

Cognitive differential diagnosis of hepatic encephalopathy in a cohort of outpatients with chronic liver disease

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Background

Covert hepatic encephalopathy (CHE) is a complex and multifactorial complication of chronic liver diseases (CLD). Other etiologies may cause neurocognitive impairment (NI) independently from the liver condition, making the differential diagnosis difficult using cognitive tests.

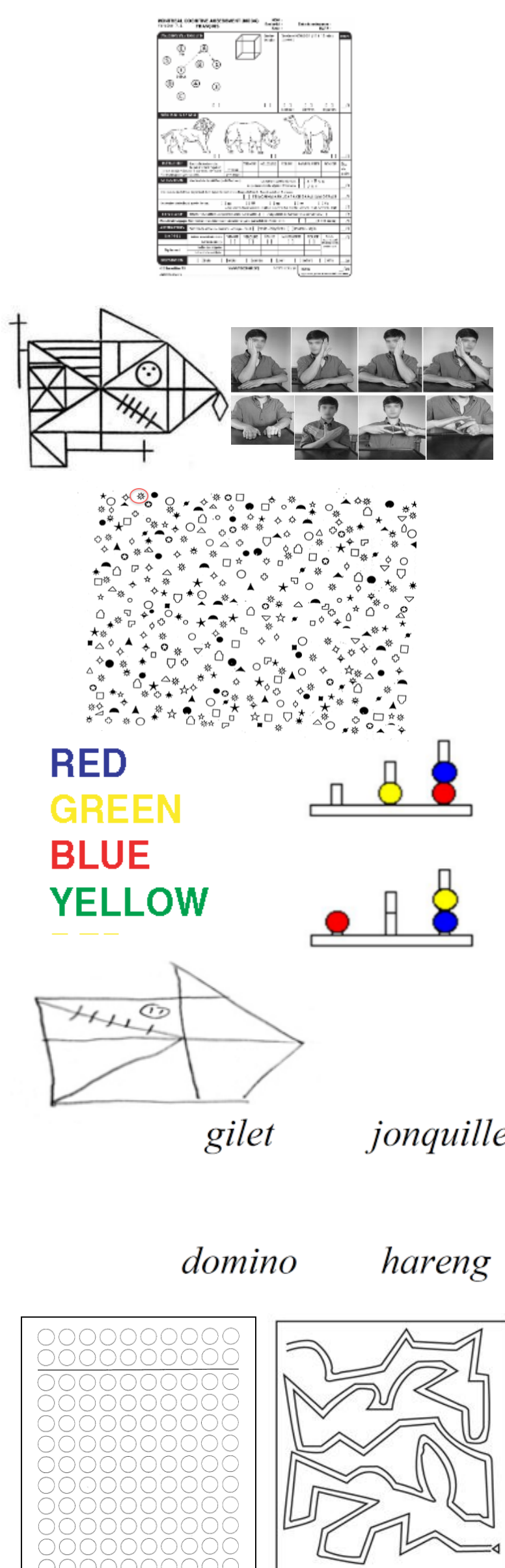
Methods

- ✓ a retrospective study of prospective cohort of patients with CLD with suspicion of CHE (Cognitive complaint or impairment) referred to our outpatient's clinics
- ✓ Multimodal work-up : hepatological and neurological examination, biomarker evaluation, Electroencephalogram, Brain MRI with spectroscopy, neuropsychological examination
- ✓ Adjudication committee involving hepatologists, neurologist and neuropsychologist for the differential diagnosis of CHE and other neurological factors (NF)

Neuropsychological evaluation

- ✓ Performed by a senior neuropsychologist in standardized conditions (several hours)
- ✓ Cognitive evaluation including validated tests :

