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A – Study Design
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Study of unilateral spatial neglect in Parkinson's patients

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SUMMARY

Background: In Africa, few studies are interested in unilateral spatial neglect (NSU) in Parkinson's disease. However, this syndrome is a deficit to detect, respond to or orientate towards meaningful stimuli (Heilman, KM 1973), observable after an injury affecting the non-dominant hemisphere for language. The significant handicap it entails justifies the need for early diagnosis and care. The NSU study is motivated by its link with neurocognitive phenomena that are important on the theoretical level (attention, visuospatial and perceptual awareness). The objective is to study USN in Parkinson's patients, followed and hospitalized at the Neurology Department of Hassan II University Hospital in Fez. The visual-graphic test that has been used to detect this pathology is that of Bell's test. The test focuses on the detection of targets placed among several stimuli on a sheet of A4 paper.

Material/ Methods: The material included 120 people: 60 Parkinsonian patients: 34 men (56,7%), and 26 women (43,3%) and 60 control subjects: 34 men (56,7%), and 26 women (43,3%). The groups were matched by age and sex. Different aspects of neglect have been observed throughout the Bell's test.

Results: It was found that total omission of bell figures was significantly influenced by age, being less frequent in the 35-49 age group in both groups, and higher in the elderly (50-80 years), as well the level of education. It have been reduced considerably with the increase in education. The hand used and the laterality had no effect; t = 3.76 degrees of freedom (df) = 108.27 and p = 0.000.

Conclusions: Unilateral spatial neglect has a negative effect in subjects with Parkinson's disease. It deserves to be systematically sought for a better clinical evaluation and therapeutic management of the patients.

Key words: Unilateral Spatial Negligence, Parkinson's Disease, Bell's test

INTRODUCTION

Unilateral spatial neglect is defined as the inability to detect, orient towards meaningful stimuli when presented in the contralesional hemi-space (Heilman, KM 1973). Unilateral spatial neglect can occur in different forms such as visuospatial, tactile, auditory and can be characterized as mild, moderate or severe. The level of impairment is classified according to the patient's performance on the standard battery. For the last 30 years there has been a great deal of research and debate about unilateral spatial neglect disorder, and its rest still theoretical, neuroanatomical, and cognitive. The interest of unilateral spatial negligence comes from the theoretical questions it poses about neurocognitive activities as complex as mental representation, visual perception, attention, space consciousness on their locations. In terms of public health, unilateral spatial neglect poses significant problems because it aggravates the disability by impeding motor rehabilitation (Appelros P et *al*., 2003; Gianfranco Denes et *al*., 1982; Jehkonen M et *al*., 2000). Dam tests are commonly used in the assessment of negligence. The subject must detect target items distributed on a sheet of paper and bar them (surrounded) with a pencil or pen, using a search strategy for the target items (bells). Compared to the test there are several, we used the Bell's test Gauthier et *al*., 1989 which allows a quantitative and qualitative evaluation of visual neglect in space.

The goal is to understand spatial neglect in Parkinson's patients is to implement a strategy of this screening tool to diagnosed the syndrome at an early stage during Parkinson's disease, with the goal of proposing a remediation method cognitive has a population unfamiliar to the test. Screening for unilateral spatial neglect is an important benefit of evaluating subjects with this pathology. Otherwise screening, rehabilitation and rehabilitation techniques are likely to reduce it, thus improving the autonomy of patients.

Understanding the mechanisms of unilateral spatial neglect and the diagnostic technique is important to provide clinicians with appropriate tools for diagnosis, treatment and rehabilitation. Research on unilateral spatial neglect may further contribute to a better understanding of the brain mechanisms of spatial processing and the neural correlates of perceptive consciousness.

MATERIALS AND METHODS

Framework and population

The study is conducted in the Neurology Department of the Hassan II University Hospital in Fes (Morocco). It includes 120 people from the Moroccan population among which 60 are Parkinson's patients and 60 control subjects. Sociodemographic and Clinical Characteristics of Parkinsonian Patients and Control Subject are presented in Table 1.

