



Cognitive Reaction Test. Standardization and Validation of its Reliability and Utility in the Diagnosis of Mild Cognitive Impairment

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[#]In Memoriam

Introduction

Ageing is usually associated with reduced processing efficiency, which can diminish the capacity of some brain areas and differs in extent among individuals [1]. Some “fluid” mental capabilities declines from early adulthood (aspects of memory, reasoning, processing speed, and executive functions) and are important for living independently, when one fluid mental domain declines others also tend to do so [2]. Early diagnosis of patients with Mild Cognitive Impairment (MCI) is very important to initiate early treatments that may slow their progression towards dementia [3]. Salthouse [4] championed the idea that processing speed might be one major cause of age associated cognitive declines in other cognitive functions. It begins by the 30s and appears to account for a substantial proportion of age-associated decline in all affected cognitive domains [5]. In this vein, it has recently been suggested that processing speed might be useful as a biological marker of cognitive aging [6]. Accurate biological and imaging markers are not accessible to all health systems; neuropsychological clinical assessment assumes a leading role, as the first approach to the target subject.

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Study Population

Hundred healthy subjects and 100 MCI patients aged 50 to 80 years entered the study; they lived relatively independently; 72% Women. The healthy subjects aged 63.21 years (SD=9.42), with 13.44 years (SD=3.60) of formal education, lived in Buenos Aires, and spoke Spanish. 100 MCI patients aged 64.56 (8.35), with 10.36 (3.76) of formal education.

Normal cognition was defined as having no cognitive concerns and scores, in the normal range, in the cognitive tests: Mini-Mental State Examination (MMSE: 29.53 ± 0.7) ; episodic memory performance as assessed by a verbal word learning test of ADAS memory subtest (2.0 ± 1.37), and executive function by Trial Making Test A & B time (A: 41.28 ± 9.14; B: 79.51 ± 26.54) and Trial

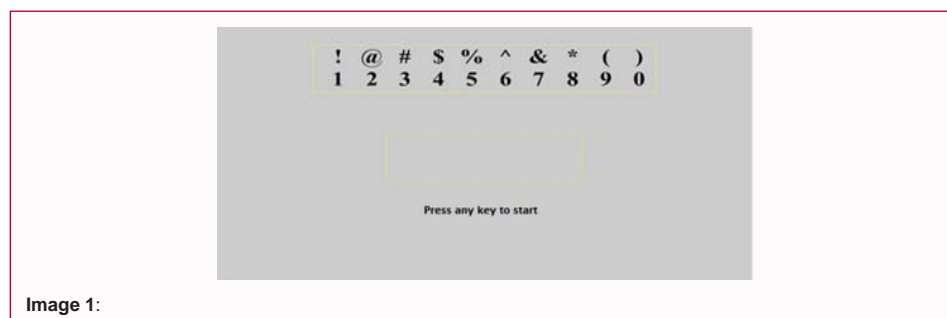


Image 1:

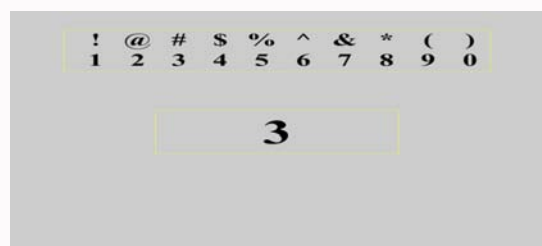


Figure 1: Motor subtest Illustrative screen.



Figure 2: Vismotor subtest: The subject must look at the numerical stimulus that appears in the screen centre and press the correct number on the keypad.

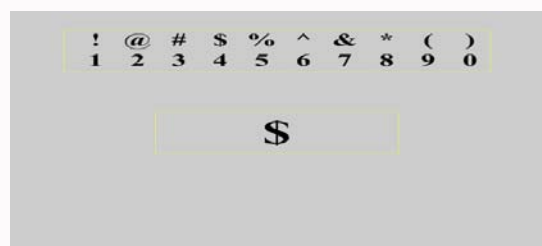


Figure 3: Cognitive subtest: Illustrative screen.

Making Test A & B errors (A: 0; B: 0), and the Clinical Dementia Rating. The recruitment and all assessments procedures were described in detail in a free-access, full protocol of the study [7].

Cognitive Reaction Test (CRT) Description

It was administered in a screen computer with millisecond accuracy. Participants had to press the numbers keys on the right keypad. Assessment Duration was 40 minutes. Each subtest consists of 60 stimuli and it records: 1- Mean Time measured in seconds, between hearing or seeing each stimulus that appear in screen, and pressing it on the keypad; 2- Total time in seconds of each subtest; 3- Mistakes made; 4- "Pure reaction time" value that indicates the patient's cognitive performance results.

The next screen is present during the administration of test: (Image 1)

The CRT is subdivided into three subtests

Motor subtest: A number appears on the screen center. The subject is instructed to look away from the screen, and to focus only on the numbers that are in the right of the keyboard. The examiner says the numbers and the subject must only press the correct key. The main objective of this subtest is that the subject gets familiar with the keyboard and exercises his fingers "Motor Time" (Figure 1).

Visomotor subtest: In this subtest, the subject must look at the screen center where a numerical stimulus appears and he must press

Table 1: CRT Mean and DS according to the age range of the Motor Subtest.

