Neurological Soft signs in HIV associated neurocognitive disorder (HAND):
an easy clinical examination for screening and early recognition

Johannes Schröder, Christina Herold and Pablo Toro
Section for Geriatric Psychiatry, Rupprecht- Karls Universität Heidelberg
Dept. of Psychiatry, Pontificia Universidad Católica de Chile

Conflicts of interest

last 5 years

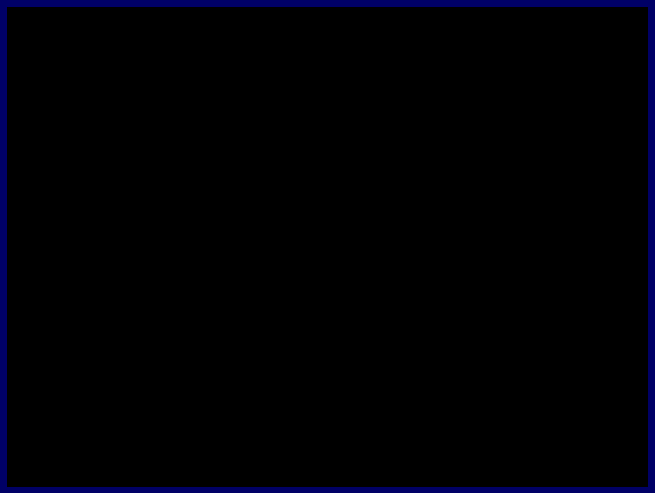
- Nothing to declare

Neurological soft signs

- comprise both, minor motor and sensory abnormalities
- are frequently found in major psychiatric disorders
- vary in the clinical course
- can be reliable assessed by using rating scales, such as the Heidelberg scale as part of the routine work up