Table 1. Sociodemographic and Clinical Characteristics of Parkinsonian Patients and Control Subjects

Variables	**Parkinson Group (*n= 60)***		**Control group (*n = 60)***		***p***
	n	%	n	%	
Sex					
Men	34	56,7	34	56,7	
Woman	26	43,3	26	43,3	
Sex ratio	1,3		1,3		
Age (years)					
Average	58,18±11,57		57,43±11,86		0,727 NS
Median	58		57		
Extremes	17 and 80		17 and 80		
	[35-49]	13 (21,7%)			
	[50-80]	47 (78,3%)			
Laterality					
Right handed	54	90	60	100	
Left handed	6	10	0		
School level					
Illiterate (NI 1)	25	41,7	25	41,7	
Primary (NI 2)	23	38,3	23	38,3	
Middle School High School (NI 3)	10	16,7	10	16,7	
University (NI 4)	2	3,3	2	3,3	
Duration of evolution (year)					
Average	5,68 ±3,7		NA		
Median4	NA		NA		
Extremes	1 and 12		NA		
[1-5]	35 (58,3%)		NA		
[6-10]	15 (25%)		NA		
[10 >]	10 (16,7%)		NA		
Hoehn et Yahr					
Stage 0	0%		NA		
Stage I1	0%		NA		
Stage III	27 (48,33 %)		NA		
Stage IV	3 (5 %)		NA		
Stage V	1 (1,7 %)		NA		
MMS 21, Stage V	1 (1,7 %)	63 ± 3,91	23,72 ± 4,28		0,40 NS

NA: not applicable; NI: level of education.

Inclusion criteria

The study includes Parkinson's patients of all ages, regardless of sex and regardless of education level (school: Illiterate NI 1, Primary NI 2, Middle School High School NI 3, University NI 4), the source. Table I details the socio-demographic and clinical characteristics of Parkinson's patients. Patients (subjects) unable to write (hold a pen) and express themselves were not included in the study as well as visually impaired patients.

The Bell's test

The Bells test was developed by Gauthier, Dehaut and Joanette in 1989. The test focuses on the detection of targets placed among several stimuli on a sheet of A4 paper. The test consists of 315 stimuli including 280 distractors and 35 bell figures, which are target stimuli. During the test, the examiner places the sheet

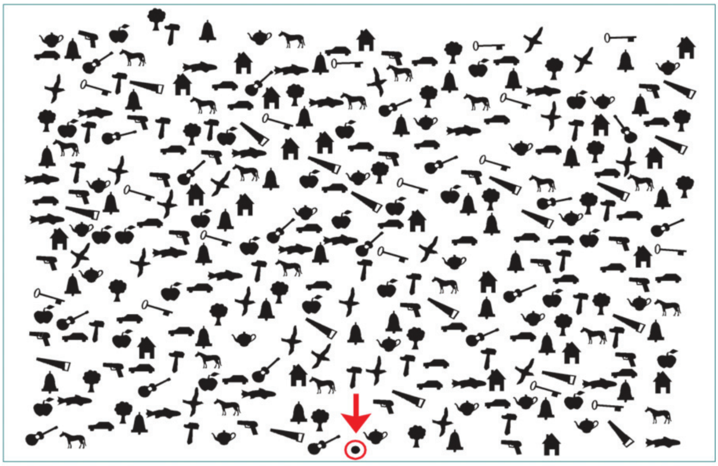

Figure 1: Bell's test, Gauthier et al., 1989

horizontally in front of the subject and asks him to surround with a pen all the bells on the sheet (Gauthier L et *al*., 1989). The bells are distributed randomly within the set of stimuli, divided into 7 columns each with 5 bells and 40 other stimuli. On the left are columns 1, 2 and 3; in the center column 4 and on the right columns 5, 6 and 7. The page is placed on the median line of the patient or subject.

There are 9 types of strategies for finding bells in an organized way: A = from right to left high, B = from left to right high, C = from right to left low, D = from left to right low, E = from top to bottom right, F = from top to bottom on the left, G = from bottom to top on the right, H = from bottom to top on the left, and I = disorganization (Figure 1).

