

Cognitive reserve: the leisure time concurs to the cognition performance and to the independence of early Huntington disease patients

S. Migliore^{1,2}, G. D'Aurizio³, S. Maffi^{1,2}, E. Scaricamazza^{1,2}, C. Ceccarelli², G. Ristori⁴, S. Romano⁴, A. Castaldo⁵,
M. Fichera⁵, G. Curcio³, F. Squitieri^{1,2}

¹ Huntington and Rare Diseases Unit, IRCCS Casa Sollievo della Sofferenza Hospital (Rome CSS-Mendel), San Giovanni Rotondo, Italy

² Italian League for Research on Huntington (LIRH) Foundation, Rome, Italy.

³ Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila, L'Aquila, Italy

⁴ Department of Neuroscience, Mental Health and Sensory Organs, S. Andrea Hospital, Sapienza University, Rome, Italy.

⁵ Department of Medical Genetics and Neurogenetics, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy.

Background: According to the Cognitive Reserve (CR) hypothesis, neuropsychological expression of brain disease is attenuated among people with higher education or active lifestyle.

Aim: The current research examines CR in patients with early Huntington Disease (HD) and aims to investigate whether the lifetime intellectual enrichment may influence cognition and independence overtime.

Methods: We enrolled 75 early manifest patients (Stage 1 and 2 of the disease according to the Total Functional Capacity – TFC) (46M/29F; age: $47,2 \pm 12,5$ y; education: 11 ± 4.43 y, CAG repeat: $43,7 \pm 2,3$) in three different ENROLL-HD sites (LIRH Foundation-Rome, IRCCS Istituto Neurologico Carlo Besta-Milan, S. Andrea Hospital -Rome). CR was assessed by the Cognitive Reserve Index questionnaire (CRIq), a 20-item international validated tool assessing CR acquired in three different areas during person's lifetime: education (CRIq_Edu), working activities (CRIq_WA) and leisure time activities (CRIq_LA). All patients were assessed, moreover, by the UHDRS (Unified Huntington's Disease Rating Scale) which includes motor, cognitive and functional domains, at baseline (t0) and at 1-year (t1) and 2-years (t2) follow-up.

Results: A correlational analysis showed a significant association between CRIq_LA decrease and: 1) the longitudinal functional impairment (i.e. the difference between the TFC score at t2 and t0 or Δ TFC) ($p < 0,05$); 2) the multidimensional progression of HD measured by the composite UHDRS (cUHDS, $p < 0,01$) (Figure 1). CRIq_LA decrease was significantly associated with the cognitive impairment increase ($p < 0,05$) at all timepoints (Figure 2). Moreover, patients with impaired CRI_LA index showed a more pronounced multidimensional and functional progression (respectively cUHDS, $p = 0,001$ - and Δ TFC, $p = 0,01$, see Figure 3) associate with poorer cognitive performance respect at normal CRI_LA index group (see Table 1).

