Neurobehavioral and Cognitive Disorders in Frontal Lobe Injured Patients

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1. Introduction

The frontal neocortex is the highest stage of a hierarchy of neural structures dedicated to the representation and execution of the actions of the organism (1). Within the boundaries of the frontal lobe diverse functions ranging from fine motor control to working memory and reasoning on to the most complex social behavior are subserved by a number of anatomically distinct regions. Patterns of neural connectivity involving frontal regions critically determine the nature and diversity of frontal lobe-affiliated function (2).

The human frontal lobe comprises the anterior half of the cerebral hemispheres with four primary functional regions: motor area, premotor area, prefrontal area, and deeper in the medial portion is the paralimbic or limbic area. Each of these areas is associated with different functions (3).

The *motor area*, also known as the voluntary area, is in charge of all specific movements in the body, of the voluntary muscles, especially fine movements, such as those of the fingers, and the lips and mouth in speaking and eating. The supplementary motor area is in charge of the coordinated contractions of many different muscles.

The *premotor cortex* or secondary motor area is involved in multiple processes: in the timing of movement, the inhibitory and modulating control of deep motor functions. The posterior parts of this cortex are involved in afferent verbal functions

The *prefrontal cortex* actively participates in attention and vigilance mechanisms and is mainly associated with planning, programming, and predictive capabilities, decision making and problem solving.

The prefrontal cortex is widely connected to the *paralimbic or limbic area*. Lesions in this area are associated with severe affective disorders such as euphoria, impulsiveness and antisocial behavior and so forth due to failure of inhibitory activity from the frontal lobes.

Patients with frontal lobe lesions produced by traumatic brain injury can show specific characteristics ranging from slight exacerbation in personality traits previous to the injury to much more serious changes in these traits. These are described at a clinical level by as pseudo-depressive and pseudo-psychopathic (4). They present a set of well grouped and defined combination of symptoms defined by specific characteristics that fit in with the different frontal syndromes proposed by authors such as Cummings (5), who groups them into three syndromes the orbitofrontal syndrome, the convexivity syndrome and the medial frontal syndrome.

There are other less obvious, although not less important, deficiencies such as the deterioration of the ability to initiate an activity, decrease/absence of motivation, deficiencies in planning, and problems in the development of a sequence of activities that lead to directed behavior of a goal. All of these functions are of capital importance in routines and daily life activities (6,7,8,9).
On the other hand, there seems to be a general agreement that frontal lobe lesions primarily affect executive functions and problem solving capabilities, but there is a serious problem for an objective exploration and diagnosis of the frontal lobe deficiencies. Generally, patients with frontal lesions tend to appear normal in most traditional psychological tests (including intelligence tests) given that most of the tests administered to them are highly structured (10). In frontal patients, deficiencies in cognitive organization are detected when they have to solve problems or organize complex information by themselves and without external help.
This work is a comparative study of executive and problem-solving deficiencies in frontal and non-frontal patients in both highly structured (Wisconsin Card Sorting Test) and little structured (Tower of Hanoi/Seville) neuropsychological tests.

1. Subjects and Procedure

1.1 Subjects

The sample was made up of a total of 40 patients that had survived serious traumatic brain injury, (GCS<9), divided in two groups of 20 subjects each, the first called Frontal Group and the second Non-frontal Group.

The subjects in the **Frontal Group** consisted of 5 women and 15 men, with ages ranging from 13 to 63 and educational levels ranging from 5 to 17 years; they had been in coma for periods ranging from 11 to 47 days; all but three of them suffered lesions derived from an accident related to motor vehicles (twelve motorcycle accidents, four car accidents, three industrial accidents and one person had been hit by a car.)

The subjects in the **Non-frontal Group** also consisted of 5 women and 15 men, with ages ranging from 15 to 44; and educational levels ranging from 5 to 17 years; they had been in coma between 10 and 30 days; 17 had suffered lesions derived from an accident with a motor vehicle (fifteen motorcycle accidents, three industrial accidents, one car accident and one person had been hit by a car).

In table 1 variables for the averages, standard deviation and ranges for age, educational level, Glasgow Coma Scale (GCS) and coma time of the groups (frontal and non-frontal) can be observed.

