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En nombre de CoRISpe-Cohorte de pacientes pediátricos con VIH de Madrid. España.

COMPENSATORY BRAIN ACTIVITY IN WELL CONTROLLED PERINATALLY HIV-INFECTED YOUNG ADULTS

FARO & NeuroCoRISpe Projects

HIV neuro psychiatry

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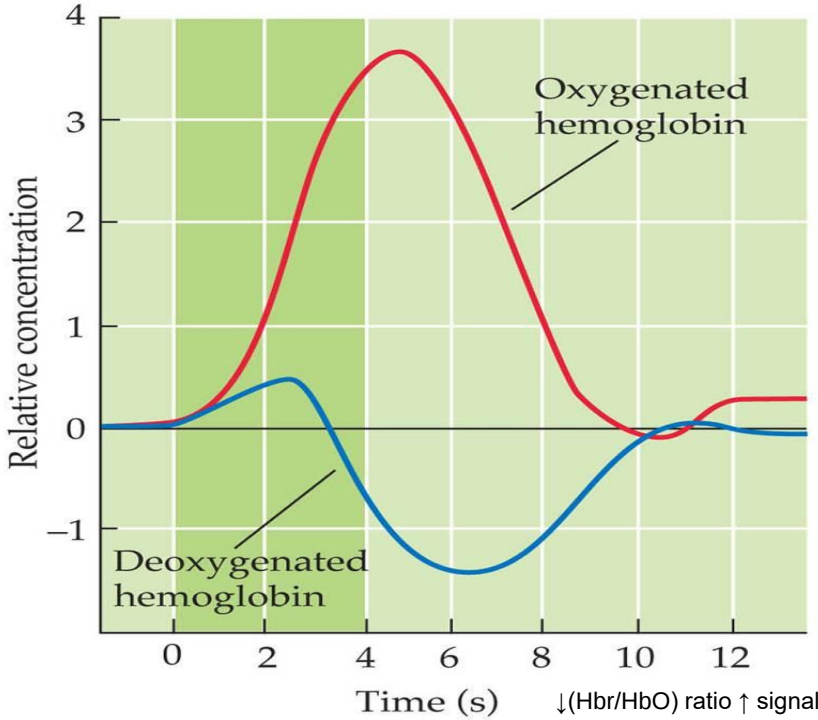
INTRODUCTION & RESEARCH GOALS

fMRI such as unique diagnostic tool is its ability to bridge the mind and the brain. It allows to relate the specific anatomical segments of our brain; its neurology and structure to our mind which makes up our higher perceptions of how we behave, learn, retain memory and make decisions. This technique can be viewed in real-time where a stimulus given to a patient can result in immediate and dynamic changes of brain activity.

Data in children and adolescents with PHIV are scarce and to our knowledge there are not studies performing fMRI while engaged in phonemic and motor tasks in PHIV patients!

Our aim was to assess the neural activity patterns using fMRI on a group of PHIV adolescents with good daily functioning and good immunovirological controlled infection compared with their peers with similar socio-demographic characteristics



↓(Hbr/HbO) ratio ↑ signal (T2)

It measures haemodynamic changes induced by regional changes in neuronal activity…

BOLD Effect (Blood oxygen level dependent)

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METHODS

Twenty right-handed young adults from 16 to 25 years of age were included in the study (10 PHIV infection and 10 HIV-, matched by age and educational level (±1 years of school).

- PHIV patients inclusion criteria: CD4 nadir >12%, CD4 > 25% plus prolonged viral suppression on cART, undetectable VL ≥ 5 years with good adherence to treatment and stable cART > 1 year.

