Changes in Cognition, Mood, and Sleep Following EFV-DTG Switch in South Africa: The CONNECT study

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BACKGROUND

WHO first line ART recently changed from EFV- to DTG-based therapy, affecting millions of PWH globally.

Both EFV and DTG have been associated with neuropsychiatric side effects.

The effect of EFV-DTG switch on cerebral function and CSF HIV RNA control is not known.

Rates of cognitive impairment and CSF escape have not been comprehensively studied in African populations.

METHODS

178 virally supressed PWH on EFV-based ART in a low-income area of Cape Town were studied at baseline. 145 were followed up at 1-year following switch to DTG.

95 sociodemographically similar people without HIV (PWoH) were recruited from the friends and relatives of PWH in the same area, matched for age and sex. 40 PWoH were followed up at 1-year to assess practice effects.

Measures:

Comprehensive cognitive testing over 7 domains

Cognitive symptoms and functioning:

- Patient's Assessment of Own Functioning Inventory (PAOFI)
- Charter Instrumental Activities of Daily Living scale (CTADL)

Mental health and sleep:

- Center for Epidemiologic Studies Depression Scale (CESD)
- Mini International Neuropsychiatric Interview (Mini) v7.0
- State-Trait Anxiety Inventory (STAI)
- Pittsburgh Sleep Quality Index (PSQI)

PWH had CSF sampling for HIV RNA quantification.

Global cognition was assessed by T-scores and low cognitive performance by global deficit score ≥0.5. Mixed effects regression models were used to investigate the effects of switch on cerebral function parameters.

CONCLUSIONS

Cognition:

- Cognitive performance improved to that of HIV-ve controls following EFV-DTG switch
- Cognitive symptoms were common in both PWH and HIV-ve controls, varied by method, and were not significantly different between groups.

This finding contrasts markedly with cognitive impairment estimates derived using HAND criteria, which suggest that ~45% of PWH have a neurocognitive disorder, with highest rates in sub-Saharan Africa.[1]

Mental health and sleep:

- Sleep quality improved following EFV-DTG switch.
- Depression rates worsened, although there were baseline differences and this requires further exploration (the effect of drug exposure and genotype is being investigated)

CSF HIV RNA escape:

- CSF escape was uncommon and generally at low levels.
- One participant developed transient asymptomatic CSF escape following EFV-DTG switch. The cause is unclear and warrants further investigation.

1. Wang et al. HAND: a meta-analysis. Neurology 2020

RESULTS

	Baseline (EFV)					Follow up (DTG)				
	PWH (N=178)		PWoH (N=95)			PWH (N=178)		PWoH (N=95)		
Variables	*n*	*M* (*SD*) or *f* (%)	*n*	*M* (*SD*)	*p*	*n*	*M* (*SD*)	*n*	*M* (*SD*)	*p*
Cognition										
Global T-score	176	47.35 (6.22)	94	49.92 (5.27)	<.001***	145	51.43 (5.79)	40	52.73 (6.16)	.215
Low PCT using GDS cut-off	176		94		<.001***	145				1[b]
Functional measures										
PAOFI total score [a]	178	21.60 (13.83)	95	22.01 (12.79)	.621[a]	145	26.54 (14.07)	40	24.62	.224[a]
PAOFI affirmative	178	52 (29.21%)	95	20 (21.05%)	.145	145	47 (32.41%)	40	10 (25.0%)	.369
CTADL total score [b]	178	2.19 (1.48)	95	1.94 (0.94)	.765[a]	145	2.58 (1.16)	40	1.98 (0.83)	.002[a]**
CTADL affirmative	178	10 (5.62%)	95	2 (2.11%)	.227[b]	145	6 (4.14%)	40	1 (2.50%)	1[b]
Mental health and sleep										
CES-D score ≥16	178	17 (9.55%)	95	21 (22.11%)	.004**	145	22 (15.17%)	40	6 (15.00%)	.979
STAI total	178	37.20 (8.03)	95	37.55 (9.43)	.747	145	36.97 (8.72)	40	35.85 (9.47)	.483
Major depressive disorder	178	1 (0.56%)	95	6 (6.32%)	.008[b]**	145	9 (6.21%)	40	2 (5.00%)	1[b]
PSQI total [c]	178	5.79 (3.59)	95	5.80 (3.94)	.765[a]	145	5.14 (3.76)	40	6.47 (3.78)	.032[a]*
PSQI total score ≥ 5	178	114 (64.04%)	95	60 (63.16%)	.885	145	68 (46.9%)	40	25 (62.50%)	.081
HIV RNA										
Plasma <1000 copies/ml	113	111 (98.23%)		NA		122	117 (95.90%)		NA	
Plasma <50 copies/ml	113	104 (92.04%)		NA		122	103 (84.43%)		NA	
CSF <1000 copies/ml	94	93 (98.94%)		NA		77	76 (98.70%)		NA	
CSF <50 copies/ml	94	92 (97.87%)		NA		77	73 (94.81%)		NA	

