

The Tower of Hanoi for Evaluating Dysexecutive Syndrome in Patients with Parkinson's: Standardization Values

Marcos Serrano-Dueñas^{1,2}, Belén Calero¹, Maite Serrano¹

¹Medicine Faculty, Pontifical Catholic University of Ecuador, Quito, Ecuador ²Movement Disorders Unit, Neurological Service, Carlos Andrade Marín Hospital, Quito, Ecuador Email: umasnhcam_fmpuce@yahoo.es

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Abstract

Objective: The Tower of Hanoi measures executive functions using non-verbal content and requires perception of position in space. The main objective of this study is to standardize the use of the TOH as a measurement tool in Parkinson's disease. **Patients and Methods:** Of the Control Group subjects, 192 (59.6%) were women, 223 subjects (69.25%) were able to perform the TOH with 3 discs. In the Parkinson's Group, there were 57 women (39.3%), and 66 subjects (45.5%) did not get past that level. **Results:** If we take the TOH (with 3 or 4 discs) as a tool for discriminating between those who have dysexecutive syndrome and those who do not, we find that the Parkinson's Group presents dysexecutive syndrome significantly more frequently than the Control Group ($p \le 0.0064$). **Conclusion:** We can conclude that dysexecutive syndrome is frequent in Parkinson's patients and it is more prevalent than in the general population.

Keywords

Parkinson's Disease, Dysexecutive Syndrome, Tower of Hanoi

1. Introduction

Parkinson's disease is a common neurodegenerative illness which affects between 1% and 3% of the population over age 65, with a slight prevalence in men over women [1].

The symptoms associated with dopaminergic degeneration of the cells of the *substantia nigra pars compacta* include motor, neuropsychiatric and autonomic symptoms [2]. Neuropsychiatric symptoms may range from minor deficits in executive function (EF) to cases of Mild Cognitive Impairment that include al-

teration of EF, which is a clear predictor of an evolution to dementia in 80% of cases [3] [4].

The executive functions refer to the capacity to perform complex motor behaviors directed toward an objective. Considering the highest and most complex of the cognitive skills, executive control includes planning, organizing, abstract thinking, and proper sequencing. This requires processing the impulses from other functions, such as memory, language, and perception [5].

The construct of "*impaired executive functioning*," or dysexecutive syndrome (DS), is often used to describe patients who have preserved intelligence and no specific cognitive deficits, but who are incapable of carrying out self-directed adaptive behaviors which are "necessary and appropriate," socially responsible, and effective [6].

Categorization of executive function, according to Lezak [6], consists of four main components: i) Volition, defined as the ability to think of one's own future needs and formulate an intention to meet them, accompanied by the appropriate motivation; ii) Planning, defined as the ability to formulate the steps necessary to achieve a goal, which requires the capacity to imagine the future, abstract and objective thought, consideration of alternatives, and hierarchical sequencing; iii) Purposive action, requires sustained attention to initiate, maintain, or stop behaviors in an organized manner; and iv) Effective performance, the capacity to monitor whether the goal has been reached, identify errors, and correct them.

The Hanoi Tower (TOH) [7] is a test used in numerous neuropsychological studies, the satisfactory completion of which requires the cooperation of multiple executive functions. The TOH measures executive functions using non-verbal content and requires perception of position in space [8].

It is considered to require the generation of a sequence of movements involving multiple steps, [8] and a selection strategy [7], while keeping the subordinate objectives and the final objective in working memory. It also requires the execution of a sequence of movements while inhibiting the execution of incorrect movements, as well as monitoring one's own performance and revising the work plans. It is considered particularly suitable for evaluating the executive function of planning [7] [8].

Unfortunately, the implementation of this test varies from author to author, and the criteria used for determining what is normal and what is pathological are diverse. Therefore, the main objective of this study is to standardize (in a normal population) the use of the TOH as a measurement tool. It will establish cutoff points for number of attempts, the number of movements, violation of the rules, and the time needed to finish the test. After that, it will use the TOH to study the presence of DS in Parkinson patients.

2. Patients, Materials and Methods

2.1. Pilot Study

All individuals included in the pilot study were residents of homes for the elderly

in the city of Quito (Ecuador), and met the following inclusion criteria: accept participation in the study, and have a score of ≥ 25 points of the Mini Mental Status Examination (MMSE) [9]. Excluded from the study were subjects who had a background of neurological and/or psychiatric illness or were taking psycho-pharmaceuticals at the time of the interview; those with significant systemic illness; and those who were illiterate.