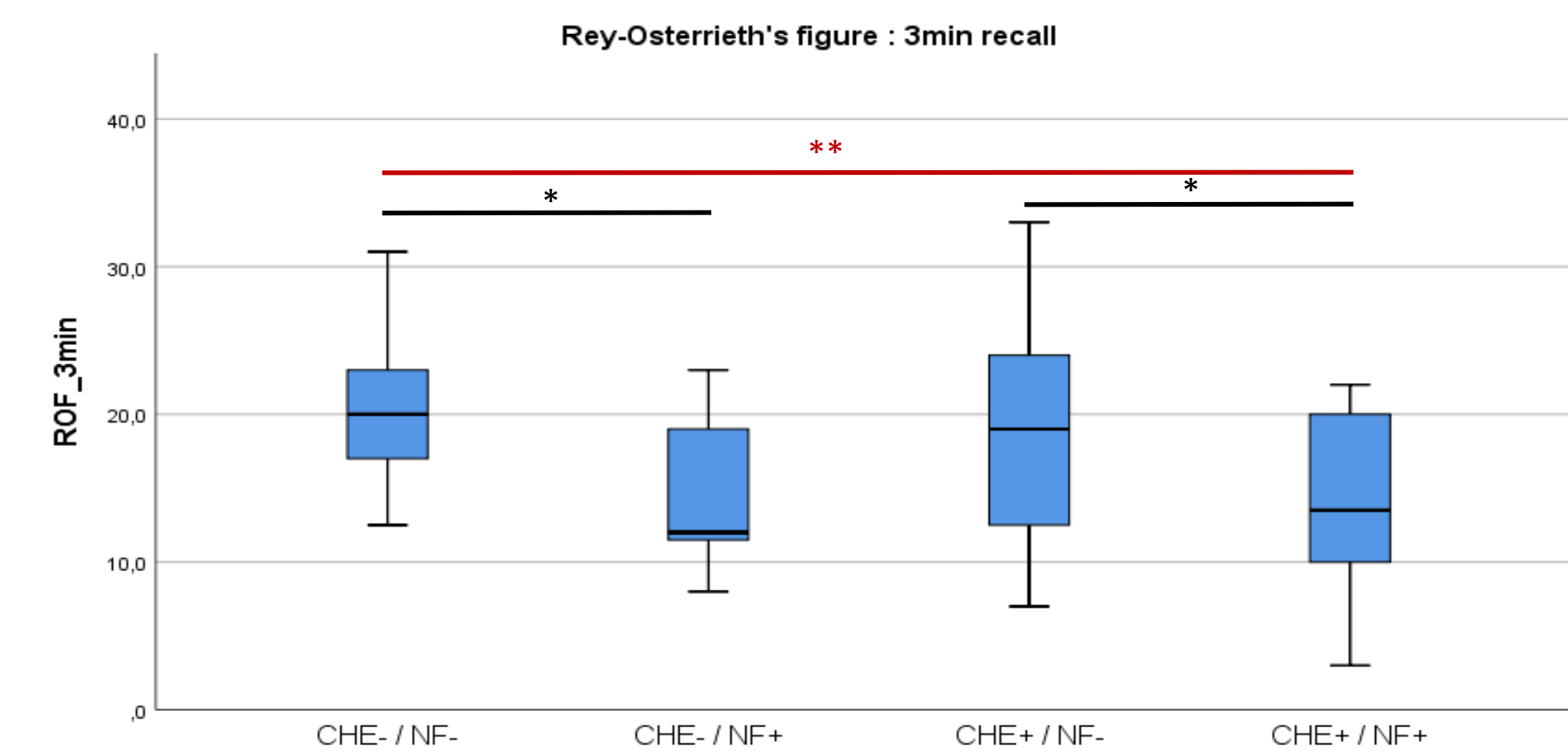
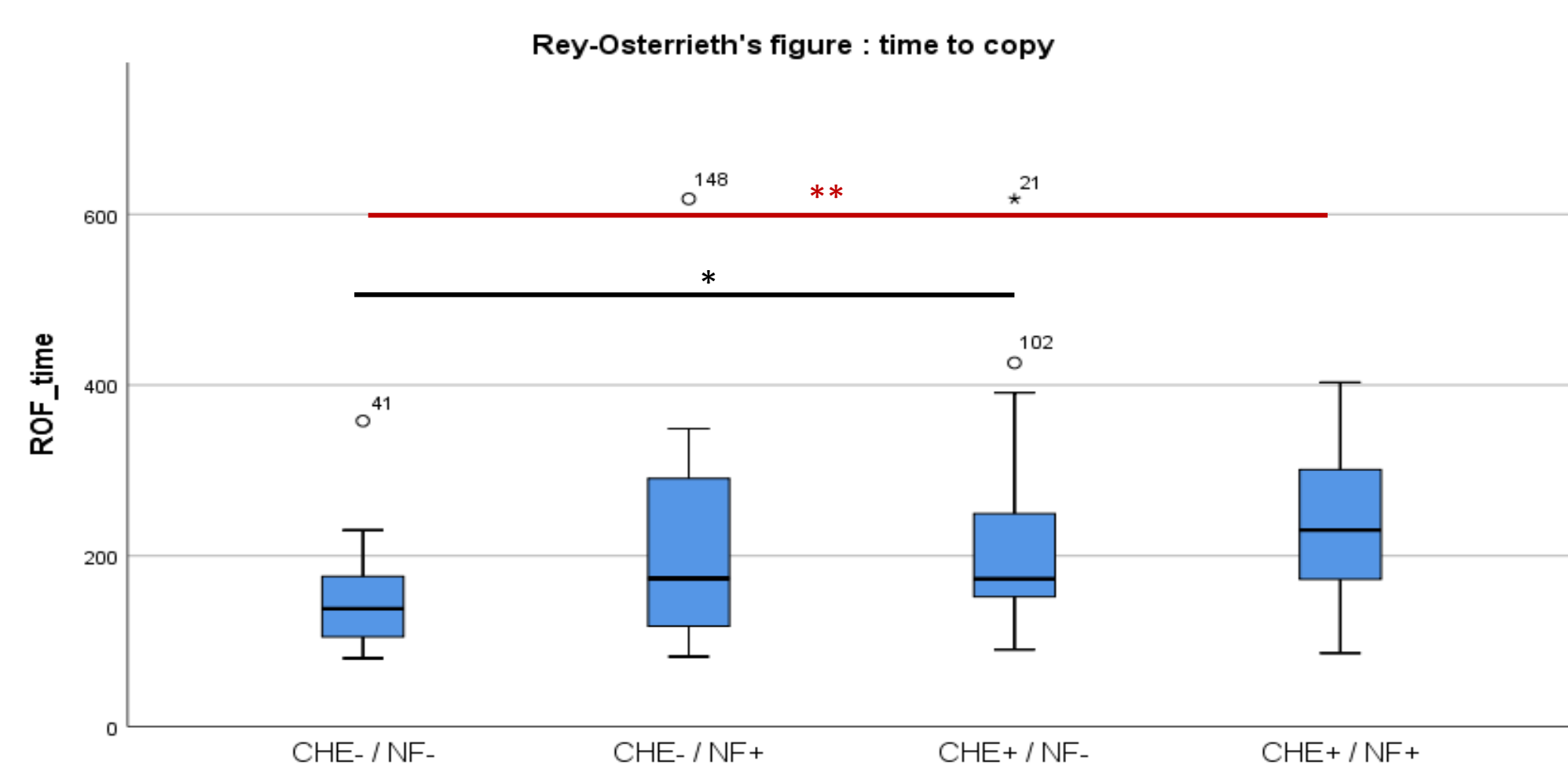
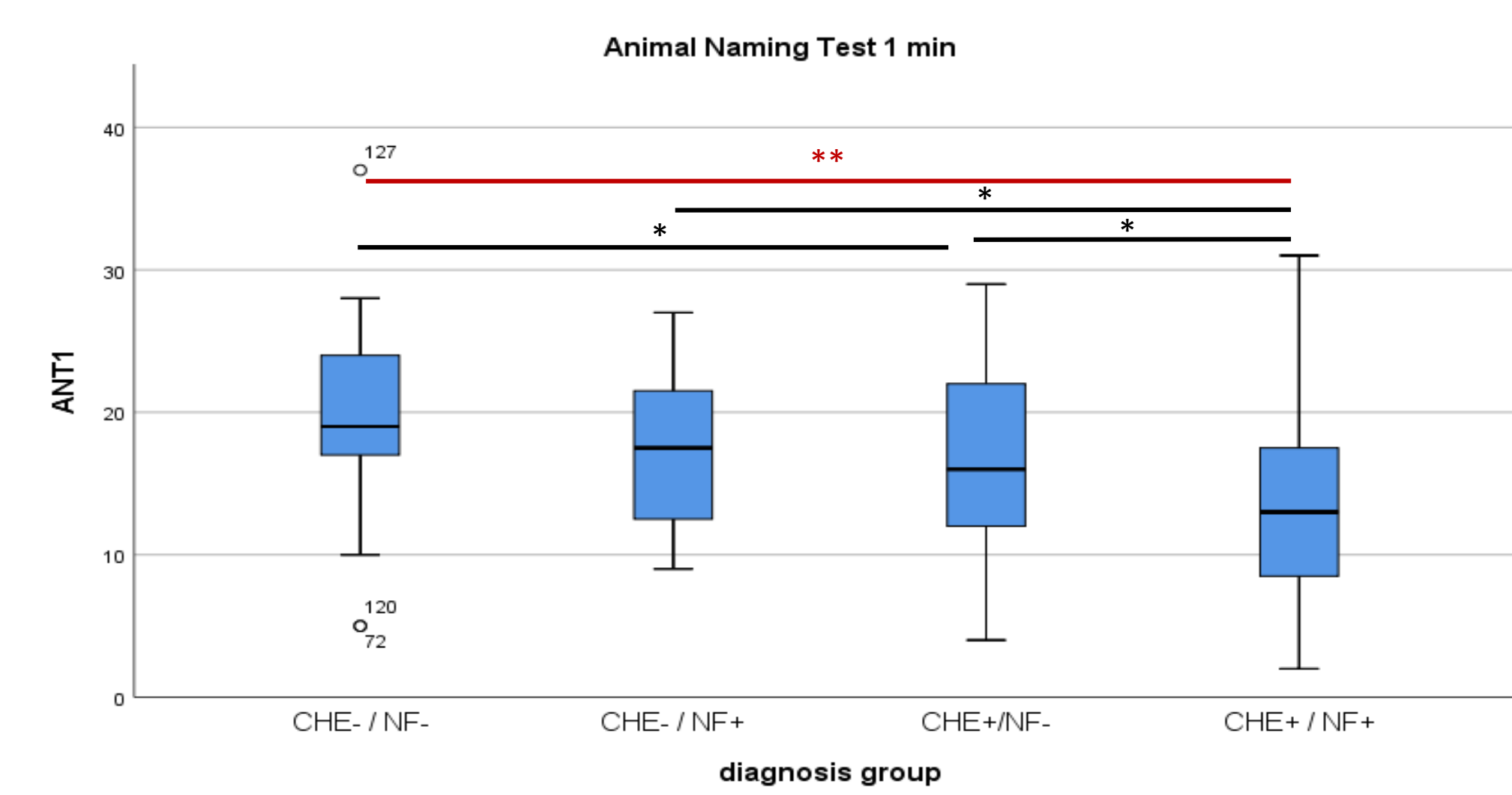
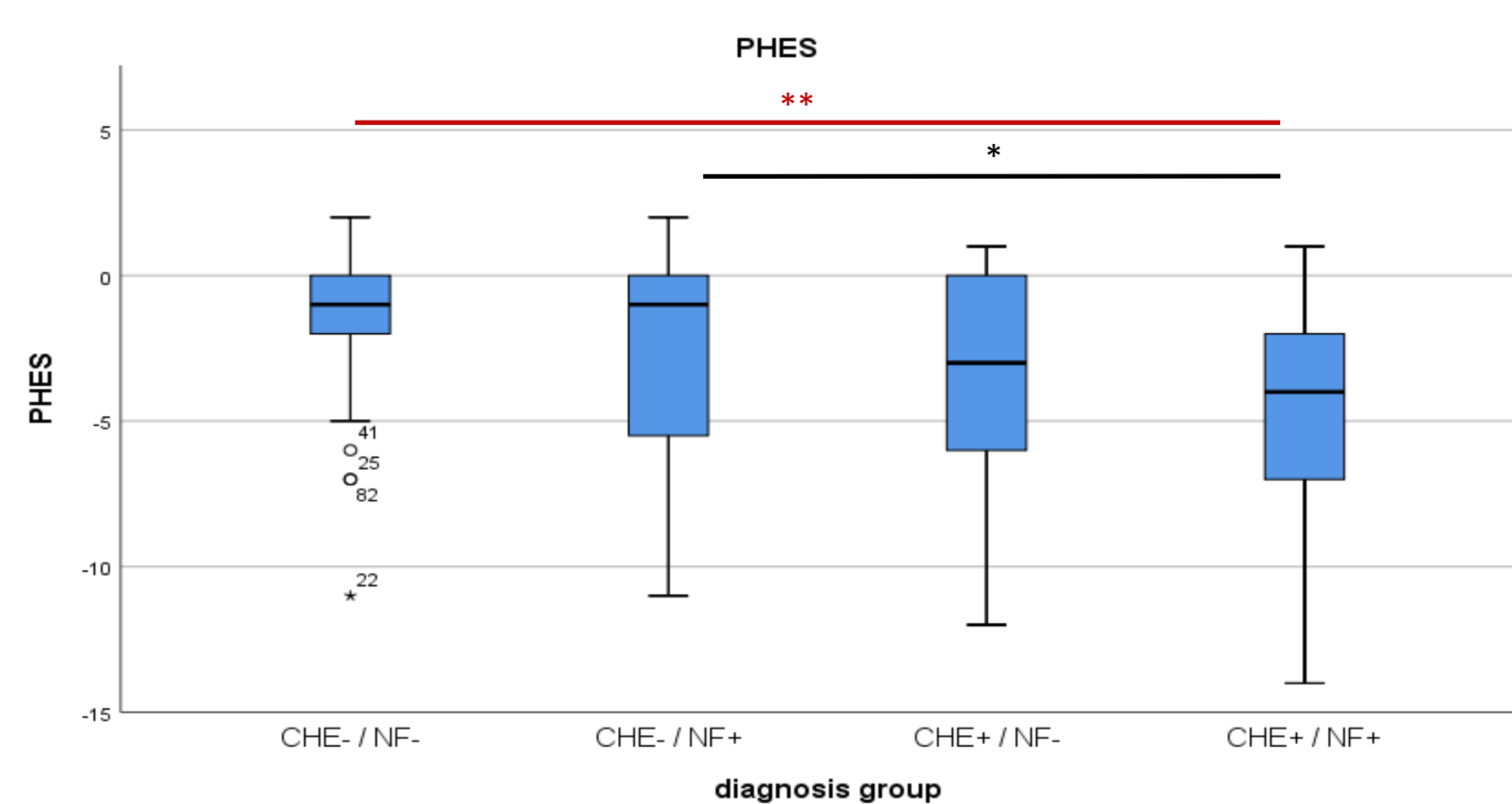
- ✓ **General cognitive efficiency** (MMS, MoCA)
- ✓ **Instrumental functions** (vision, praxis, language)
- ✓ **Attention** (cancellation tasks, encoding, intensity)
- ✓ **Psychomotor speed** (timed tasks)
- ✓ **Executive functions** (organization, inhibition, flexibility, strategy)
- ✓ **Memory** (recall and recognition of verbal or visual information : Rey's Figure, Free and Cued Selective Reminding Test)
- ✓ **Tests validated for HE diagnosis** (PHES, ANT)