Table 1. Cognitive, mental health, sleep and HIV viral load at baseline and follow up in PWH and PWoH

[a] Higher score on PAOFI indicates worse functional impairment; [b] Higher score on CTADL indicates worse functional impairment; [c] Higher score on PSQI indicates worse sleep

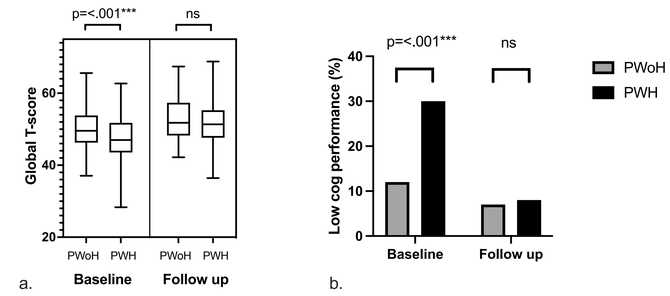


Figure 1. Cognitive performance by a) global T-score and b) GDS at baseline (EFV) and follow up (DTG). Improvements in PWoH over time relate to practice effects.

Mental Health outcomes (PWH only)			
CES-D score ≥16	Odds ratio	95% *CI*	*p*
Timepoint (baseline versus follow-up)	6.53	1.42 – 30.06	.016*
CES-D score ≥16[a]			
Timepoint (baseline versus follow-up)	5.45	1.11 – 26.77	.037*
Emotional/mental impact of COVID pandemic	0.95	0.50 – 1.82	.886
MINI – MDD dx			
Timepoint (baseline versus follow-up)	11.71	1.47 – 93.57	.020*
STAI Total	Estimate	95% *CI*	*p*
Timepoint (baseline versus follow-up)	-0.07	-1.37 – 1.23	.915
Sleep outcomes (PWH only)			
PSQI Total	Estimate	95% *CI*	*p*
Timepoint (baseline versus follow-up)	-0.63	-1.24 – -0.02	.042*
PSQI Total score ≥ 5	Odds ratio	95% *CI*	*p*
Timepoint (baseline versus follow-up)	0.37	0.20 – 0.66	.001**

Table 2. Linear mixed effects regression models showing effects of EFV-DTG switch on mental health and sleep

CSF HIV RNA escape (ie. CSF HIV RNA > plasma)

Baseline (EFV): 1/94 (1.1%):

- Plasma <50, CSF HIV RNA 150 copies/ml

Follow up 3/77 (3.9%):

- Plasma <50, CSF 70 copies/ml
- Plasma <50, CSF 81 copies/ml
- Plasma 448, CSF 4204 copies/ml*

*This participant had plasma 91, CSF <50 copies/ml at baseline. LP was repeated at 5 months without change in ART: Plasma 170, CSF <50 copies/ml.

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