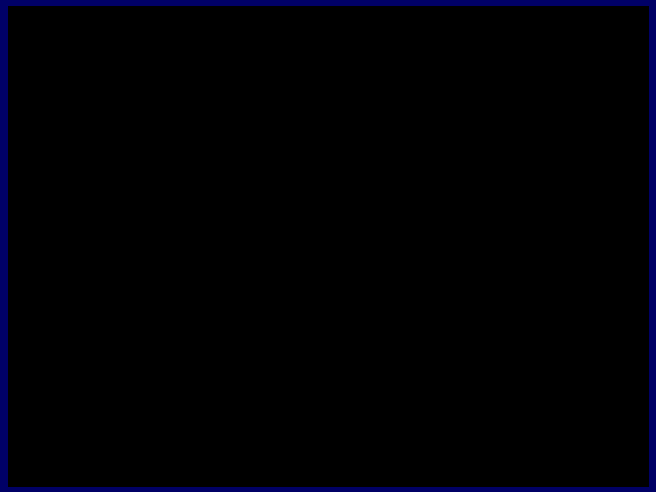
Schröder et al., 1992

typical motor NSS in patients with schizophrenia vs. controls

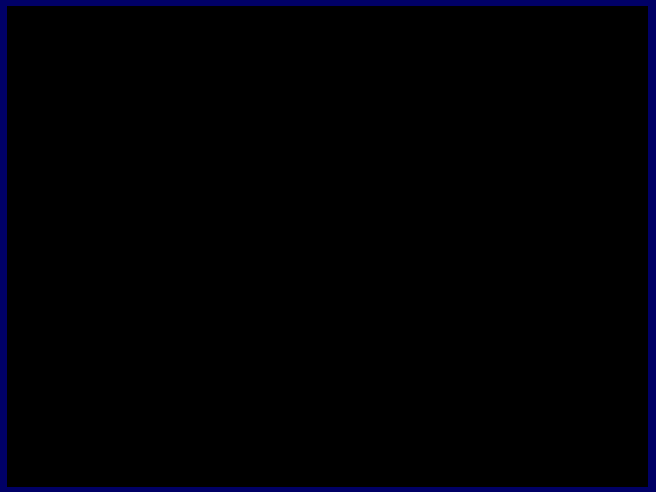


Fist- edge palm, control

Fist- edge palm, schizophrenia



Finger- to- thumb, control



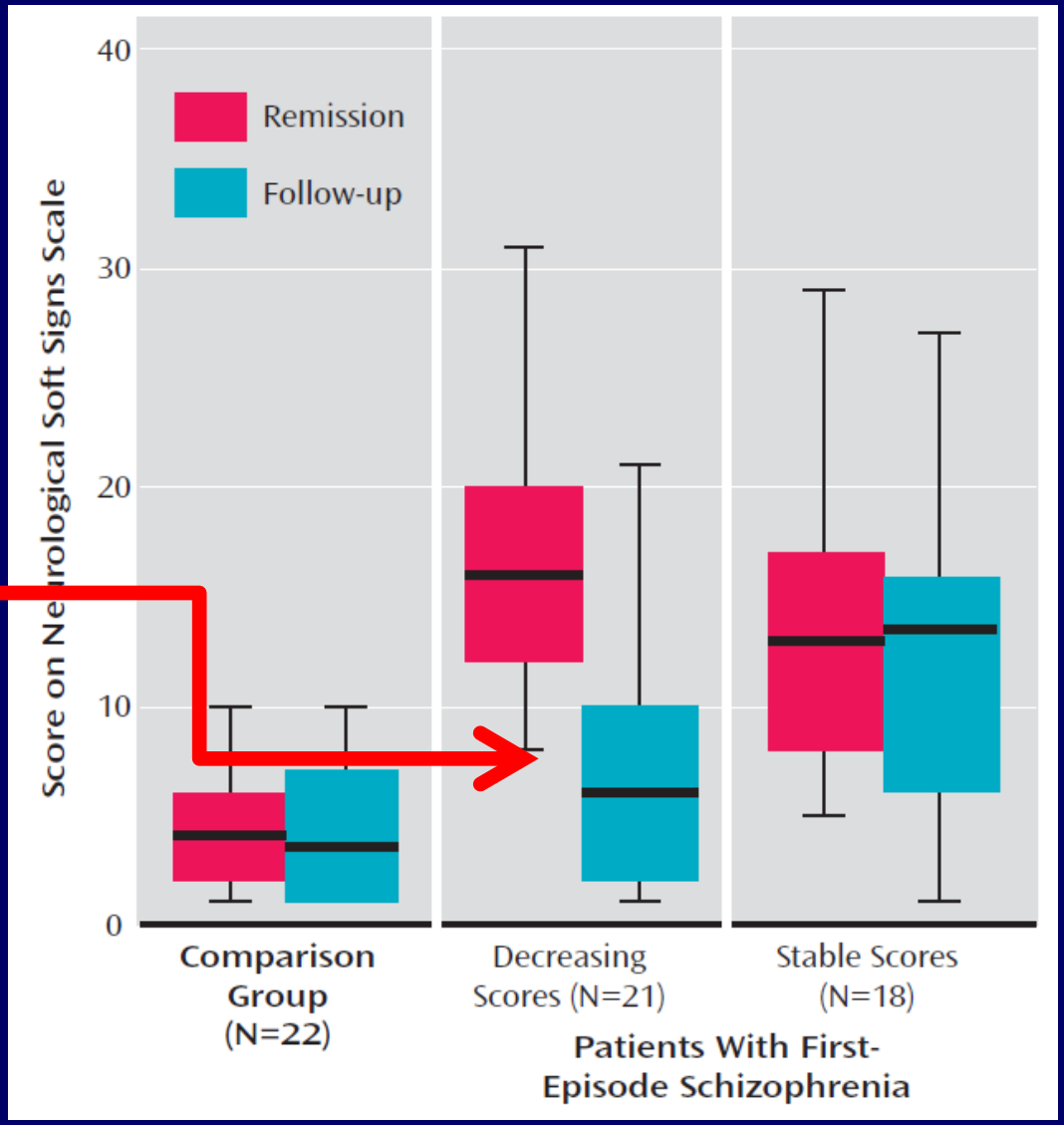
Finger- to- thumb, schizophrenia

NSS in first episode schizophrenia & controls

*results of a **longitudinal study** over 14 months*

Genetic loading ?

Niethammer, 2000



Bachmann et al., 2005; see Prikyl et al., 2012 for similar results

Cognitiv correlates of NSS chronic schizophrenia vs. healthy controls

NSS / neuropsychology	NSS total Score	motor coordination	sensory integration	complex motor tasks	right/left and spatial orientation	hard signs
Logical memory I	-0.40***/-0.32*	-0.38***/-0.2[illegible]	-0.20/-0.27*	-0.45***/-0.15	-0.35**/-0.14	-0.12/-0.12
Logical memory II	-0.36***/-0.28*	-0.35**/-0.20	-0.15/-0.26*	-0.46***/-0.22	-0.29*/-0.07	-0.09/0.03
Digit span forward	-0.19/-0.[illegible]	-0.09/-0.16	-0.05/0.05	-0.30**/0.27*	-0.32*/0.14	0.04/0.02
Digit span backward	-0.33**/-0.26*	-0.36**/-0.35**	-0.13/-0.08	-0.38***/-0.21	-0.30**/-0.02	-0.06/0.12
Trail making test A	0.57***/0.41***	0.45***/0.20	0.18/0.17	0.57***/0.29*	0.60***/0.54***	0.42***/-0.02
Trail making test B	0.40***/0.52***	0.37***/0.25	0.16/0.29*	0.41***/0.42***	0.44***/0.32*	0.11/0.19
Autobiographic memory - semantic	-0.07/-0.09	-0.04/0.10	0.05/-0.25	-0.06/-0.07	-0.04/-0.12	-0.16/-0.00
Autobiographic memory - episodic	-0.36**/0.02	-0.33**/0.00	-0.13/-0.04	-0.38***/0.04	-0.37***/-0.06	-0.05/0.13
Autobiographic memory - episodic details	-0.28*/0.04	-0.27*/-0.02	-0.10/-0.00	-0.27*/0.17	-0.35**/-0.05	-0.04/0.04
Theory of Mind - total	-0.54***/-0.45***	-0.50***/-0.15	-0.36**/-0.14	-0.49***/-0.28*	-0.44***/-0.62***	-0.16/-0.23
Theory of Mind - questions	-0.59***/-0.48***	-0.56***/-0.25	-0.40**/-0.17	-0.46***/-0.27*	-0.46***/-0.47***	-0.24/-0.31*
Theory of Mind - order	-0.42***/-0.26	-0.40**/-0.06	-0.29*/-0.12	-0.43***/-0.18	-0.39**/-0.44***	0.03/0.02
Reading Mind in the Eyes Test	-0.40***/-0.08	-0.35**/-0.07	-0.09/-0.02	-0.45***/-0.08	-0.43***/-0.09	-0.21/0.06