At the end of the test, the rating covers six main variables: 1) the number of omissions of targets in the left side, 2) the number of omissions of targets in the right side, 3) the number of omissions of targets in the middle, 4) the total number of omissions, 5) the column of the first bell surrounded and 6) the time of handover.

A result is considered pathological when: 1) the first dam is after the fifth column, 2) the number of total omissions is greater than 5 for the age group 20-34 years, greater than 6 for the tranche age 35-49, greater than 7 for the 50-80 age group, 3) the difference between omissions (left omissions - right omissions) is greater than 2 or 3 when the number of years of schooling Patient ≤ at 8 years since the preparatory course (CP), 4) the time of completion is greater than 183 seconds (Gauthier L et *al*., 1989).

The mini-mental state

The mini-mental state (MMS) is used to detect major neurocognitive disorder. The Mini mental state is a tool for evaluating cognitive functions in 30 questions. It explores temporospatial orientation, attention, learning, memory, mental arithmetic, language, and praxis. Total score is between 0 and 30, the rating is scored as a result (wrong answer 0 and correct answer 1), the evaluation time is 5 to 10 minutes (Folstein MF et *al*., 1975).

Statistical analysis

In the statistical analysis, the characteristics of the patients and control subjects are expressed as a percentage for the qualitative variables and as an average ± standard deviation for the quantitative variables. Chi-square and t Student tests were used to compare the variables. *p*-value <0.05 is considered statistically significant. The data was analyzed with Excel 2007, the Statistics for Windows Social Science software version 21 (SPSS Inc., Armonk, New York, USA).

RESULTS

Comparisons of the results of the bell's test, between Parkinsonian and control groups is presented in Table 2. It was found that total omission of bell figures was significantly influenced by age, being less frequent in the 35-49 age group in both groups, and higher in the elderly (50-80 years), as well the level of education. It have been reduced considerably with the increase in education. The hand used and the laterality had no effect; t = 3.76 degrees of freedom (df) = 108.27 and p = 0.000.

The difference in left and right omissions (OG - OD) was significant between the two Parkinsonian groups and controls subject, with t = 3.99 ddl = 85.77 and p = 0,000. Omissions are discreetly more important in Parkinson's patients. It was weak, and significant in control subjects. Total selection errors were very rare among subjects with a high level of education, with no influence of the variables.

The handover time was very influenced by age, as it increased steadily with him, especially in the 50-80 age group. By examining the value of the total omission correlation coefficient, r = - 0.327 with p = 0.000 the effect of the relationship between the two variables is large and very strong relationship.

Table 2: Comparisons of the results of the bell's test, between Parkinsonian and control groups

Variables	**Parkinson Group (*n= 60*)**		**Control group (*n = 60*)**		***p***
	n	%	n	%	
Number of total omissions					
Average	13,66±10,30		7,46±7,56		**0,000**
	35 to 499,39±7	552,93±3,40			**0,012**
	50 to 80	14,85±10	718,85±7,96		**0,003**
Difference of omission (OG-OD)					
Average	2,67±2		781,07±1,3		**0,000**
35 to 49	1,62±1,60		0,50±0,650		**0,034**
50 to 80	14,85±10,7		18,85±7,96		**0,003**
Testing time					
Average	171,77±27, 11		118,13±14,95		**0,000**
35 to 49	177,68±24,32		119,86±20,83		**0,000**
50 to 80	170,13±27,85		117,61±12,90		**0,000**