A first phase included a pilot study conducted with 63 subjects, of which 29 were men (46%). There were 31 subjects (49%) with only basic education (1 - 6 years); 21 subjects (33%) with a medium level of education (7 - 12 years); and 11 subjects (18%) with higher education (\geq 13 years). The objective of this phase was to determine: (i) When to consider a movement as having been made; (ii) When to consider an attempt complete; and (iii) How many attempts to allow the subject to make.

The TOH used in the study consisted of a wooden base $(24 \times 9 \times 1 \text{ cm})$ supporting three vertical posts of equal diameter (0.5 cm) and height (6 cm), and equidistantly spaced (7.5 cm), with five wooden discs of varying sizes and colors, from smallest to largest as follows: 4 cm-brown; 5 cm-yellow; 5.5 cm-blue; 6 cm-green; and 6.5 cm-red. Each disc had a hole in the center of 1.3 cm, which would fit onto any of the three posts. Discs of varying sizes and colors were used because color is considered to be a complementary dimension to size [10].

All subjects were encouraged to perform the test using the fewest number of moves and in the shortest time possible. The rules were explained using examples: 1) Move only one disc at a time. 2) Do not place a larger disc on top of a smaller one. 3) Do not place a disc to one side or keep it in your hand while moving another disc. In general, these are the rules most often used [11].

From this pilot study we obtained the following criteria: i) A movement was considered a movement if and only if the disc left the post. In other words, if the subject took a disc, lifted it, and placed it back on the same post without removing it, that was not counted as a movement. In addition, any violation of the rules was considered an extra movement. ii) An attempt ended under the following conditions: ii.i) when the subject did not want to continue, ii.ii) when the subject could not continue, or ii.iii) when the subject wanted to start over. iii) Up to 5 attempts were allowed.

The minimum number of movements required to solve the TOH task can be represented by the formula $(2^n) - 1$, with *n* being the number of discs on the first bar at the beginning of the test [7]. When the test is done with three discs, the minimum number of movements needed to complete the task would be $(2^3) - 1 = 7$. Doing the task with 4 or 5 discos would require a minimum of $(2^4) - 1 = 15$ or $(2^5) - 1 = 31$ movements, respectively.

2.2. Standardization Study

The standardization study included 322 subjects. The same as in the pilot study, all were residents of homes for the elderly in the city of Quito, Ecuador, called

the Control Group (CG). The relevant demographic data was obtained from all of them (sex, age, and years of education). First the TOH test was administered. After that, the MMSE, the CLOX-1 and the CLOX-2 were administered [12].

Briefly, the CLOX consists of two sections, each one evaluated with a maximum of 15 points, where more points indicate better and more correct completion. The CLOX-1 consists of asking the subject to draw a clock that indicates a specified time. An overall evaluation is made of whether the drawing looks like a clock, and after that various details are considered: the circle, the hands, the sequence and distribution of the numbers, etc. The cutoff point for presentation of DS is considered to be $\leq 10/15$. The CLOX-2 consists of copying a clock, with the same evaluation criteria. The cutoff point for DS is considered to be $\leq 12/15$.

Study with Parkinson Patients

The subjects were 145 consecutive patients who were ambulatory, diagnosed with PD according to the criteria of the United Kingdom Parkinson's Disease Society Brain Bank (UKPDSBB) [13], and who are regularly attended at the Abnormal Movement Unit of Neurology Services at Carlos Andrade Marin Hospital (HCAM) in Quito, Ecuador. This group was called the Parkinson Group (PG)

Exclusion criteria were the presence of: i) illiteracy; ii) serious concomitant illness; iii) blindness or daltonism; iv) hypoacusis; or v) amputation of a limb. The study was approved by the Teaching and Research Manager of HCAM. All patients involved provided their written informed consent.

General demographic descriptors were obtained from all subjects. In addition, the following scales and tests were administered: (1) Functional assessment, with the SPES-SCOPA [14]; limitations to daily living activities, using the Schwab & England scale (S&E); stage of illness, with Hoehn & Yahr (H & Y); cognitive status with the MMSE [9]; emotional status with the Hospital Anxiety and Depression Scale (HADS) (self-administered under supervision) [15]; quality of life with the Parkinson's Impact Scale (PIMS) (self-administered under supervision) [16]; psychosocial status with the SCOPA-Psychosocial (SCOPA P-S) [17]. Finally, the subjects were evaluated with the Clinical Impression of Severity Index for Parkinson's Disease (CISI-PD) [18].