1.2 Procedures

All of the subjects had been discharged from the Neurotrauma ward of one of the most important hospitals of Seville at least one and a half months before participating in the study.
All of the subjects had suffered traumatic brain injury. Computerized axial tomography (CT) and other neurological data of these subjects confirmed the presence of brain injury when admitted to the hospital.
The subjects of the frontal group showed frontal injury contrasted by the CT. Subjects of the non-frontal group showed brain injury without involvement of the frontal lobes according to the CTs.
Two computerized versions of classic tests were used for assessing functions associated with the frontal lobe. The computerized version of the **Wisconsin Card Sorting Test** (WCST) (11,12) was used. This test was devised to study “abstract behavior” and “shift of set”.

	Frontal Group				Non-frontal Group			
	Age	Educ.	G.C.S.	T. coma	Age	Educ.	G.C.S.	T. coma
M	29.75	9.7	5.9	23.05	25.25	10.2	6.1	18.45
SD	14.07	3.09	1.56	9.58	9.50	3.48	1.483	6.525
R	13-63	5-17	3-9	11-47	15-44	5-7	3-9	10-30

Men: 15 Women: 5

Table 1. Averages, Standard Deviation and Ranges for the subjects' scores in the variables of Age, Educational level, G.C.S. and Time in coma for frontal and non-frontal groups.

Subjects can choose from a set of 64 cards represented on a computer screen each having one to four symbols: a triangle, a star, a cross or a circle, in one of four colors: red, green, yellow or blue. There are no identical cards. The task consists of placing the card one at a time under four stimulus cards, following a principle that the subject must deduce from the pattern of the computer's responses to the placement of the cards. For example, if the principle is color, correct placement of a red card would be under a red triangle, regardless of the symbol or number, and the computer responds positively. The subject starts to place cards and the computer tells him or her if each placement is correct or not. After a determined amount of correct placements in a row, the computer shifts the principle. The only indication of the shift being a change of pattern in the "right" and "wrong" feedback. Testing begins with color as the basis for sorting, shifts to form, to numbers, back to color and so forth. The test continues up until the subject has made the required amount of correct placements.

In the present study, the following dependent variables were used: Total time used in completing the test; average time or temporal average the subject took in responding to each of the items making up the test; errors or mistakes made according to criteria determined by the computer; and the number of categories reached.

The computerized version (40, 13) of the **Tower of Hanoi/ Seville** (14, 15, 16, 17) was also used. This task consists of three different colored beads and three different pegs, displayed on a computer screen. The beads are placed in a starting configuration, and the subjects must move them onto the third peg in the minimum number of moves possible. The subjects must complete this task without knowing about a restriction they must overcome to solve the problem. This means that the subjects are not told of the restriction that they cannot put a large bead over a smaller bead. When they make a mistake, the computer lets them know by emitting a beeping sound and by not allowing the larger bead to be put over the smaller ones. Test administration is the same for all groups and sexes. This test focuses on reasoning, problem solving and learning capacity (18, 19, 20). The task is a transformation problem in which the subject is asked to reach a goal by performing a series of movements using planning strategies (16) in which the subject must build a tower on peg 3 identical to a previously presented tower on peg 1.

The dependent variables studied in the Tower of Hanoi/Seville were: Errors or movements not permitted, the total number of movements and total time taken to complete the test. The errors could be of two types: Type 1 when the subject tries to move a disk onto a smaller one, and Type 2 when the subject tries presses the bar to move a non-existent disk.

2. Results

Statistical analysis of the data was carried out at the Laboratory of Human Neuropsychology of the Department of Experimental Psychology of the University of Seville. This was done using the statistical pack SPSS/PC+ (V.3.3.a.) on an IBM compatible computer.

In order to confirm that the differences in scores in the different tests were due to the independent localization variable of the lesion and not its magnitude, the seriousness of the lesions in both groups was checked as a step prior to analyzing the data obtained in this study. This was done through discriminant analysis of the SPSS/PC+.

The results obtained in the different tests can be seen in table 2 where the averages and standard deviations of the two groups (Frontal and Non-frontal) are presented for each of the variables studied.