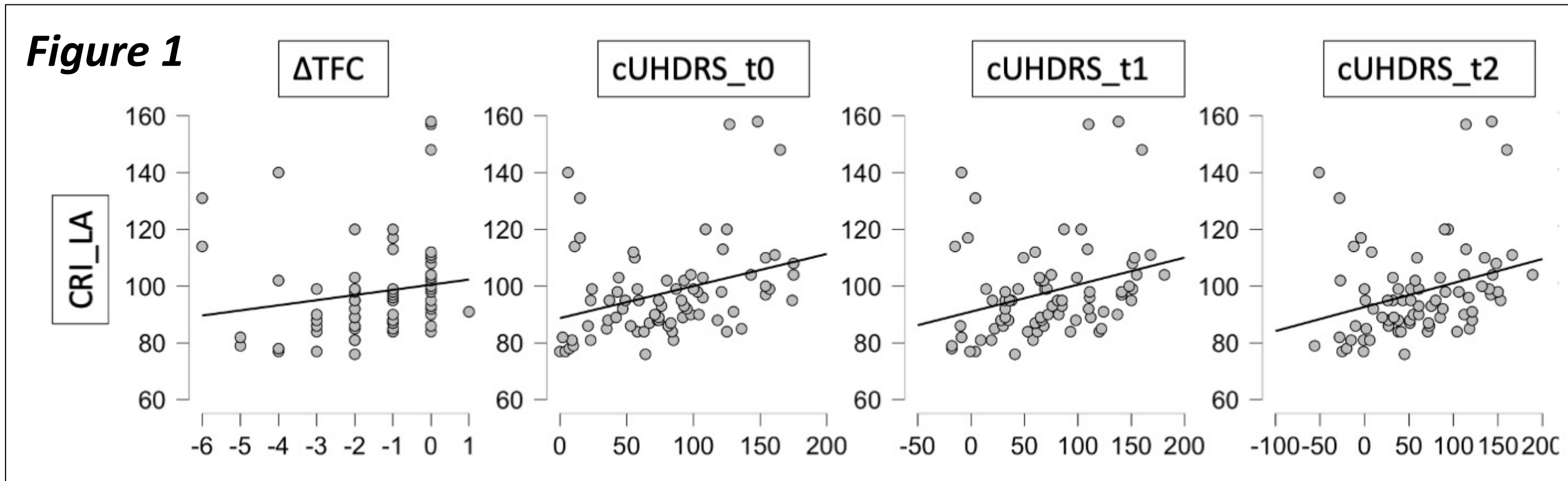
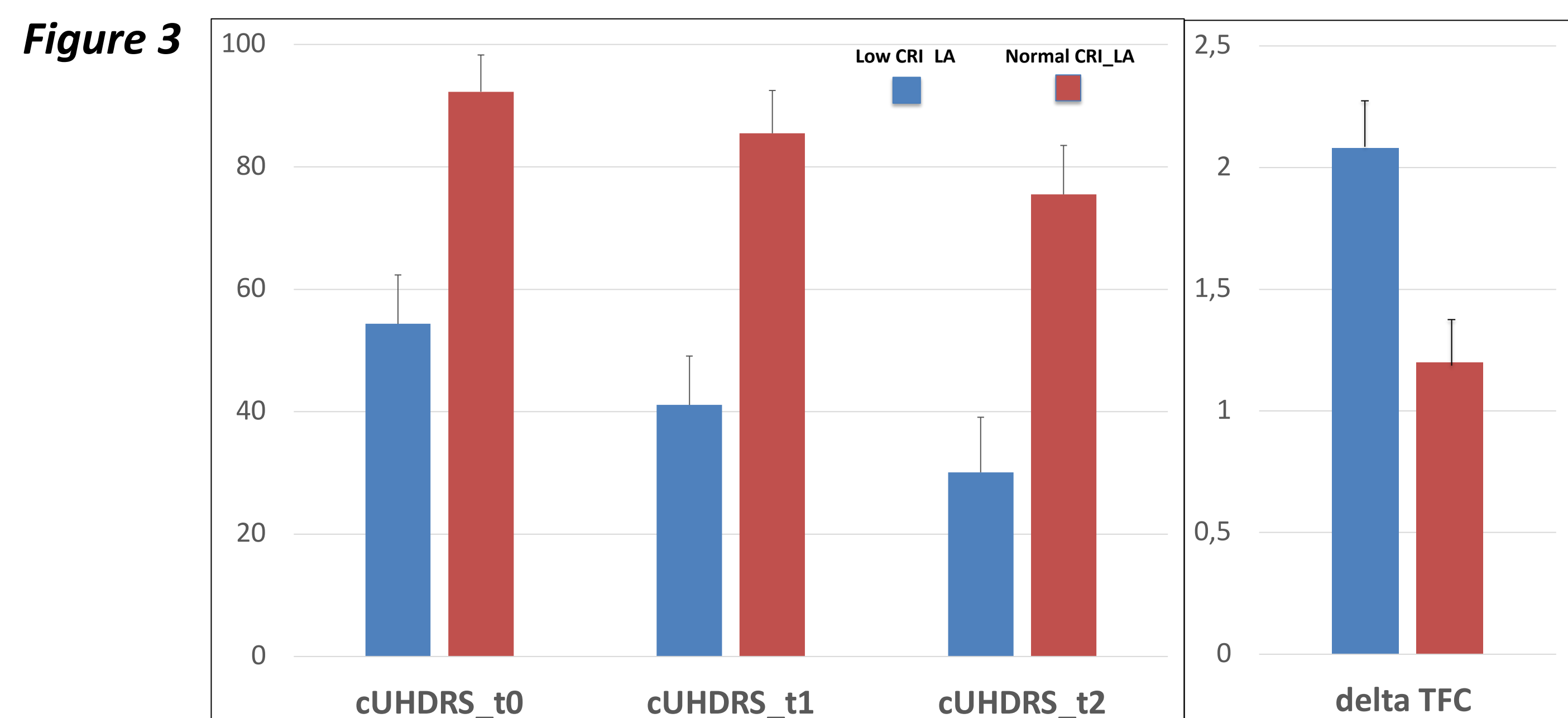
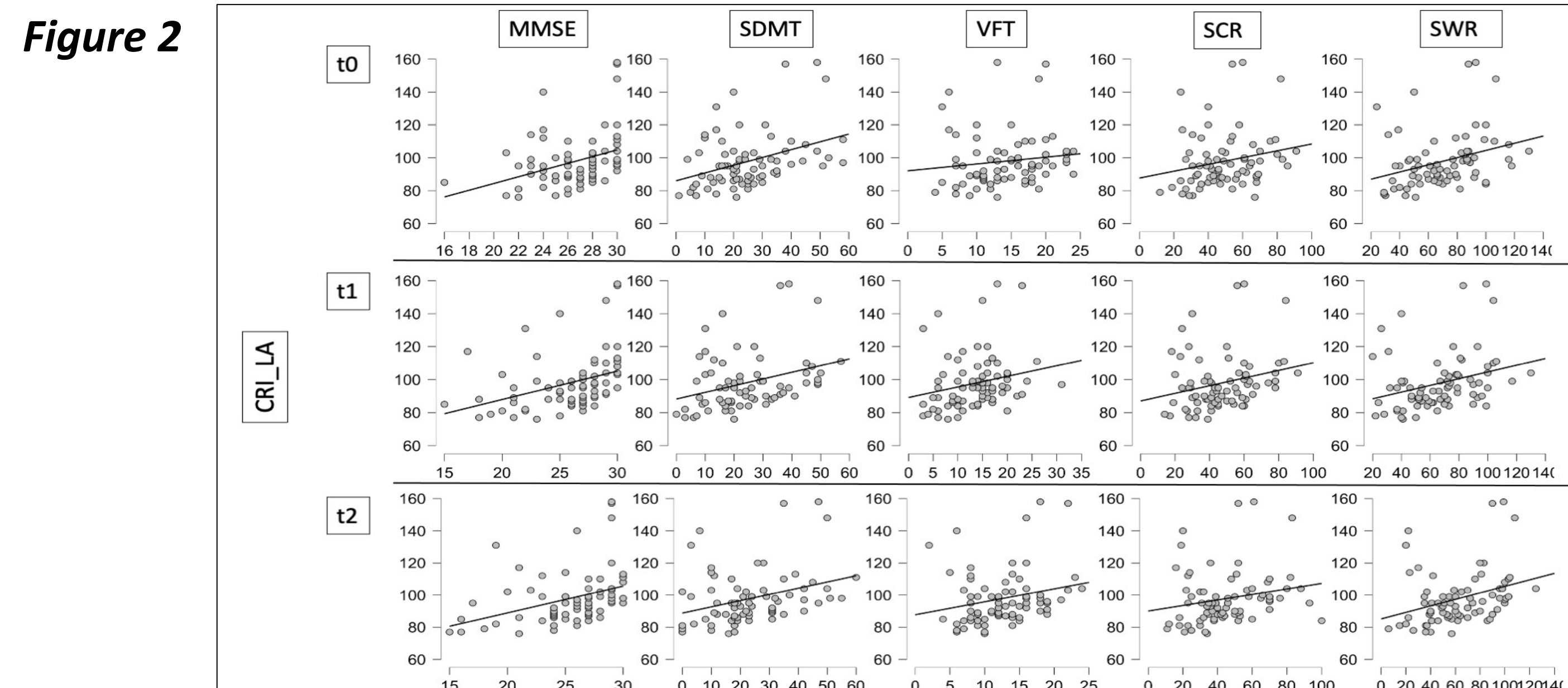