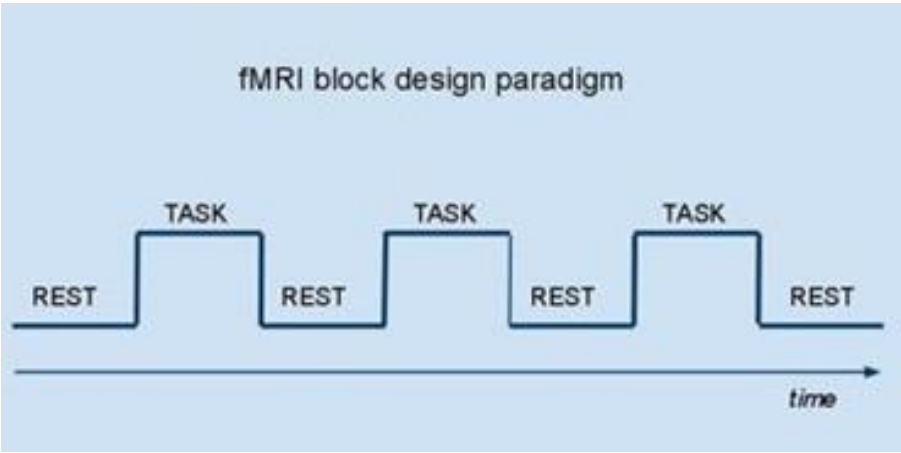
- PHIV patients exclusion criteria: (1) encephalopathy or AIDS category C3, (2) history of active drug abuse during pregnancy, HCV, (3) psychiatric disease, drug or alcohol abuse, (4) prematurity and (5) poor performance with daily living activities.

Psychological and Neurocognitive Profile

- *Psychosocial questionnaire, BDI, STAI, PSQI y SF-36*

1. Intelligence (KBIT)
2. Attention and Processing speed (Digit Span-Forward, TMT A, Coding)
3. Executive function (TMT B, Phonological and Semantic Verbal Fluency, Luria-DNA Battery-Attention Control subtest, Digit Span-Backrward- Sequencing)
4. Motor skills (Finger Tapping Test)

→ SPSS



Verbal fluency task
Motor task
→ FSL

RESULTS

Clinical features of PHIV participants

Immunovirological variables	
STAGE B (n, %)	10 (100%)
CD4 Median and IQR (cls/mm3)	781 (588-781)
CD4 Median and IQR (%)	38 (33-40)
NADIR CD4 cells/mm3 (median, IQR)	222 (123-388)
NADIR CD4 % (median, IQR)	14.5 (13.2-18)
Antiretroviral therapy	
Median age at HIV diagnoses	2.7 (0.3-6.3)
Median age at start ART	5.2 (1.4-6.9)
Median age at the start of cART	7.2 (4.3-11.1)
Time of treatment with cART	13.7 (9.6-15.8)
Median number of ART regimens	6 (5-8)
Median number of cART regimens in years (median, IQR)	6 (4-8)
Time of viral load <50 cop/ml (years)	9.5 (6-11.8)
Current treatment situation	
Good adherence to treatment (n, %)	10 (100)

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RESULTS

Demographic and cognitive measures

	Patients	Controls	P value
Demographic Characteristics	**n(%)**	**n(%)**	
Caucasian	8 (80%)	7 (70%)	0.356
Born in Spain	8 (80%)	8 (80%)	1
Age at assessment in years (median, IQR)	19 (17-22)	20 (17-21)	0.854
Female gender	7 (70%)	5 (50%)	0.361
Currently working	3 (30%)	0 (0%)	0.211
Exercise regularly	6 (60%)	8 (80%)	0.403
Good sleeper	7 (70%)	4 (40%)	0.178
Single	6 (60%)	4 (40%)	0.398
Years of education (median, IQR)	11 (10-12)	12 (10-12)	0.371
Cognitive measures	**Mean (SD)**	**Mean (SD)**	
IQ	-0,017 (0,54152)	-0,069 (0,53276)	0.970
Processing speed and Attention	-0,226 (0,75948)	-0,172 (0,68855)	0.850
Executive function	-0,033 (0,52493)	-0,094 (0,48356)	0.821
Phonological verbal fluency	-0,1670 (0,7589)	-0,535 (0,50112)	0.309
Fine motor skills	1,800 (0,57246)	1,961 (0,31519)	0.405
Finger Tapping Test (dominant hand)	2,088 (0,59503)	0,595 (0,2203)	0.307