Patients at evaluation / differential diagnosis

	All patients (n= 164)	Patients CHE- (n=61; 37%)		Patients CHE+ (n=103; 63%)		p-value
		No neurologic factors CHE- / NF- n=43 (26%)	Neurologic factors CHE- / NF+ n=18 (11%)	No neurologic factors CHE+ / NF- n=62 (38%)	Neurologic factors CHE+ / NF+ n=41 (25%)	
Men, n (%)	105 (64)	22 (51)	13 (72)	42 (68)	28 (68)	0.23
Age, year, mean (SD)	56.7 (12.6)	52.8 (13.4)	58.2 (16.6)	56.6 (11.9)	60.2 (9.9)	0.026*
Etiology of chronic liver disease, n (%)						
Cirrhosis	127 (77)	26 (60)	17 (94)	49 (79)	35 (85)	0.009**
Heavy drinking	79 (62)	16 (37)	14 (78)	25 (40)	26 (63)	0.003**
MASH	68 (54)	10 (23)	6 (33)	35 (56)	17 (41)	0.007**
Virus	20 (16)	5 (12)	1 (6)	8 (13)	5 (12)	0.859
Mixed causes	49 (39)	7 (16)	6 (33)	21 (34)	15 (37)	0.154
Child-Pugh class (A/B/C)	29/78/12 (24/66/10)	12/10/2 (50/42/8)	6/9/2 (35/53/12)	7/36/4 (15/76/9)	4/23/4 (13/74/13)	0.004**
MELD score	12.5 (4.5)	10.0 (3.5)	10.7 (3.5)	14 (4.8)	13.1 (4.2)	<0.001**
Vascular liver disease	38 (23)	15 (34)	1 (5)	14 (23)	8 (20)	0.08
Previous TIPS placement, n(%)	47 (29)	9 (21)	4 (22)	21 (34)	13 (32)	0.452
Previous episode of hepatic encephalopathy, n(%)	115 (70)	21 (49)	10 (56)	50 (80)	34 (83)	0.001**
Specific medication for hepatic encephalopathy, n (%)	113 (69)	20 (47)	9 (50)	50 (80)	34 (83)	<0.001**
Comorbidities, n(%)						
Diabetes	60 (37)	11 (26)	6 (33)	30 (48)	13 (32)	0.091
Obesity at time of evaluation	43 (27)	8 (19)	1 (5)	21 (34)	13 (32)	0.039*
Active alcohol abuse at evaluation	14 (8)	5 (12)	2 (11)	2 (3)	5 (12)	0.305
History of brain damage	26 (15)	2 (5)	3 (17)	6 (10)	14 (34)	0.001**
Ischemic stroke	14 (8)	0 (0)	2 (11)	3 (5)	9 (22)	0.006**
Head trauma	12 (7)	2 (5)	1 (5)	4 (6)	5 (12)	0.564
Anxio-depressive disorder	32 (20)	10 (24)	6 (33)	11 (18)	5 (12)	0.251
Psychiatric disease	9 (5)	5 (12)	0 (0)	2 (3)	2 (5)	0.186
Psychotropic drug medication	39 (24)	13 (30)	5 (28)	15 (24)	8 (20)	0.657

Cognitive tests



Conclusion : The diagnosis of HE based on NI is complicated. Validated tests (PHES, ANT) can be sensitive for HE but for other neurological damage as well, they are also found to be worse in patients with mix causes of NI. The assessment of memory seems to be sensitive for differential diagnosis between CHE and other Neurological factors. Developing tests including processing speed and memory could represent a promising tool for differential diagnosis of CHE.