When administering the TOH, time was not counted whenever the PD was causing slowness of movements. The same steps were followed as in the standardization phase. All patients were evaluated in the best functional status (time ON).

3. Results

Of the CG subjects, 192 (59.6%) were women. They had mean values \pm SD as follows: 64.5 \pm 15.2 years of age; 9.5 \pm 5.1 years of education; 27.6 \pm 1.4 points on the MMSE; 9.9 \pm 2.9 points on CLOX-1; and 12.7 \pm 2 points on CLOX-2 (**Table 1**).

From those subjects, the following results were obtained: 223 subjects (69.25%) were able to perform the TOH with 3 discs; 171 subjects (76.68% of the preced-

Male = 130; Female = 192	Median	Mean ± SD	Range	Skewness	Kurtosis
Age	64	64.52 ± 15.25	53	0.02	-1.24
Education	8	9.53 ± 5.16	29	0.87	0.66
MMSE	28	27.66 ± 1.47	4	0.16	-1.47
Clox-1	10	9.96 ± 2.9	12	-0.35	-0.62
Clox-2	13	12.71 ± 2.05	10	-0.99	1.05

Table 1. Statistics descriptives of Control Group (n = 322).

MMSE: Mini Mental Status Examination.

Table 2. Values in the realization of the Tower of Hanoi (50^{th} percentile) Control Group (n = 322).

N	Attomato	Movemente	Time (minutes)	Violations of the rules			
	IN	Attempts	Movements	Time (minutes)	R1	R2	R3
3 DISCS	223 (69.25%)	2	9	1.22	1	1	1
4 DISCS	171 (53.1%)	2	23	3.16	1	2	1
5 DISCS	96 (29.7%)	2	58	6.2	1	2	1

Doing the task with 3 or 4 or 5 discos would require a minimum of $(2^3) - 1 = 7$; $(2^4) - 1 = 15$ or $(2^5) - 1 = 31$ movements, respectively. The rules: R1) Move only one disc at a time. R2) Do not place a larger disc on top of a smaller one. R3) Do not place a disc to one side or keep it in your hand while moving another disc.

ing) with 4 discs; and 96 subjects (56.14% of the preceding) with all 5 discs. The 50th percentile was taken as the standard value, for the number of movements, attempts, time required, and rule violations. That is, with three discs, at the easiest level of the TOH, 99 subjects (30.75%) presented DS (**Table 2**); 110 subjects (34%) had scores equal to or less than 10 on the CLOX-1; and 81 subjects (25%) had scores equal to or less than 12 on the CLOX-2.

Within the CG, if we take into account the CLOX-2 scores, we find that 128 subjects obtained scores equal to or less than 12, which means they had DS. Ninety-nine subjects were not able to perform the TOH with three discs. In comparison to the CLOX-2, the TOH correctly diagnosed 90.99% with DS; sensitivity of 100.00%; specificity of 77.34%; positive predictive value of 87%; negative predictive value of 98.99%; maximum positive verisimilitude indicator of 4.41, and negative of 0.01.

In the PG, there were 57 women (39.3%) and 88 men (60.7%) with mean values as follows: age, 67.1 years; duration of illness, 8.3 years, with a dosage of 692.8 mg of levodopa daily (**Table 3**). Their distribution according to H&Y stages was the following: 17 patients in Stage I (12.1%); 31 in Stage II (21.2%); 74 in Stage III (50.8%); and 23 in Stage IV (15.9%).

Their CLOX-1 scores showed that 71 subjects (48.9%) had scores less than or equal to 10, while with the CLOX-2 scores, 48 patients (33.1%) had scores equal to or less than 12, which means they presented DS.