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Anxiety, depression and QoL

	Patients	Controls	P value
Psychological testing	**Mean (SD)**	**Mean (SD)**	
STAI- Trait	0,021 (1,46827)	-0,246 (0,91895)	0.405
STAI- State	-0,544 (0,88425)	-0,787 (0,84363)	0.762
SF-Physical Functioning	1,034 (0,07589)	0,979 (0,23154)	0.914
SF- Role Functioning-Physical	0,905 (0,77476)	1,089 (0,19290)	0.942
SF-Role Functioning-Emotional	0,43 (0,79690)	0,594 (0,77792)	0.330
SF-Energy Fatigue	0,416 (0,78155)	0,885 (0,75850)	0.159
SF-Emotional Well Being	-0,291 (0,98293)	0,219 (0,74314)	0.222
SF-Social Functioning	0,389 (0,63048)	0,585 (0,77476)	0.102
SF-Pain	0,531 (0,68125)	0,944 (0,5288)	0.042*
SF-General Health	0,783 (1,08395)	0,995 (1,03680)	0.732
SF-Health Change	0,1430 (0,9224)	0,361 (0,89386)	0.491
BDI (% normal)	6 (60%)	8 (80%)	0.232

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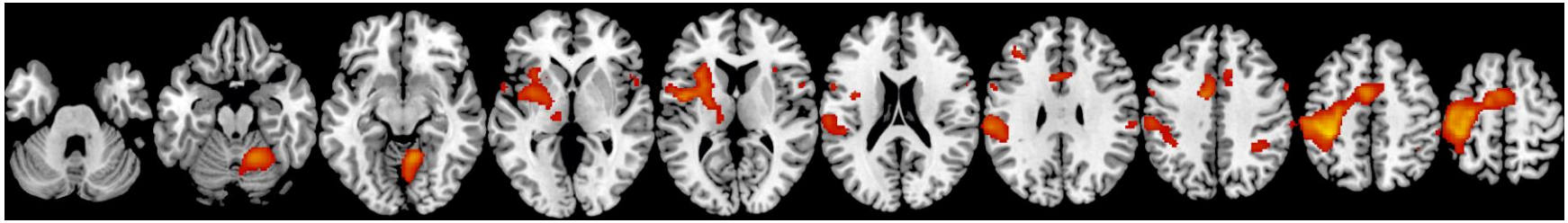
RESULTS

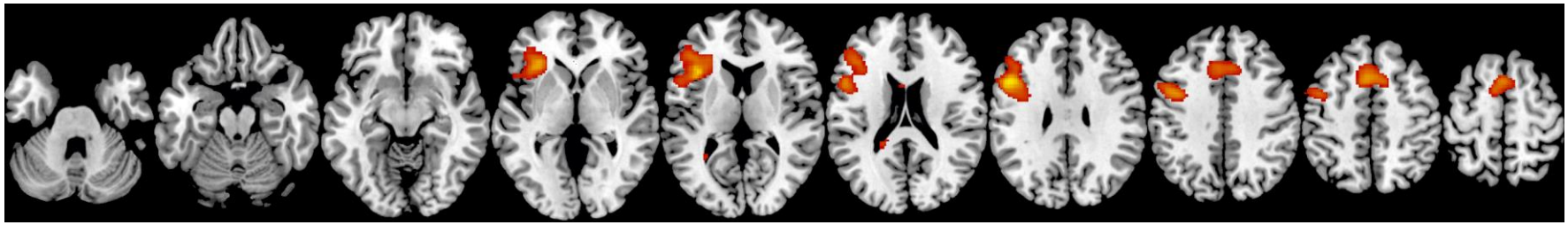
fMRI

Patterns of brain activation (all participants) during ‘finger motion + touching tips vs rest



Left Motor Cortex (LMC; -36, -34, 50)
Right Cerebellum (RC; 8, -54, -10)
Intraparietal Sulcus (IS; 34, -44, 40)
Ventral Premotor Cortex (VPC; 60, 6, 38)