For the variables total time (WCSTOT) and total errors (WCSTER) in the WCST it can be seen that the subjects of the frontal group took more total time (obtained higher scores) and made more errors (obtained higher scores) than the subjects of the non-frontal group. The scores of both variables present statistically significant differences given that the variable total time presents $t= -3.22$ ($p=0.003$).

Regarding the average time (WCSTME) and categories (WCSTCA) variables, it can be observed that the group of frontal subjects took more average time (obtained higher scores) than the non-frontal group in executing this task. As to the number of categories, the group of non-frontal subjects obtained higher scores than the frontal subjects in this task. The scores of both variables are statistically important given that subjects obtained $t= -3.16$ ($p=0.003$) in average time and $t= -1.17$ (p=0-040) for the variable categories

In the Tower of Hanoi/Seville tests the scores of variables of total time (TOWTIE) and total movements (TOWMOV) it can be seen that the frontal group took more total time (got higher scores) than the non-frontal group. At a statistical level there exist significant differences in both variables given that total time performance in the tower was $t= -4.13$ ($p= 0.007$) and $t= -2.09$ ($p=0.043$) for the variable total movements.

For the variables errors type 1 (TOWER1) and errors type 2 (TOWER2) of the same test one observes that the frontal subjects made more type 1 mistakes (got higher scores) and also made more type 2 errors (higher scores) than the non-frontal subjects. Significant differences exist at the statistical level in both variables given that type 1 error $t= -4.58$ ($p=0.000$) and for type 2 error $t= 2.42$ ($p=0.020$).

	Frontal Group		Non-frontal group	
	X	SD	X	SD
WCSTOT	857.950	363.238	592.750	119.413*
WCSTME	4.317	1.459	3.072	0.570*
WCSTER	69.500	24.252	47.550	18.520*
WCSTCA	1.650	1.890	2.750	1.832*
TOWMOV	48.65	60.058	20.000	11.872*
TOWTIE	391.95	201.219	188.500	90.107*
TOWER1	12.50	7.900	3.95	2.560*
TOWER2	5.894	10.252	0.35	0.587*

Table 2. Averages and Standard Deviations for the different variables studied in the frontal and non-frontal groups. (*) significant scores at a statistical level)

3. Discussion

The results we obtained in this study are similar to those obtained by other authors.
In the WCST, the variables total time and mean time show significant differences between the groups, suggesting that the subjects with frontal lobe lesions are slower than the non-frontal group in carrying out the task. It seems that this slowness is related to the difficulty frontal patients have in classifying and categorizing.
The second variable studied, total number of errors, shows that the subjects with injury to the frontal lobe lesions obtained a higher score than the group of subjects with non-frontal injury. The subjects with frontal injury were not able to learn to not repeat errors they had made in later intents. In the same way, these subjects did not efficiently use feed-back presented on the activity they had already performed, causing them to repeat the same mistakes over and over again although they were warned that these mistakes were being made. The errors most frequently repeated by frontal subjects are classified as perseverative, a consequence of typical impulsive behavior in frontal lesion patients. Our work coincides with that of Milner, (21, 22) who demonstrated, using the same test, that a group of patients with epileptogenic focal points and its consequent resection in the prefrontal dorsolateral area of the cortex showed a poorer performance on the test than the groups of subjects with injury in other areas of the brain. In Miller's work the variable that best distinguished subjects with lesions in the prefrontal dorsolateral cortex was the number perseverative errors made. In later years different researchers working with groups of neurological patients with different etiologies have confirmed these discoveries using this test.
Drewe (23) reached conclusions similar to ours studying the results of WCST performance in subjects with different cerebral lesionss. He found that subjects with frontal lesions showed significantly more errors classified as perseverations than other subjects. Robinson, Heaton, Lechman and Stilson (24) carried out a study with 132 normal subjects and 8 groups of subjects with cerebral lesions in different areas. In this study the group of subjects classified as normal had fewer persevered answers than the total sample of subjects with injured brains, and within this group, the group with frontal injury performed the task more poorly than the non-frontal group of subjects. Van der Broek and Bradshaw (25) found in their study that impulsive behavior and perseverations are associated with disorders that affect the frontal lobe.
Weinberger, Berman and Zec (26) found a relative increase in prefrontal dorsolateral areas during the execution of the WCST while using Xenon 133 to determine regional cerebral blood flow (rCBF), specifically in the prefrontal right dorsolateral area. Different researchers found many more perseverative errors in subjects with injury to the right frontal lobe when compared to subjects with injury to the same area of the left lobe (24). Overall, the evidence suggests that performance on the WCST, particularly perseverative responses, is especially sensitive to the functioning of the frontal lobe and in particular to that of the prefrontal dorsolateral area.
Referring to the number of categories achieved by each group in our study, the subjects from the non-frontal lesion group obtain more categories (better scores) than those in the frontal lesion group. The experimental and clinical evidence show that subjects with frontal lesions are not able to either categorize or group different elements by the physical characteristics of the stimulus, and if they do, this categorizing is very poor. Patients with frontal lesions have a diminished classifying capability. The ability to change criteria in relation to feedback obtained from the environment is also diminished. Therefore, subjects with these le-