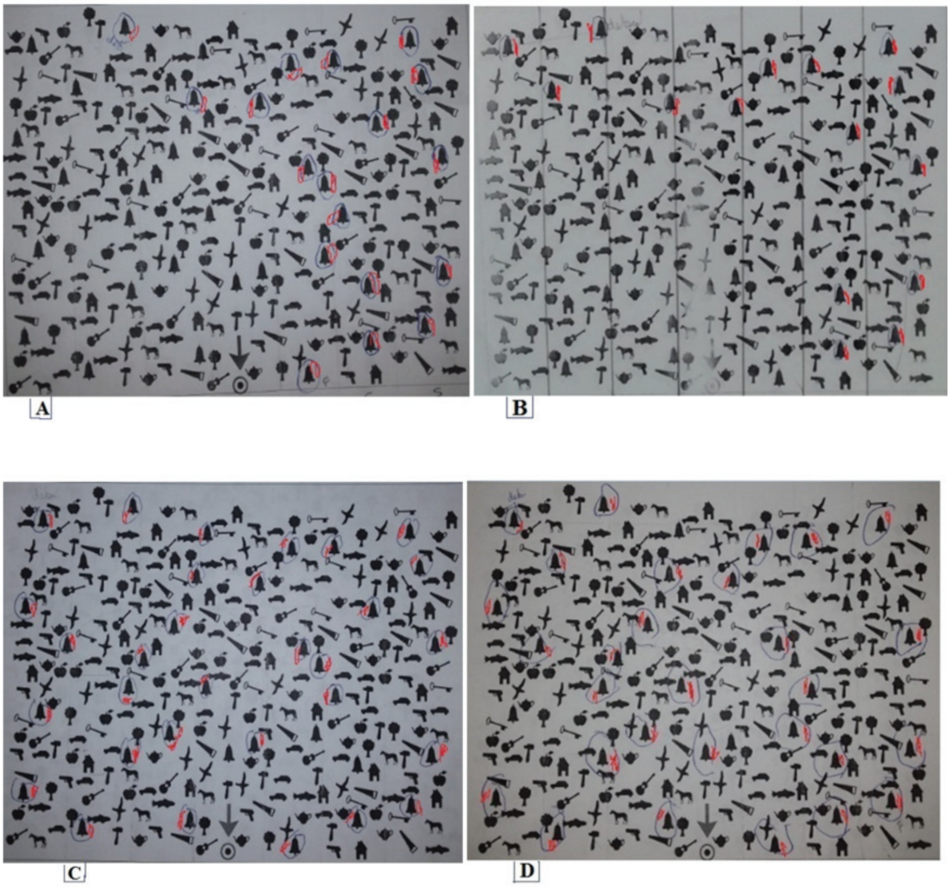

Fig. 2. Examples of the results in Parkinsonian patient and in control subject: A: the result of a 63-year-old Parkinsonian patient with disease duration of 7 years, primary education level N2, and visual scanning strategy E; B: Outcome of a Parkinsonian patient aged 57 with a 3-year disease course, illiterate N 1, and visual scanning strategy B. C: the result of a 68-year-old control subject; Primary education level N2 and visual scanning strategy B. D: result of a 67-year-old control subject; illiterate N1 and visual scanning strategy B

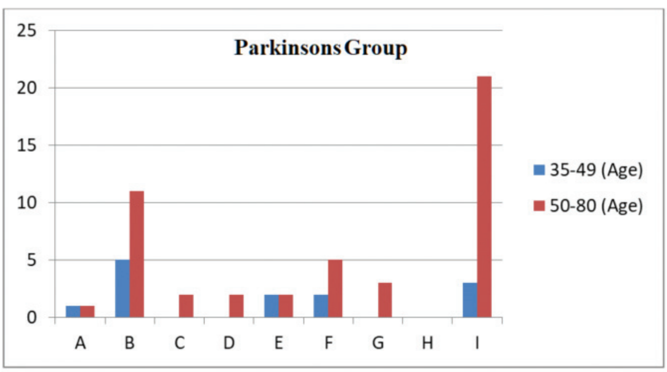

Fig. 3. Visual scan strategy results of the test, in the Parkinsonian group.