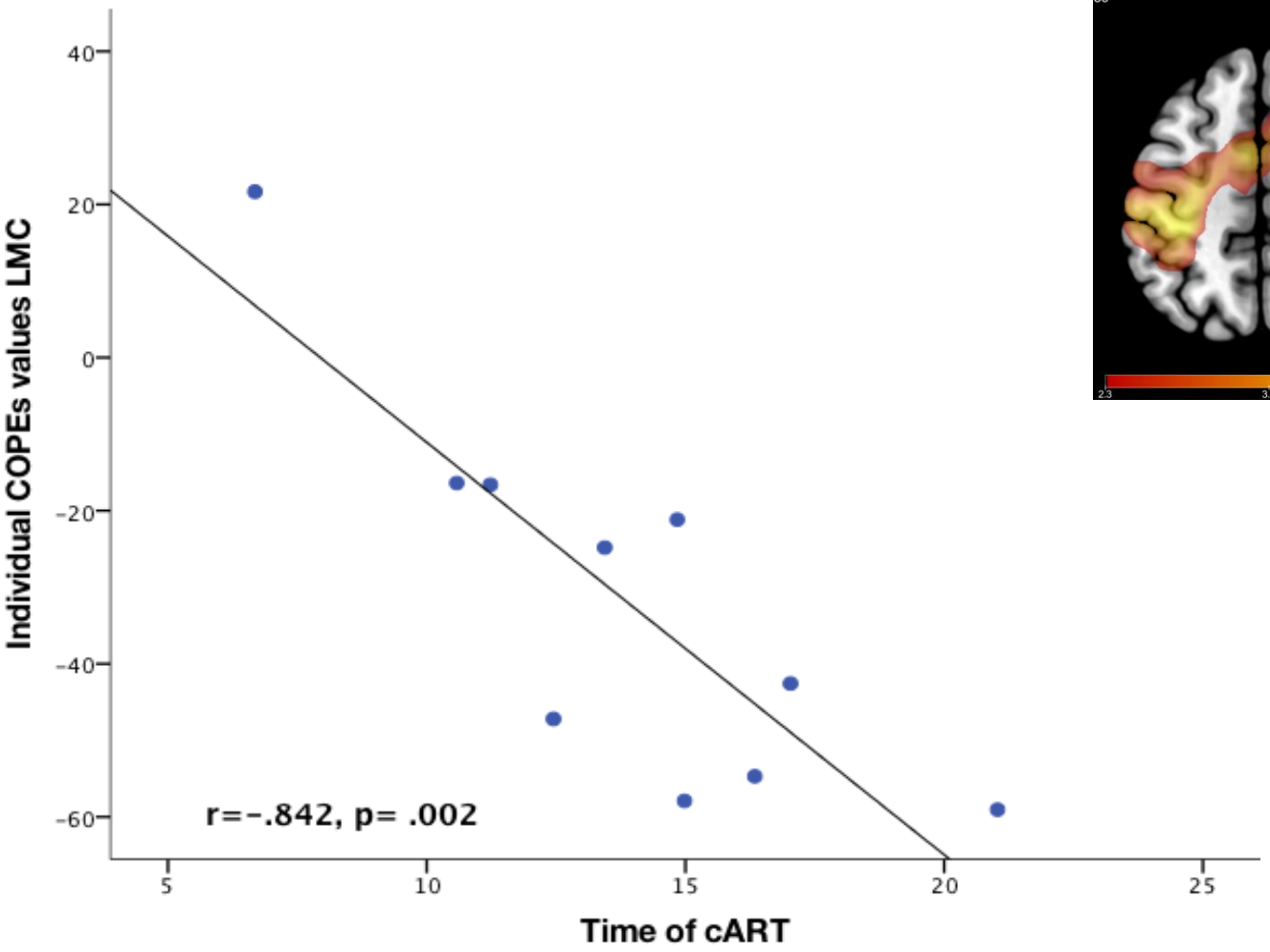
Patterns of brain activation (all participants) during letter retrieval (b, ‘words from letter vs word repetition’)



Left Inferior Frontal Gyrus (IFG; -50, 12, 30)