With the TOH and three discs, the easiest level of that test, 66 subjects (45.5%) did not get past that level; 31 patients (39.2%) did not manage to get past the

Male = 88; Female = 57	Median	Mean ± SD	Range	Skewness	Kurtosis
Age	67.5	67.1 ± 10	52	-0.36	0.15
Education	8	9 ± 4.5	21	0.92	0.42
Years of disease	6	8.38 ± 6.5	26.3	1.15	0.73
Years with l-dopa	6	6.2 ± 4.5	18	0.65	-0.15
Dose	750	692.8 ± 312.3	1250	-0.50	0.17
SPES-SCOPA 1	16	17.1 ± 5.2	25	0.27	-0.09
SPES-SCOPA 2	8	9.4 ± 3.6	19	0.76	0.67
SPES-SCOPA 3	2	3.3 ± 3.3	12	0.88	-0.11
SPES-SCOPA Total	28	29.9 ± 10.8	51	0.55	-0.01
Schwab & England	70	70.3 ± 16.2	80	-1.13	1.22
MMSE	29	27.5 ± 3.4	19	-2.55	8.10
Clox-1	11	9.8 ± 3.4	15	-0.75	0.03
Clox-2	13	12.7 ± 2.6	13	-1.93	4.50
HADS anxiety	9	8.7 ± 4.1	18	-0.16	-0.60
HADS depression	8	7.8 ± 3.7	16	0.30	-0.32
PIMS	19	18.8 ± 8.7	38	0.10	-0.55
SCOPA P-S	12.5	11.8 ± 6.1	22	0.14	-1.17
CISI-PD	11	11.1 ± 4.2	18	0.36	-0.27

Table 3. Descriptive statistics of Parkinson's Group (n = 145).

4-disc level; 20 individuals (41.6%) were able to do it with all 5 discs.

If we take the CLOX-2 as the standard and compare the TOH with 3 discs (in both cases the easiest levels of both tests), we find that the TOH correctly diagnosed 86.21%; sensitivity of 80.41%; specificity of 97.92%; positive predictive value of 98.73%; its equivalent negative of 71.21%; and positive verisimilitude indicators of 38.6 and negative of 0.2.

When we compare those who successfully completed the TOH in the CG with those who were successful in the PG we find that the age of the Parkinson's patients was significantly older. With three discs, Parkinson's patients made more movements and more attempts before being able to complete the TOH. Similar behavior was seen with 4 discs. With 5 discs the only significant differences were in age (the subjects with PD were older) who also performed more movements (**Table 4**).

The variables of success or failure and rule violations were significantly greater in Parkinson patients at the 3- or 4-disc levels, but this did not happen with 5 discs, where the differences tended to disappear (Table 4).

When we analyze the results in the PG, comparing those who had success with the TOH to those who failed, we find that age and years of education were always significantly less in those who were successful. The same was seen with the scores on CLOX-1 and CLOX-2, on the PIMS and on the SCOPA-Psychosocial (Table 5).

1 DISCS	CONTROL n = 223	PARKINSON n = 79	
3 DISCS -	mean ± sd	mean ± sd	— p≤
Age	60.73 ± 14.82	65.58 ± 10.32	0.009
Education	10.46 ± 5.48	9.88 ± 4.51	0.409
MMSE	27.78 ± 1.5	28.51 ± 1.5	0.000
Clox-1	10.2 ± 2.92	10.39 ± 3.27	0.637
Clox-2	12.92 ± 1.95	13.24 ± 1.73	0.202
Attempts	1.88 ± 0.97	3.89 ± 2.18	0.000
Movements	8.96 ± 1.68	9.78 ± 3.83	0.010
	CONTROL n = 171	PARKINSON n = 48	
4 DISCS -	mean ± sd	mean ± sd	— p≤
Age	59.2 ± 14.28	67.09 ± 9.6	0.001
Education	11.07 ± 5.74	10.11 ± 4.79	0.299
MMSE	27.86 ± 1.51	28.5 ± 1.39	0010
Clox-1	10.31 ± 2.91	10.2 ± 3.24	0.819
Clox-2	13.07 ± 1.9	13.37 ± 1.62	0.323
Attempts	1.82 ± 0.97	3.52 ± 1.99	0.000
Movements	23.26 ± 5.09	27.02 ± 18.34	0.018
- D1000	CONTROL n = 96	PARKINSON n = 28	
5 DISCS -	mean ± sd	mean ± sd	— p≤
Age	55.62 ± 13.77	66.27 ± 10.14	0.000
Education	12.09 ± 5.84	10.81 ± 4.34	0.294
MMSE	28 ± 1.54	28.42 ± 1.36	0.203
Clox-1	10.4 ± 2.85	10.92 ± 2.86	0.404
Clox-2	13.32 ± 1.68	13.58 ± 1.17	0.471
Attempts	2.06 ± 1.13	3.04 ± 1.53	0.000
Movements	56.41 ± 13.14	61.07 ± 49.24	0.384

 Table 4. Comparison between control subjects and patients with Parkinson who could make the Tower of Hanoi (t test).