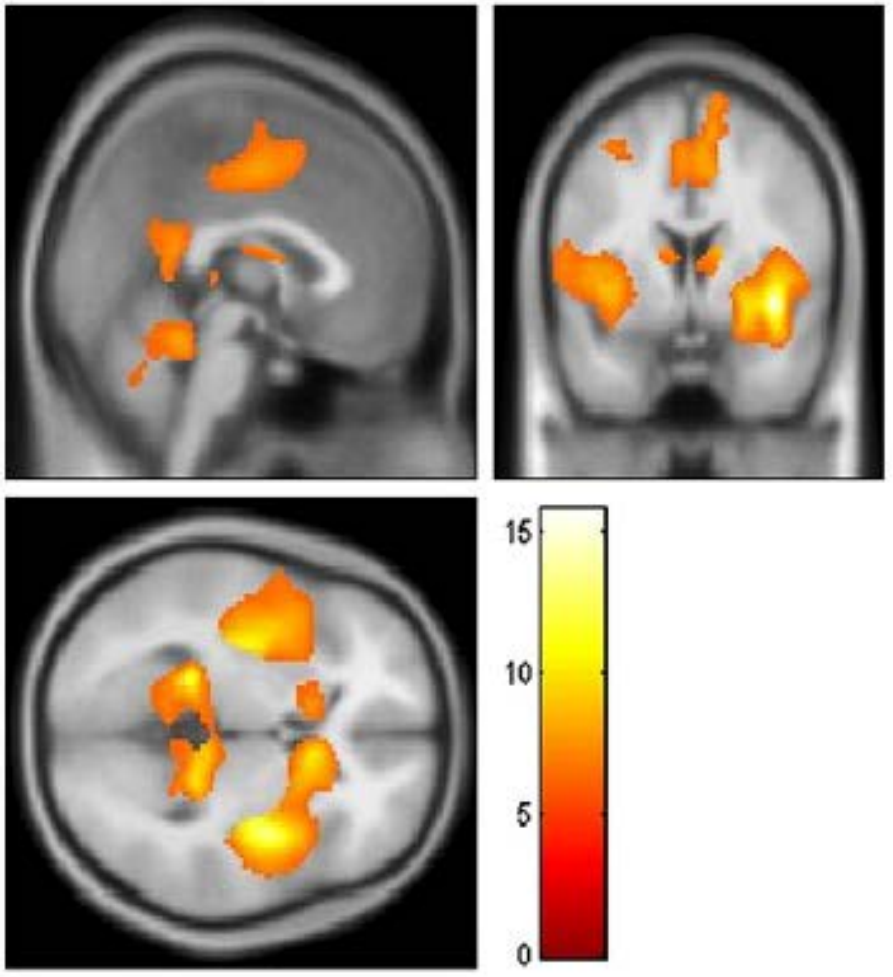
*p≤0.05, **p≤0.01, ***p≤0.001

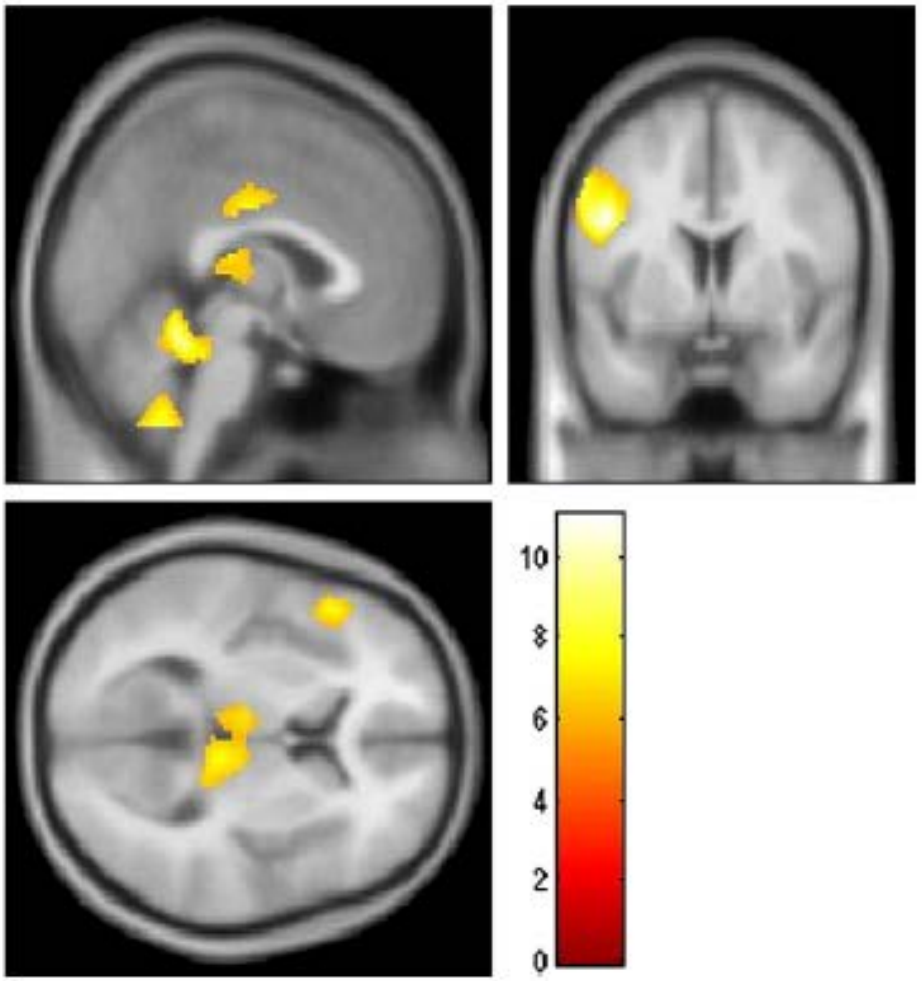
Herold et al., 2017

Neurological soft signs and gray matter changes: A longitudinal analysis in first-episode schizophrenia