RESULTS

Individual brain activity and time of cART



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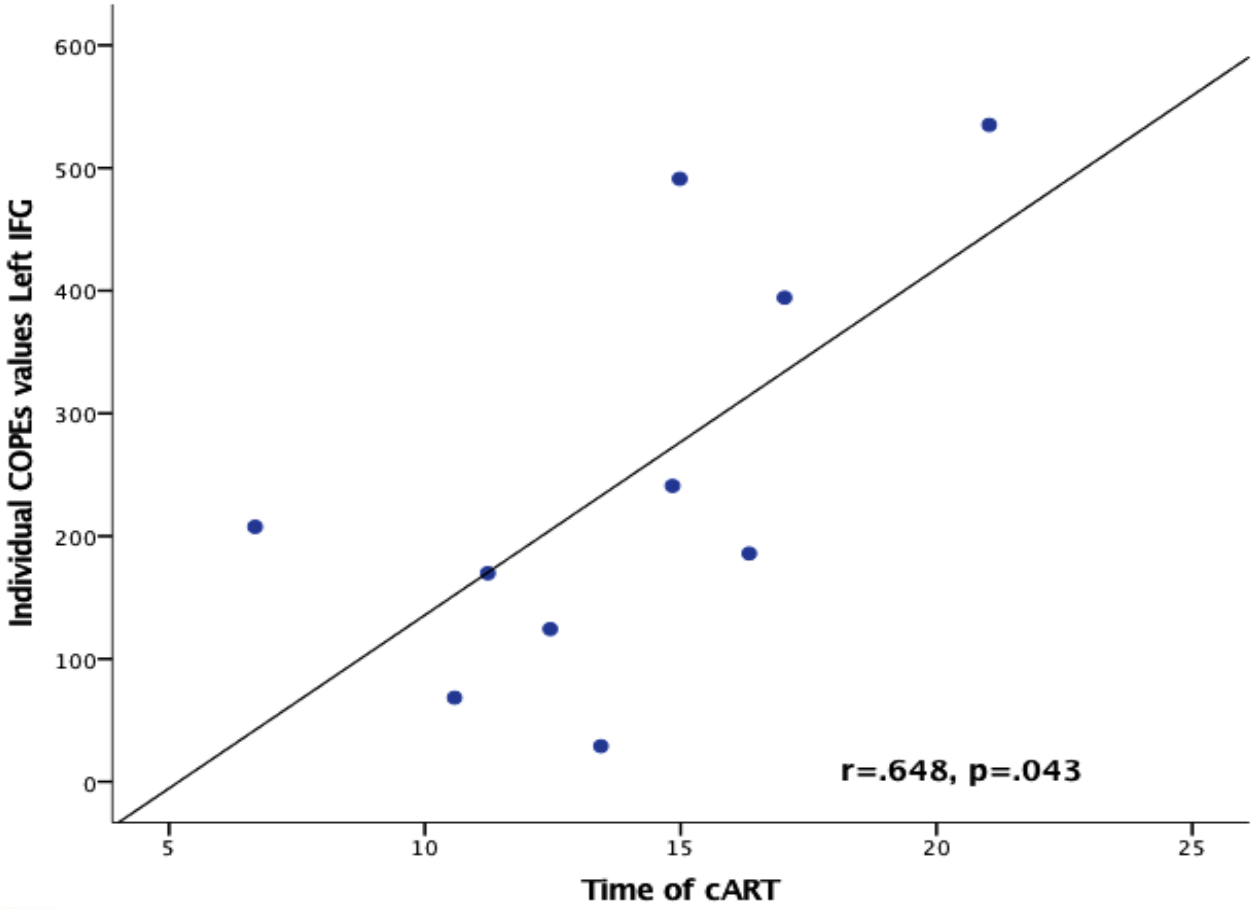