MMSE: Mini Mental Status Examination.

4. Discussion

The basic objective, which was to standardize the use of the TOH, and the standard values of each of its stages, has been achieved for the sample of population with no evidence of cognitive decline. We were able to standardize its use. The 50th percentile was used as the standard value. Of this normal population, 30.75% presented DS when evaluated with the TOH. In the PG, 45.5% presented DS. To our knowledge, there is no reference indicating that this type of standardization has ever been done for both groups, subjects with no neurological illness and subjects with Parkinson's. We noticed that, overall, the CLOX-1 scores in our CG were lower than those obtained by Menon *et al* [19] and by Crowe *et al* [20]. Age does not seem to be the element that would justify this difference, even though the subjects studied by Menon were younger than those studied by Crow. The MMSE scores were not different from ours either.

We believe that the difference is due to education level. It is already known that education level affects execution and results on CLOX-1 [21].

If we accept the suggested cutoff points for CLOX-1 and CLOX-2 [12], one of the first conclusions we could make from this study is that more DS was found in the CG (34% and 25% respectively) than with the TOH (30.75%). In other words, the CLOX test is more sensitive than the TOH.

When we compare the CG subjects to the PG subjects, who were able to do the TOH with 3 discs, we find that the PD patients had significantly more rule violations than the Control Group subjects, required more moves and more attempts to be able to complete the test, and that the differences were significant (**Table 4** and **Table 5**). The Parkinson patients were older and had better scores on the MMSE. There were no differences in their CLOX-1 and CLOX-2 scores. The CG and the PG were almost the same in completing the TOH with 4 discs, but with 5 discs there were no differences. In other words, the most demanding test with the TOH did not reveal any differences between the healthy subjects and the Parkinson patients.

If we take the TOH (with 3 or 4 discs) as a tool for discriminating between those who have DS and those who do not, we find that the PG presents DS significantly more frequently than the CG ($p \le 0.002$ and $p \le 0.0064$, respectively) (Table 5).

	3 DISCS				4 DISCS					5 DISCS						
	(success)	(failure)	Total	X²	p≤	(success)	(failure)	Total	X²	p≤	(success)	(failure)	Total	X²	p≤	
CONTROL	223	99	322	0.55	0.000	171	52	223	7 42	0.0064	96	75	171	0.07	0 7865	
PARKINSON'S	79	66	145	9.55	0.002	48	31	79	7.42		28	20	48	0.07 0	0.7805	
		Ru	ıle 1			R			Rule 1			Rule 1				
CONTROL	83	140	223	28.63	20.62		84	87	171	1.27	0.2502	73	23	96	0.01	0.0000
PARKINSON'S	57	22	79		0.0000	28	20	48	1.27	0.2595	21	7	28	0.01 (0.9098	
		Ru	Rule 2		Rule 2			Rule 2								
CONTROL	31	192	223	~~~~	0 0000	34	127	171	24.67 0.00	0 0000	22	74	96	0.52 [¥] (0.4695	
PARKINSON'S	49	30	79	69.38	0.0000	27	21	48		0.0000	4	24	28			
		Ru	ıle 3				Rule 3			Rule 3						
CONTROL	20	203	223		0 0000	13	158	171	11.00		2	94	96	2.24 [¥] (0.1344	
PARKINSON'S	48	31	79	89.69	0.0000	12	36	48	11.22	0.0008	3	25	28			

Table 5. Comparison between control subjects and patients with Parkinson's who could make the Tower of Hanoi (X² test).

Y: X² with Yates correction. The rules: R1) Move only one disc at a time. R2) Do not place a larger disc on top of a smaller one. R3) Do not place a disc to one side or keep it in your hand while moving another disc.