sions will have poor scores in these kinds of tasks. As Glosser and Goodlass (27) point out, poor scores on number of categories indicate deficiencies in response flexibility, self-regulation and attention and, as Milner (22) points out, are specifically associated to frontal dorsolateral lesions.

In a study done by Arnett, Rao, Bernardin, Grafman et al. (28), three groups of subjects were used in which two of the experimental groups presented lesions to the frontal lobe of differing degrees. Upon administering the WCST they found that subjects with frontal damage obtained significantly fewer categories and made more total errors than control group subjects. The number of errors made was directly related to the amount of injured tissue in the frontal lesion subjects groups.

In another study by Corcoran and Upton, (29) comparing the performance of this task in two groups of patients, one with frontal lesions and the other with lesions in the hippocampus, they observed the same results as Arnett et al (28). The explanation these authors accept is that working memory problems presented in hippocampal lesions are also crucial for the execution of this task.

Errors in maintaining sorting strategies can be caused by different deficiencies ranging from secondary cognitive mistakes to simple inattention, or from difficulties in ignoring irrelevant stimuli that disperse attention far from the strategy being used for sorting. These mistakes are evaluated in the test through conceptual answers given by the subject. Luria presented a view of this test and its relation to neurocognitive activity when he wrote, “The regulation of activity directed towards a goal and the modulation of impulsive answers, both activities evaluated with the WCST, are mediated by prefrontal areas” (8).

Lezak (9) maintains that poor performance on the tests can be due to different types of intellectual deficiencies. The subject may have difficulty in doing different sorting activities according to the criteria of the category followed, which could indicate an alteration of concept forming abilities. This problem generally occurs with patients that have an injured frontal lobe, especially those with injury to the left and specifically the medial area of this lobe. Common errors made by subjects with these pathologies concern difficulties in changing classification categories (23).

In reference to the causes of poor performance on the WCST, Fernández-Ballesteros and León-Carrión, (30) state that the causes are an incapacity to form concepts based on an abstraction of elements to classify; inadequate strategies for checking hypotheses; difficulties in changing sorting strategies when the one in use is inadequate; cognitive rigidity or perseveration of categories. These same authors observed that normal subjects would go from one form of sorting to another frequently depending on the nature of the material to be classified. However, Golstein and Scheerer (31) and Hanfman and Kasanin (32), among others, maintain that subjects with cerebral lesions, and generally in the frontal lobe, tend to formulate sorting strategies linked exclusively to just one model of representation of reality. When a subject sorts objects he or she considers rules with common attributes which allow him or her to identify all the members of a given category. Frontal lesion subjects make mistakes because they do not know how to use feedback information. Thus they do not introduce changes in their behavior that helps to discover new sorting strategies.