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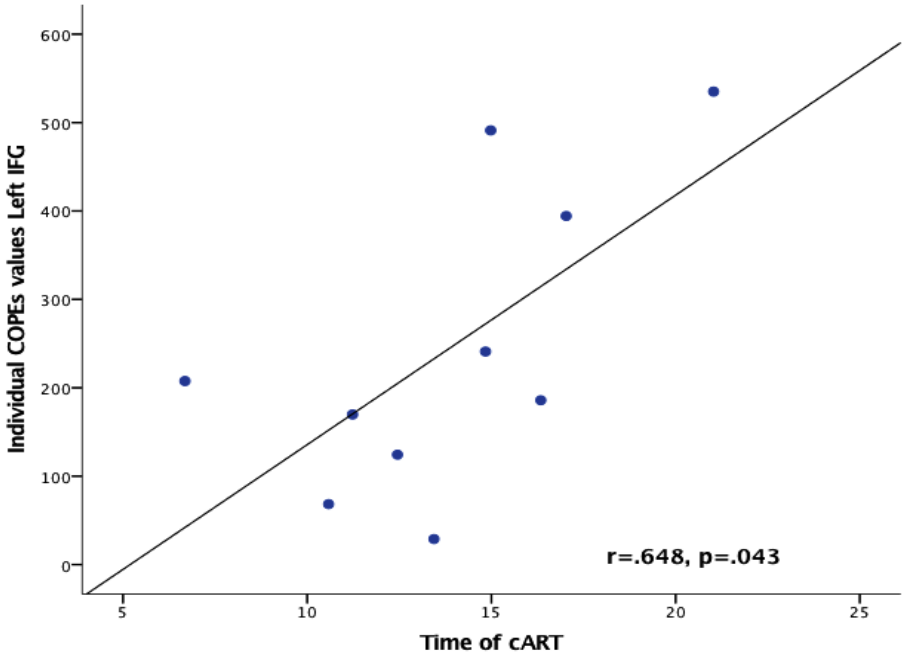