Li Kong [a,1], Silke Bachmann [b,*,1], Philipp A. Thomann [a], Marco Essig [c], Johannes Schröder [a]

Schizophrenia Research 134 (2012) 27–32

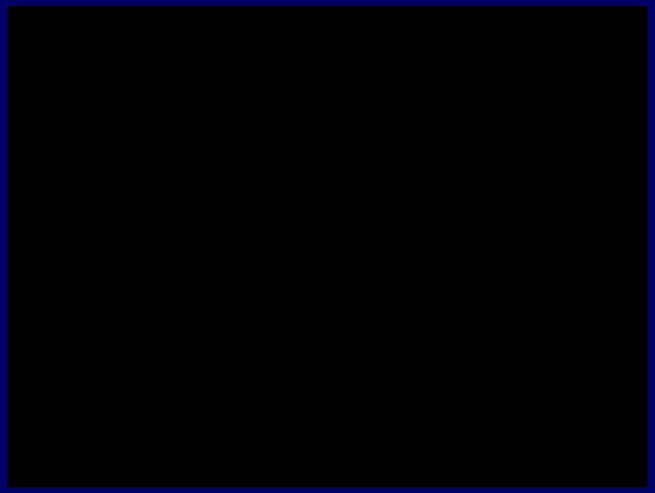




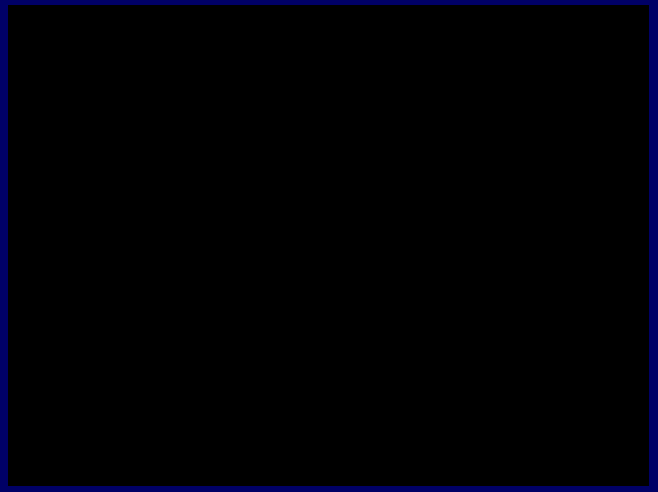
PANSS	51.2	44.2	50.1	52.8
	9.8	9.9	13.6	22.8

[a] Repeated measures analysis of variance (df = 1.18).