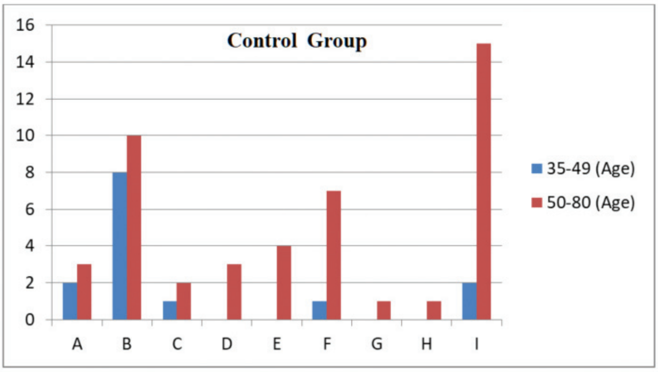

Fig. 4. Visual scan strategy results of the test in the control group

Fig. 2 shows the examples of the results in Parkinsonian patients and in control subjects. The subject should surround (checked) all the bells distributed among visual distractors symmetrically (Gauthier L et *al*., 1989). It was found that the majority of the Parkinson patients began by circling (ticking) the bell located in the first three columns on the left.

Fig.3 illustrates the visual scanning strategy distribution of the bells in Parkinsonian patients, the result showing that a large number of patients use the disorganized strategy that is followed by B. In addition there is lack of strategy H.

Fig. 4 illustrates the visual scanning strategy distribution of the bells in the control group. The results shows that the majority of subject controls, having age range between 35-49 uses visual scanning strategy B, while those of age range 50-80 uses disorganized strategy I, as well as strategy B and F.

DISCUSSION

In this study, two groups of subjects were analyzed, Parkinson's patients and subject controls for comparison of outcomes regarding unilateral spatial neglect, (hand-use, lateralization, attentional and visuospatial performance). We will discuss the main effects observed in Parkinson's patients and the problem of the limits of variation in control subjects, which make it possible to decide on the pathological nature of patient performance.

From our results, it is important to highlight the level of education (school), we found that the total omission increases with the level of education, and age. The higher the level is higher the less omission of the bells. He suggests that lower-level subjects have less control over the quality of their achievement. This result is similar to the study by Rousseaux M et *al*., 2001 and different from the study presented by Gauthier L et *al*., 1992 who observed a weak influence of age and lack of impact of school level. Regarding the time of treatment, in Parkinson's patients the presence of motor disorder including triad, tremor, akinesia and rigidity has an impact on the time of realization. Other studies have emphasized the effect of educational level on the time of achievement, in certain perceptual-motor tasks (Ruff RM et *al*., 1993). The intervention of motor decline in the hand and upper limb Smith et *al*., 1999 appeared unlikely, given the nature of the variable. Other studies have noted the effect of age on omission and time to completion (Lezak M 1995). The analysis of the results shows that Parkinson's patients need more time to perform task tasks compared to control subjects, so have pointed out that Parkinson's respond more slowly and omit more bells than control subjects. In addition, the MMS scores must be qualified by the level of education (schooling). It is noted that a patient or control subject having a low level of education and a duration of evolution of the advanced disease, reduce the cognitive performance during the MMS; similar to the study Christian Pradier et *al*., 2014 which confirms a strong correlation between the MMSE score and education in patients with neurodegenerative disease.

In addition, the difference in average left and right omissions was significant between the two groups. In contrast, Parkinson's patients left and right omission are similar and different from control subjects, as is the study by Vingiano W 1991, who had shown right inattention to spatial stimuli in a dam test. For total omissions, a number greater than 6 for age groups 35 to 49 and greater than 7 for age groups 50 to 80 should be considered a priori to be pathological in most subjects, and if Older subjects and those with low levels of education should be taken into account. These points of information are relatively similar to those of the authors Gauthier and Joanette 1992; Gauthier, L., Deahut, F., Joannette, Y 1989, according to their studies the subjects aged 18 to 28 years did not omit more than 2 bells in each hemi-space (space of the central column not included), those of 50 to 81 years not more than 3. The majority of the patients and subjects controls began to checked (targeted) the bells located in the first three columns, no topics that started beyond.

When performing or evaluating the bell's test, it is important to point out that the majority of Parkinson's patients and control subjects in the age group 50 to 80 have used strategy B and I. there is the lack of strategy H in the Parkinsonian group. Regarding the cognitive performance of the subjects, the maximum number of bells omitted in the visual fields was two and three depending on the level of education (school), so we can say that greater than or equal to two or three, omitted bells may suggest that 'hemi-negligence in the corresponding visual side, corroborated with the study of Oliveira de CR et *al*., 2016 these may be appropriate according to level of education (school) and age. According to Gautier et *al*., 1989 left or right omissions of bells suggest a syndrome of hemi-negligence as well as the total sum of bells omitted.

