	[-0.84, 0.54]	-	
Receiving NNRTI-based cART	0.84	[-0.29, 0.33]	-	
Current CD4⁺ Count, *per 100-cell increase*	0.08	[-0.02, 0.29]	0.75	[-0.13, 0.19]
Nadir CD4⁺ Count, *per 100-cell increase*	**0.01**	**[0.10, 0.68]**	**0.04**	**[0.02, 0.55]**
CPE score 2007, *per 1.0 score increase*	0.51	[-0.52, 1.03]	-	
CPE score 2010, *per 1.0 score increase*	0.89	[-0.29, 0.33]	-	
IHDS, *per 1.0 score increase*	**0.001**	**[0.17, 1.74]**		

Summary

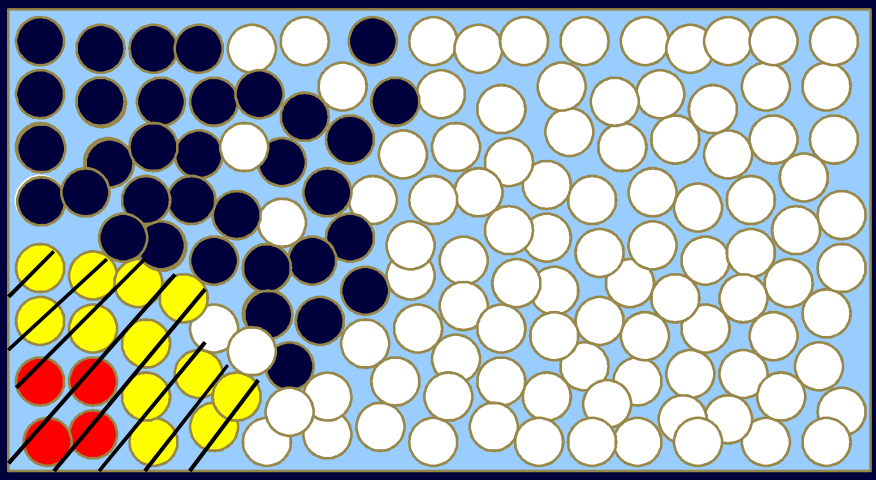
Many cohorts have reported high rates of HAND, cART status widely variable

In this cohort of neurologically-asymptomatic adults on suppressive cART, the rate of NCI was 19% - only just exceeds rates in HIV-negative populations

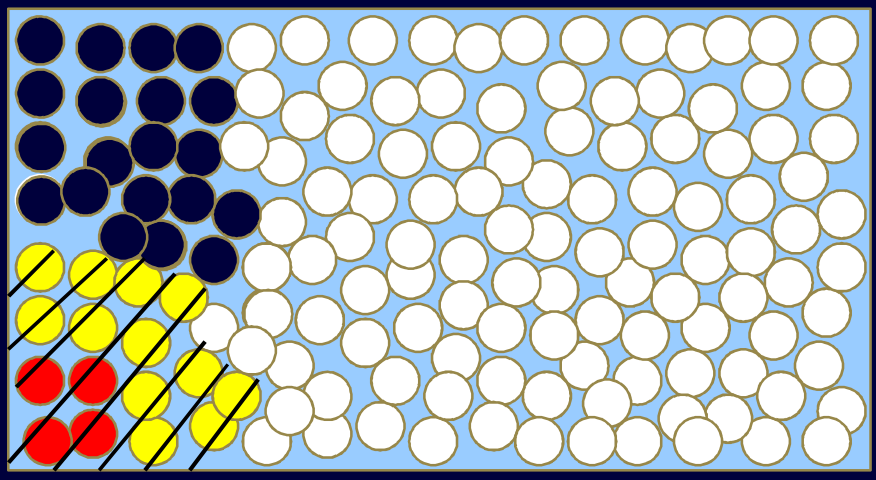
Evidence of HIV-disease effect as nadir CD4+ cell count associated with poorer cognition

No association with cART drug class or CPE score

Summary – subjects stable on cART



Summary – subjects stable on cART



Conclusions

One of first studies to investigate NcP in a cohort of asymptomatic patients on effective therapy, which represents large proportion of our clinic population

Further work required to establish rates of NCI in symptomatic and untreated subjects

Acknowledgements

All patients who participated in research

Staff at St Mary's HIV Outpatient Department

Staff at *Cogstate*^{TM}, Melbourne, Australia for assistance with data analysis techniques