NSS in patients with Alzheimer´s disease

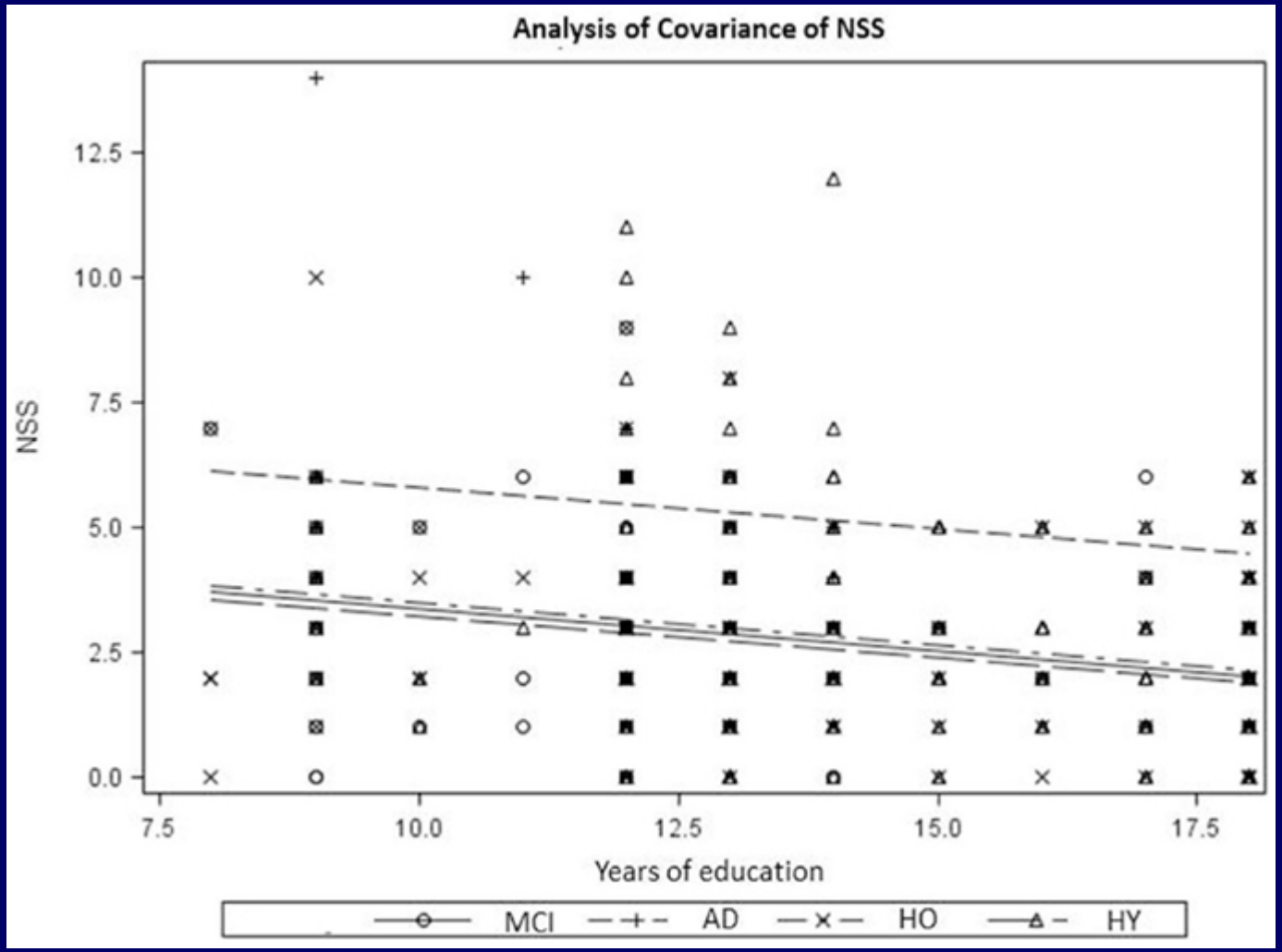


Fist- edge palm; AD



Finger-to-thumb + mirror movements; AD

NSS and cognitive reserve



Urbanowitsch et al., 2015

NSS as clinical markers of CNS involvement in HIV infection

- may facilitate the differential diagnosis of HAND
- 2 motor signs (fingertapping, fist-edge-palm test) are incorporated as motor speed + psychomotor speed in the HIV dementia scale
- may contribute to the development of more specific preventive and treatment strategies

NSS are clinical markers of neuropsychological deficits & CNS involvement in HIV.....

..... and may therefore facilitate the differential diagnosis of HAND

Heidelberg Scale Subscale and Test
1. Motor coordination
Ozeretzki's test
Diadochokinesis
Pronation/supination
Finger/thumb opposition
Articulation
2. Sensory integration
Gait
Tandem gait
2-point discrimination
3. Complex motor tasks
Finger-to-nose test
Fist-edge-palm test
4. Right/left and spatial orientation
Right/left orientation
Graphesthesia
Face/hand sensory test
Stereognosis
5. Hard signs
Arm-holding test
Mirror movements

Heidelberg NSS-Scale

- **Three point rating scale**
  (max. 81 points)
- **High internal consistency**
  Cronbach's α: 0.85/0.89
  - **test-retest reliability**
    rtt=0.80, p<0.001
  - **interrater reliability**
    r=0.88, p<0.005

Schröder et al., 1992
Bachmann et al., 2005
Valenzuela et al., 2014

Neurological soft signs in HIV associated neurocognitive disorder

- 87 HIV infected patients from Santiago de Chile
  - no history of head injury trauma or opportunistic infections of the CNS
  - no acute psychiatric diseases and no history of substance abuse
  - Structural MRI to exclude secondary brain changes
- 39 healthy controls were recruited from the community
- Cantab: attention and psychomotor speed, episodic + working memory, executive function, visuoperception.
- “paper pencil”: verbal fluency

Toro et al., submitted

Methods: Psychiatric clinical evaluation

- Semistructured psychiatric Interview SCID I, for DSM IV-TR (First MB et al. 2002)
  - Hamilton depression scale (Hamilton M. 1967)
  - Hamilton anxiety scale (Hamilton M. 1959)
  - Philadelphia Geriatric Center – Instrumental Activities of Daily Living (PGC – IADL) (Lawton MP et al. 1969)
- HAND was diagnosed using NIMH and NINDS criteria

Methods: Neuropsychological testing

- Cambridge Neuropsychological Test Automated Battery (CANTAB)

  - attention and psychomotor speed (RTI, MOT)
  - episodic memory (PAL),
  - working memory (SWM)
  - executive Function (SOC, IED)
  - visuoperception (MOT).
- “paper pencil”: phonological and semantic verbal fluency