Our results might be interpreted in the light of microgenetic theory (Brown 2015). It is in the cortex that perception and action reach the level of conscious decision. The brain forms articulated pictures or representations of what is out there in the world, and of what has been out there in the world, and the play of these images constitutes conscious perception. What is more – and this has only recently begun to be a subject of interest for neuropsychology (Pachalska, MacQueen and Cielebak, 2017) – the cortex is capable of forming pictures and/or

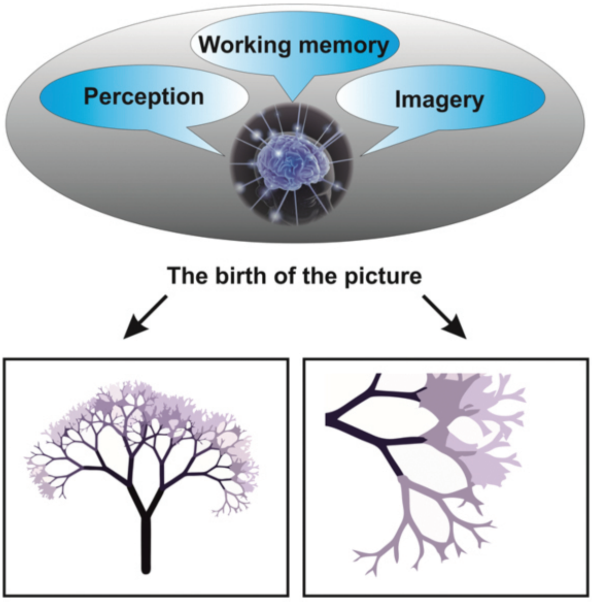

Fig. 5. The direction of brain and organism evolution, in full exteriorization, detachment and modulation of the process of perception
Source: Pachalska, Góral-Półrola, Mueller et al. 2017, with modification

images (see: Fig. 5) of what might be or could be out there, or could have been, or should have been, and was not.

It is not that hard to form a coherent theory of how the brain forms an image of something the eyes are seeing or have seen, but it is quite another thing to explain how the "mind's eye" works in terms of brain structure and function.

For the present purposes, however, the most important fact about the cerebral cortex is that both perception and action at this stage are characterized by detail, discrimination, and analysis. The reptilian brain sees a large moving object, to be avoided, or seized, or ignored; the paleomammalian brain sees a human figure, producing an affect, positive or negative; the cortex sees features, details, a face, and can put a name to it, or not. The complexity of perception results from the fact that these three images come into existence independently and sequentially, though there is only one perceiver and one object, and the entire process takes milliseconds to complete. The conscious mind, then, typically experiences its perception as a single, simple act of seeing. According to microgenetic theory, however, this single act is a multi-layered actualization, the tip of an iceberg that floats to the surface and then subsides, containing within itself the traces of all that has gone before, in phylogeny, ontogeny, and microgeny in norm and in pathology, including unilateral spatial neglect in Parkinson's patients (Pachalska 2019).

CONCLUSION

Screening for unilateral spatial neglect, which, despite its frequency, may go unnoticed and often remains poorly diagnosed in terms of its public health consequences. On the theoretical level, a better understanding of the syndrome will make it possible to propose more adapted models of the normal functioning of space consciousness, processes of mental imagination and visual-spatial attention. On the neuro-anatomical level, the debate begins to evolve thanks to the new imaging techniques (notably MRI), which make it possible to consider unilateral spatial negligence as a pathology of the right hemispheric parietofrontal networks involved in attention and consciousness. from space. It is necessary to emphasize this, that evaluation by standardized tools is important for the detection of attention deficit disorder especially in the diagnosis of unilateral spatial neglect disorder. It would be ideal to multiply the means of detection in the field of unilateral spatial negligence, for an early diagnosis and allowing as soon as possible to put in place a follow-up reducing its impact.

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