	3	DISCS	4 DISCS			5 DISCS			
	success = 79	failure = 76		success = 48	failure = 31		success = 28	failure = 20	
	Mean ± SD	Mean ± SD	p≤	Mean ± SD	Mean ± SD	p≤	Mean ± SD	Mean ± SD	p≤
Age	65.6 ± 10.3	69.1 ± 9.3	0.044	63.1 ± 11.1	68.1 ± 9.6	0.048	62.3 ± 10.1	68.2 ± 9	0.046
Education	9.9 ± 4.5	8.1 ± 4.4	0.023	11.1 ± 4.8	8.5 ± 4.1	0.047	12.8 ± 4.3	9.2 ± 5.3	0.044
Years of disease	7.7 ± 6	9.2 ± 7.2	0.187	7.4 ± 5	8.2 ± 7.5	0.592	7 ± 5.3	7.7 ± 4.9	0.629
Yearswith l-dopa	5.7 ± 4.4	7 ± 4.7	0.122	4.7 ± 2.9	6.3 ± 5	0.133	5.6 ± 4.6	6.9 ± 5.3	0.393
Dose	677.4 ± 294.8	712.5 ± 335	0.523	660.3 ± 324.5	705.4 ± 241.1	0.528	612. 5 ± 329.2	697.1 ± 322.4	0.387
SPES-SCOPA Total	29.1 ± 10.3	31.1 ± 11.5	0.287	28.4 ± 8.7	29.4 ± 11.2	0.686	26.5 ± 9.3	31.7 ± 12.1	0.114
Schwab & England	71.9 ± 15.5	68.4 ± 17.1	0.229	75.4 ± 12.3	69.8 ± 16.9	0.134	71 ± 16.5	68.8 ± 17.5	0.674
CISI-PD	11 ± 3.7	11.4 ± 5	0.571	10.4 ± 3.2	11.3 ± 4	0.314	10.9 ± 4.5	11.7 ± 3.5	0.952
MMSE	28.5 ± 1.5	28.1 ± 1.6	0.136	28.5 ± 1.7	$28{,}5\pm1.4$	0.922	28.4 ± 1.4	28.6 ± 1.5	0.516
Clox-1	8.4 ± 3.3	9.9 ± 3.6	0.026	7.2 ± 3.2	10.7 ± 3.4	0.032	7.3 ± 3.5	10.9 ± 2.9	0.033
Clox-2	13.2 ± 1.7	11 ± 3.3	0.007	13.8 ± 1.9	11.4 ± 1.6	0.024	13.1 ± 2.1	10.6 ± 1.2	0.029
HADS anxiety	7.9 ± 3.7	9.8 ± 4.4	0.008	7.3 ± 4.5	8.3 ± 3.2	0.252	8.3 ± 2	8.3 ± 3.9	0.393
HADS depression	7.5 ± 3.9	8.3 ± 3.6	0.242	7.3 ± 4.1	7.8 ± 3.7	0.585	7.3 ± 4.3	10.3 ± 3.9	0.045
PIMS	18.4 ± 8	21.5 ± 9.7	0.044	16.3 ± 7.6	20.1 ± 8.3	0.041	17.6 ± 9.8	23.8 ± 5.7	0.028
SCOPA P-S	9.4 ± 6.4	12.5 ± 5.9	0.047	9.8 ± 5.6	12.7 ± 6.8	0.030	10.5 ± 6.9	13.9 ± 6.9	0.022

Table 6. Comparison Parkinson's patients who could and could not make the Tower of Hanoi (*t* test).

In comparing the Parkinson patients who were able to successfully complete the TOH with 3, 4, or 5 discs, consistent differences were found in age and years of education. The successful patients were younger and had more years of education (Table 6).

There were also differences in the CLOX-1 and CLOX-2 scores, with better results for the Parkinson's patients who were able to do those tests. There were no differences in MMSE scores. Likewise, the Parkinson's patients who could not do the test, *i.e.*, those with DS, consistently had significantly lower quality of life as measured on both the PIMS and the SCOPA-Psychosocial. It has been previously shown that DS is accompanied by lower quality of life in Parkinson's patients [22] [23] [24].

One of the limitations of this study is that the CG was different from the PG. They were younger and had more years of formal education, elements which could cause confusion.

5. Conclusions

The TOH provides the right properties of sensitivity, specificity, and others, compared to the CLOX-2. The CLOX-1 and CLOX-2 could be considered screening tools [12], and the TOH recommended as an evaluation of planning, the alteration of which is considered to be a supportive criterion for a diagnosis of DS [25]. It is useful and easy to administer.

We can conclude that DS is frequent in Parkinson's patients; that it is more prevalent than in the general population; that it will be seen in subjects with more years of age and fewer years of formal education; that the MMSE does not show any association with the presence of DS; and that these patients will have a poorer quality of life.

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