HIV-Associated Neurocognitive disorders

HAND

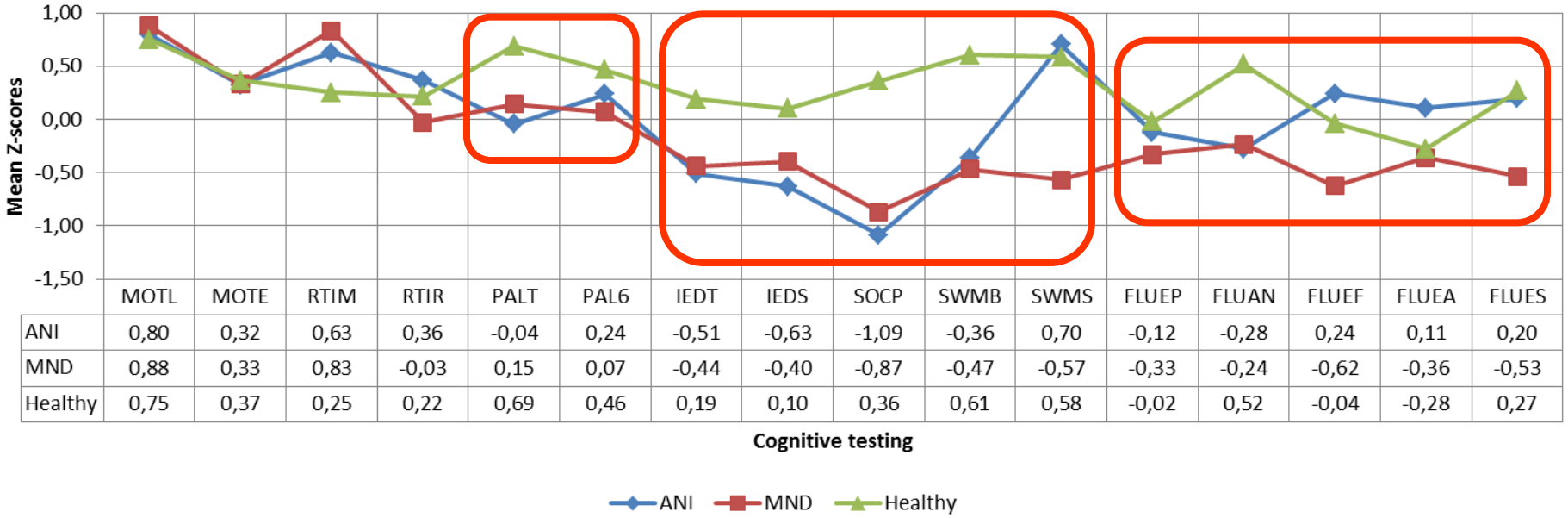
	No preexisting Cause	Delirium is absent	Acquired Impairment in ≥2 Cognitive Abilities	Interferes with Daily Funtioning
Asymptomatic Neurocognitive Impairment (ANI)	✓	✓	✓	NO
Mild Neurocognitive Disorder (MND)	✓	✓	✓	Mild
HIV-Associated Dementia (HAD)	✓	✓	Marked	Marked

Antinori et al., 2007

clinical group characteristics

Variable	Control	HIV - healthy	HIV - ANI	HIV – MND	ANOVA or X^2
n	39	28	18	21	
Age	42.7 ± 11.8	37.5 ± 8.9	45.0 ± 13.4	39.4 ± 8.5	n.s.
gender (%males)	100%	100%	100%	100%	
educational level	14.8 ± 3.8	16.0 ± 2.7	15.1 ± 2.0	15.3 ± 3.0	n.s.
lifetime depression n (%)	0	17 (60.7)	10 (55.6)	14 (66.7)	n.s.
lifetime substance abuse n (%)	0	3 (10.7)	1 (5.6)	3 (14.2)	n.s.

Neuropsychological profiles



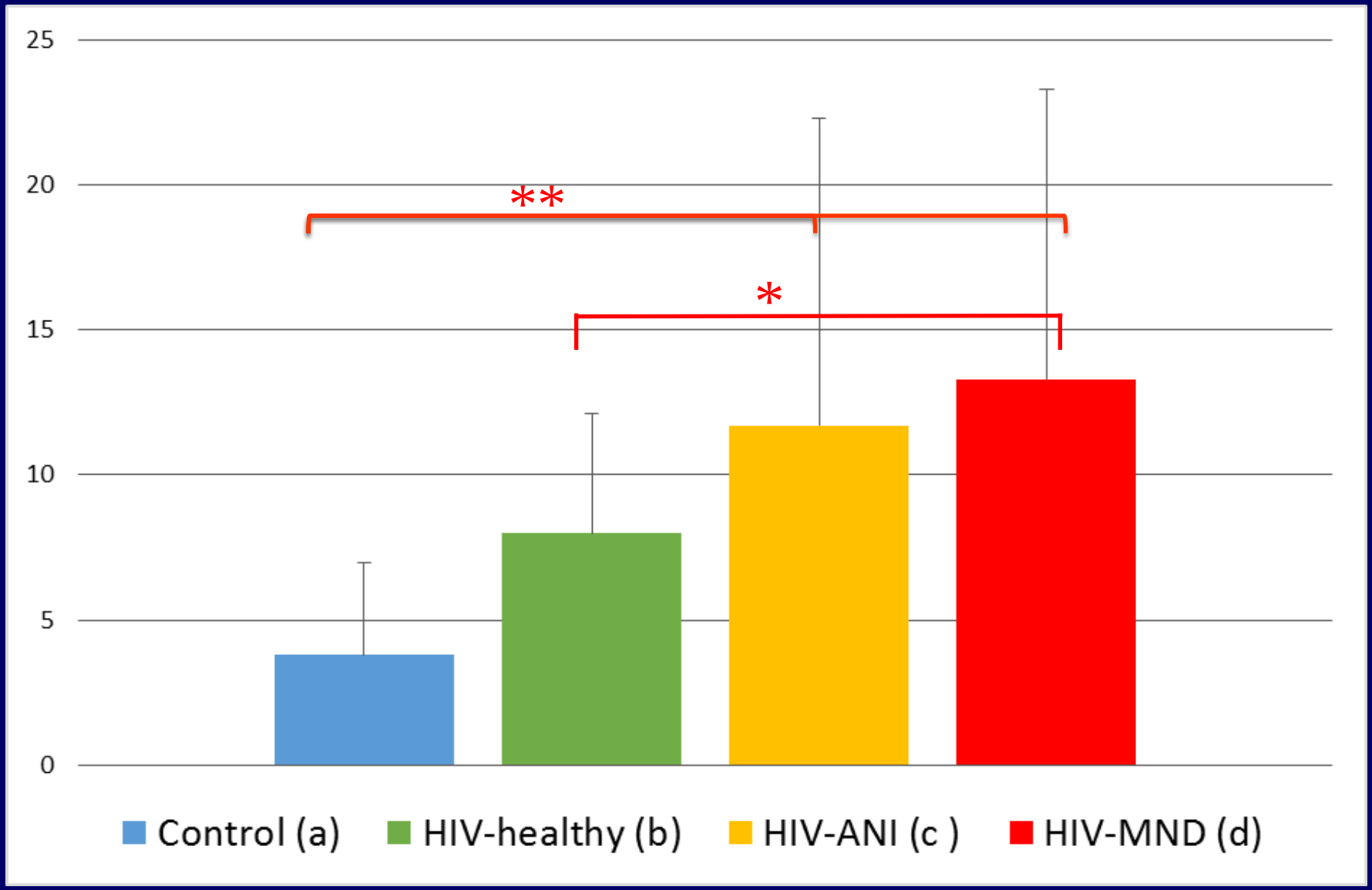
	MOTL	MOTE	RTIM	RTIR	PALT	PAL6	IEDT	IEDS	SOCP	SWMB	SWMS	FLUEP	FLUAN	FLUEF	FLUEA	FLUES
ANI	0,80	0,32	0,63	0,36	-0,04	0,24	-0,51	-0,63	-1,09	-0,36	0,70	-0,12	-0,28	0,24	0,11	0,20
MND	0,88	0,33	0,83	-0,03	0,15	0,07	-0,44	-0,40	-0,87	-0,47	-0,57	-0,33	-0,24	-0,62	-0,36	-0,53
Healthy	0,75	0,37	0,25	0,22	0,69	0,46	0,19	0,10	0,36	0,61	0,58	-0,02	0,52	-0,04	-0,28	0,27