Table 1		CRI_LA impaired Group (n=24) Mean ± SE	CRI_LA normal Group (n=51) Mean ± SE	p
Cognitive variables - Baseline	MMSE	25.34 ± 0.60	26.98 ± 0.37	0.019
	SDMT	17.54 ± 1.70	28.58 ± 1.92	0.001
	VFT	11.87 ± 0.84	14.94 ± 0.75	0.016
	SCR	41.41 ± 3.19	52.88 ± 2.42	0.007
	SWR	58.75 ± 4.39	75.02 ± 3.35	0.006
Cognitive variables - 1 year follow-up	MMSE	23.62 ± 0.74	26.78 ± 0.41	0.0001
	SDMT	16.04 ± 1.84	28.06 ± 1.91	0.0001
	VFT	10.7 ± 1	14.94 ± 0.8	0.003
	SCR	39.25 ± 2.71	50.17 ± 2.63	0.013
	SWR	54.16 ± 3.92	72.6 ± 3.49	0.002
Cognitive variables - 2 years follow-up	MMSE	23.08 ± 0.8	26.56 ± 0.41	0.0001
	SDMT	15.5 ± 1.81	27.12 ± 2.02	0.001
	VFT	10.29 ± 0.74	13.58 ± 0.69	0.005
	SCR	36.75 ± 3.81	49.17 ± 2.78	0.012
	SWR	48.42 ± 4.58	69.16 ± 3.73	0.002



Conclusion: We believe that the CR deserves to be deeply explored in HD. Our findings suggest that higher is the CRI Leisure time, lower is the progression of HD with a more preserved independence and cognitive status overtime.