Age Range (N)	Motor Subtest Mean (SD)		
	Total Time	Average Time	Errors
50-54 (n=21)	79.71 (9.08)	1.34 (.13)	.10 (.30)
55-59 (n=20)	83.19 (11.08)	1.38 (.18)	.25 (.55)
60-64 (n=18)	77.49 (10.68)	1.29 (.17)	.06 (.23)
65-69 (n=13)	82.21 (8.99)	1.37 (.15)	.38 (.65)
70-74 (n= 9)	88.11 (8.03)	1.46 (.13)	.44 (.72)
75-80 (n=19)	87.61 (10.32)	1.45 (.17)	.68 (.74)
50-54 (n=21)	79.71 (9.08)	1.34 (.13)	.10 (.30)

the correct number on the keyboard (Figure 2).

Cognitive subtest: In the screen center appears a symbol corresponding to a specific number in the keypad. The subject must press the matching number in the keypad (e.g, the \$ symbol corresponds to the number 4) (Figure 3).

Results

The test was administered to 100 controls and to 100 MCI between 50 and 80 years to establish whether CRT may differentiate them, and use pure cognitive reaction time as a useful indicator between both populations. The results of the test showed significant statistical differences in favor of "controls" (CRT patients: 133.87 vs. CRT controls: 67.14, Mann-Whitney test $p < 0.0001$).

In order to validate the proposed instrument, the result obtained by the subjects was correlated with the other cognitive test administered. The results showed moderate positive correlations of CRT with cognitive test that measure: a) global cognitive impairment (CDR); b) attention (TMT A); c) executive function (TMT B), and d) memory (ADAS memory subtest). The CRT has a negative correlation with the MMSE, which is an expected result as it evaluates global cognitive function. In all cases, the Mann-Whitney U test showed statistically significant differences: MMSE, CRT patients: 137.17 vs. CRT controls: 63.83 $p < 0.0001$; memory evaluation subtest of the ADAS scale, CRT patients: 132.36 vs. CRT: 68.64, $p < 0.001$; TMT A, time: CRT patients: 129.89 vs. CRT controls: 71.11, $p < 0.0001$; CRT patients errors: 110.00 vs. CRT controls: 91.00 $p < 0.0001$; TMT B CRT time: 140.04 vs. CRT controls: 60.97, $p < 0.0001$, TMB errors :CRT patients 132.50 vs. CRT controls: 68.50, $p < 0.0001$.

The normative values and SD of the TRC were those obtained in the control group. Control subjects CRT values are displayed in Table 2 and 3. Subjects with 1 SD above mean, age ranged have a diagnosis of possible cognitive deterioration and those subjects with CRT greater than 2 SD of the mean, age ranged, have a diagnosis of

Table 2: CRT Mean and SD according to the age range of the Vismotor Subtest.

Age Range (N)	Vismotor Subtest Mean (SD)		
	Total Time	Average Time	Errors
50-54 (n=21)	84.40 (21.49)	1.40 (.35)	.33 (.57)
55-59 (n=20)	83.41 (13.46)	1.38 (.22)	.15 (.36)
60-64 (n=18)	83.40 (24.85)	1.39 (.41)	.33 (.48)
65-69 (n=13)	86.69 (17.18)	1.44 (.28)	.38 (.65)
70-74 (n= 9)	95.77 (11.65)	1.59 (.19)	.56 (1.01)
75-80 (n=19)	90.36 (12.34)	1.50 (.20)	.37 (.76)
50-54 (n=21)	84.40 (21.49)	1.40 (.35)	.33 (.57)

Table 3: CRT Mean and SD according to the age range of the Cognitive Subtest and the Pure Cognitive CRT Indexes.

Age Range (N)	Cognitive Subtest Mean (SD)			TRC Pure Cognitive
	Total Time	Average Time	Errors	
50-54 (n=21)	139.50 (26.90)	2.32 (.44)	.52 (.87)	55.14 (22.02)
55-59 (n=20)	146.73 (33.15)	2.44 (.55)	.50 (.68)	64.82 (24.28)
60-64 (n=18)	152.25 (39.53)	2.53 (.65)	.39 (.60)	69.28 (35.76)
65-69 (n=13)	158.43 (38.47)	2.63 (.64)	.85 (.80)	71.74(33.15)
70-74 (n= 9)	161.55 (34.54)	2.69 (.57)	1.00 (1.32)	65.77 (26.71)
75-80 (n=19)	153.94 (23.07)	2.58 (.37)	.95 (1.35)	64.04 (27.49)

probable cognitive impairment.

Discussion

The CRT is a useful test for assessing cognitive decline, slow processing speed and working-memory alterations. We present normative data of a representative sample of participants over 50 years old from Argentina. It is a new and a very sensitive assessment computerized tool, of easy implementation and for subject of different educational level. This test measures speed of information processing, visuomotor time and cognitive reaction time. In addition to, learning, attention and working memory. All these are cognitive functions of great value for the differential diagnosis of Normal controls- MCI.

MCI patients reacted more slowly and made more errors than healthy individuals. These results can be interpreted as an inadequate cognitive processing. These results correlated directly with the rest of the tests used (MMSE, ADAS, TMT-A and TMT-B).

The lack of stratification by education is a weakness of this work. However, each individual is self-control, only counts the ability of brain reaction. The same happens with patients who have a hypo kinetic syndrome, since motor and visuomotor times are subtracted from the cognitive, and the resulting time is the pure cognitive reaction to the stimulus.

The CRT is an effective tool for diagnosis and assessment, since both the response time and the errors committed are sensitive indicators of early cognitive deterioration.

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