declarative memory

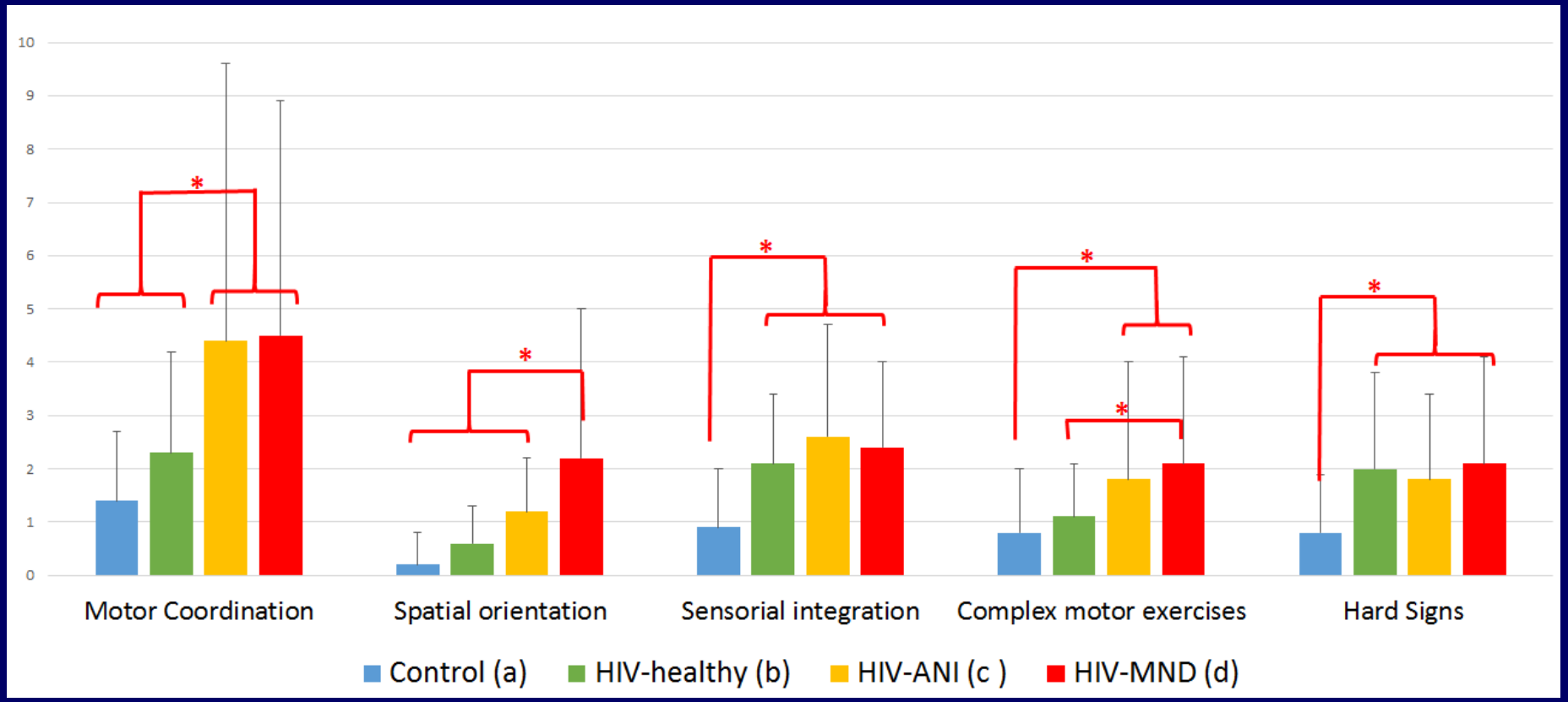
executive functions

verbal fluency

Total NSS score by cognition



NSS subscales



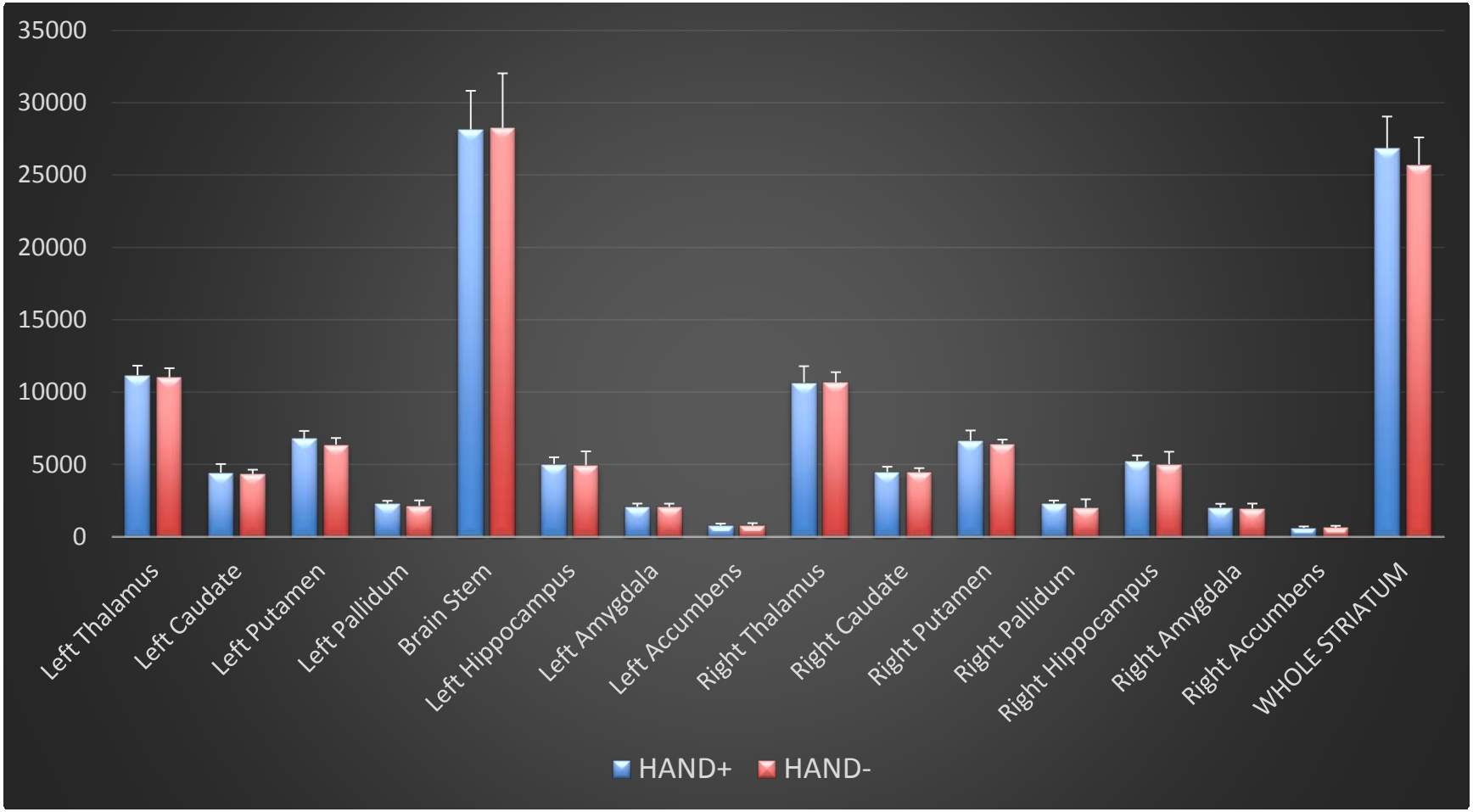
* $p < 0.05$

Cognitiv correlates of NSS: patients with HIV

	NSS total	Motor Co-ordination	ri/le & spatial orientation	Integrative functions	Complex motor tasks	Hard signs
pair ass. Learning	**.58****	**.59****	**.58****	**.32***	**.36****	.16
Reasoning (IEDT)	.20	.13	.16	.11	.15	.21
Stocking of Cambridge	-.15	**-.28***	-.14	-.05	-.12	**-.25***
Spatial working memory	**.37****	**.38****	**.34****	**.24****	**.25****	.08
Fluency: animals	**-.35****	**-.32****	**-.48****	-.23	**-.25***	.01
Fluency: letters	**-.37****	**-.28***	**-.37****	**-.30***	**-.35****	-.13

Brain changes in HAND+ v/s HAND-

Mean volumes (mm^3) for brain structures by cognitive status



Toro et al 2015

Conclusions/ Discussion

1. Neurological soft signs discriminate HAND- from HAND+ patients
   - Total NSS Score
   - Motor coordination
   - Spatial orientation

2. Neurological soft signs facilitate early recognition of HAND

COLABORADORES:

Depto de enfermedades infecciosas UC

Dra. María Elena Ceballos

Lab. Neurociencias cognitivas

Dr. Nicolás Crossley, Dr. Tomás Ossandon, Dr. Francisco Aboitiz

Neuropsicología

Ps. Gonzalo Forno, Ps. Fernando Henríquez

Radiología UC

TM Patricio Díaz, TM José M. Allende

Universities of Heidelberg & Leipzig

Dr. C. Herold, Prof. Dr. Johannes Schröder, Prof. Dr. Peter Schönknecht

ESCUELA MEDICINA UC

Dr. Juan Ignacio Reculé, Prof. Dr. Pablo Toro

José Pesenti, Daniela Valenzuela, José Ignacio Otayza, Luis Cofré, Francisca Inostroza