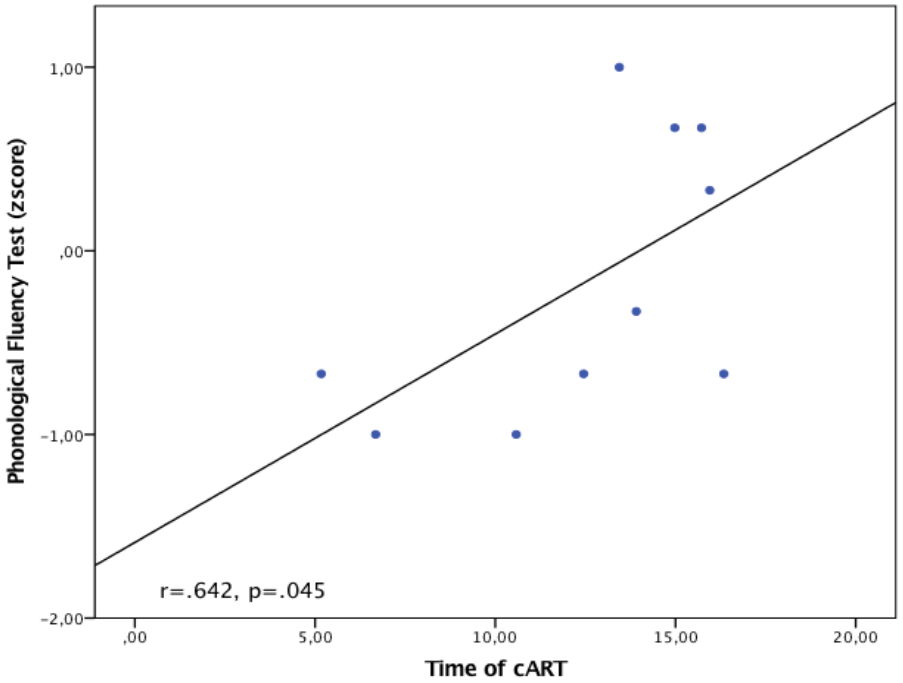

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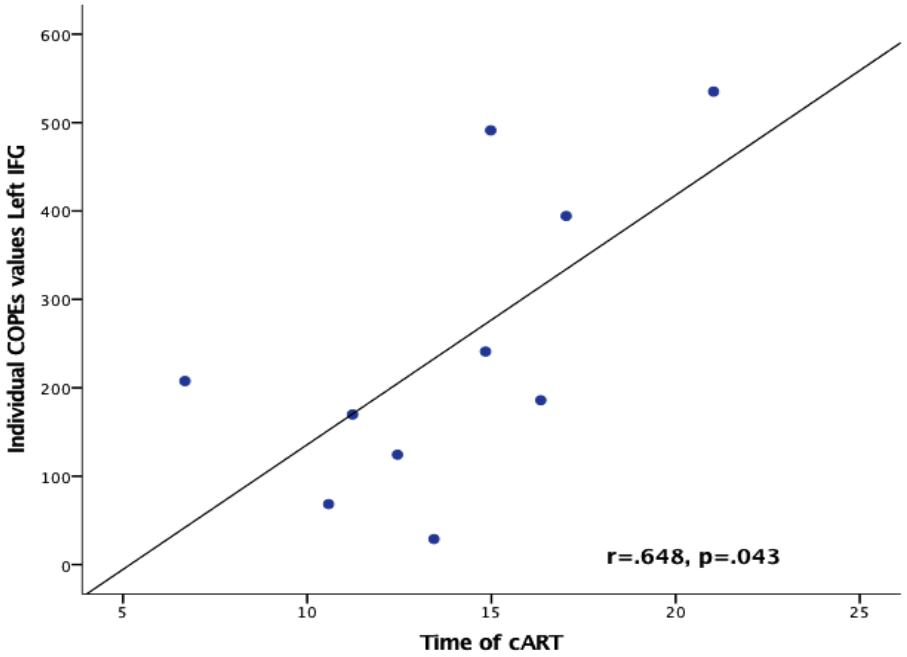

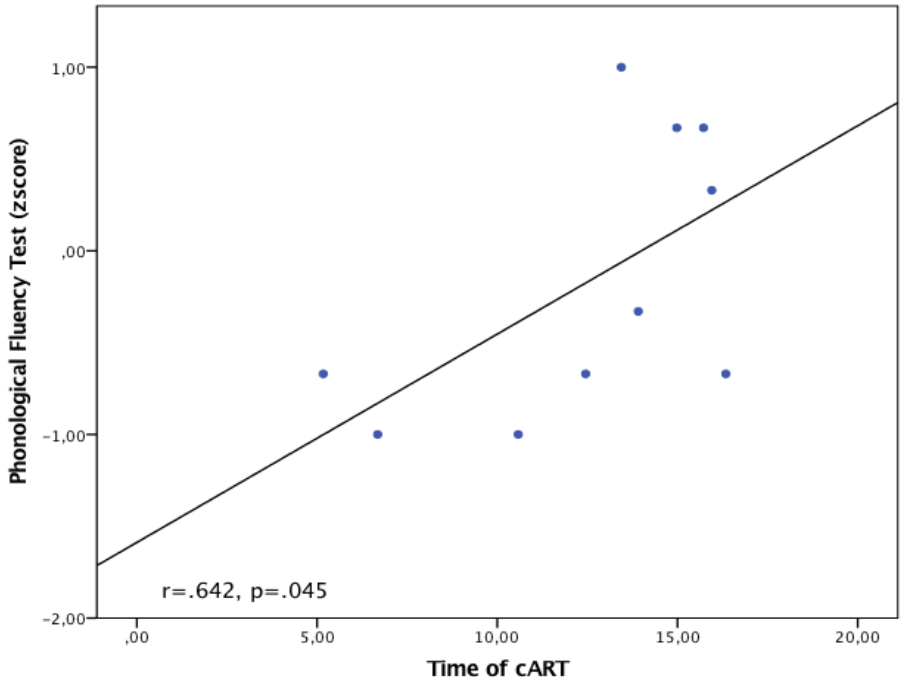

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- *Thames, A.D. & cols. (2016) "Increased subcortical neural activity among HIV+ individuals during a lexical retrieval task." Neurobiol Dis.; 92(Pt B): 175–182.

Basal ganglia (Thames et al., 2012).

CONCLUSIONS

- Our results showed that there were no significant differences between HIV + and HIV- groups neither on psychometric tests nor in fMRI activity for motor and verbal phonological fluency tasks.

- Brain activity in the left motor cortex and left IFG within the HIV patients group was related to time on cART.

¿Compensatory mechanisms?

- Possible use of fMRI as a potential biomarker, facilitating an earlier diagnosis of possible neural alterations in PHIV patients.

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