These same results are confirmed and complemented when the scores obtained by patients in the Tower of Hanoi/Seville are analyzed. The results show that in all of the dependent variables that have been studied in the Tower of Hanoi/ Seville test, subjects with frontal lobe injury obtained higher scores than non-frontal subjects. Similar to the results using the WCST, frontal subjects took longer, used more movements and made more errors. In general, subjects from the frontal injury group showed a poorer performance on the test than subjects in the non-frontal group. These results indicate that the Tower of Hanoi/ Seville is a good tool for the assessment of the ability of a given subject to reach a goal, and the capability to break a global problem into subsets that are more easily solved. This task requires the active search for possible solutions to the problem and requires generating and executing non-routine spatial movement sequences in order to satisfactorily reach the solution. The search for possible solutions takes up an important portion within spatial working memory. The solution must be kept in short term spatial memory and then passed on to the proper motor sequence before being executed. This is the necessary procedure to evaluate the complexity of the prefrontal system. The ability to solve the Tower of Hanoi/ Seville requires modulation and control of the most fundamental cognitive abilities. Problem solving abilities are put to work, activated when a pattern of unusual or new behavior which needs the organization of "sets" of established cognitive abilities is initiated or when we need to change our habits. To solve the Tower of Hanoi/Seville, the initial movement has consequences on the following movement and those of each consecutive movement. Thus, when making a decision to execute a movement considered correct, the subject must keep in mind the localization of each one of the disks and what the next movements to be made are. Subjects must look through interrelated stages, decisions and testing points (10).

The results show that, as a group, the achievements of the non-frontal lesion group reach more sophisticated levels in their strategies. Subjects with frontal lesions have limited capacity for using strategies and their cognitive activity routines, whether habits or automatic, are inadequate to solve the problems they face. This work indicates that in order to reach the final goal in the Tower of Hanoi/Seville, the capabilities to initiate an activity (drive) and to maintain it during the execution time, to establish a plan for this activity, to establish and to direct the proper order of sub-goals, to understand the complexity of the situation, to understand the rules of the task, and finally, to check the established hypothesis, are all necessary. All of these constitute the executive functions.

In the Tower of Hanoi/Seville the total time score can be interpreted as an index of the subjects information processing speed. The lower the scores, the better the system's integrity and efficiency. Shallice (33) proposed that in this test the subjects were required to formulate a plan to reach the correct solution. This plan should include a global solution that is, at the same time, broken down into several sub-goals that should be properly sequenced in order to reach the main goal. This author found specific deficiencies of total time in the performance of this test by patients with left frontal lobe lesions, leading to the conclusion that these deficiencies were due to errors associated with executive planning functions. It seems that patients with frontal injury use more time "thinking" or blocked about the strategies to be followed in order to solve the Tower of Hanoi/Seville. As Golstein, (34), Blumer and Benson, (4), Luria, (8), and Lishman, (35) point out, subjects with frontal injury demonstrate a specific slowness and give apathetic responses when executing this type of task. Also, Alivisatos and Milner, (36) found in their work with this type of patient that there is an increase in reaction times in these tasks.

The total number of movements score may indicate the subject's ability to use learning strategies. This is the most important score to be taken into account when checking the integrity of the prefrontal circuits. The lower the scores, the better the system's learning strategies and the better the use of feed-back mechanisms related to it (37).

Type 1 errors can be interpreted as an index of learning capacity. Type 2 errors can also be interpreted as an index of information on the integrity of the system, indicating that subjects with many errors of this type are unable to comprehend the task presented. An alternative interpretation of Type 2 errors is associated with a high degree of subject impulsiveness (37). Globally, the total number of errors can be associated with direction mechanisms and executive system feed-back. As with the other variables studied, the lower the scores the better the integrity of those mechanisms. This would be in agreement with Shallice's (33) explanation, who, using the test of the Tower of London, established that the nature of errors made by frontal subjects was an indication that they have difficulty establishing a plan of action without being able to establish a proper order of sub-goals.

As pointed out by Owen, Downes, Sahakian, Polkey and Robbins (38), a possible explanation for errors made by these patients is that subjects affected by frontal lesions are incapable of generating, evaluating, refining and/or revising a solution to the problem presented to them before making any movement. Therefore, the inadequate plan they follow leads them to a non-valid solution, generating in turn a higher number of errors and taking much more time to carry out. These authors offer a different perspective and go on to point out another explanation: the capacity of these patients to retain a sequence of spatial movements in short term memory for a period of time long enough to allow them to properly carry it out is altered. They conclude pointing out that these mistakes can also be explained by the incapacity of these patients to transpose a certain cognitive plan to the correct motor sequence, or, that they are simply incapable of executing that motor sequence.

In the model proposed by Egan, (39) it is suggested that errors in searching for solutions to a given problem come from the failure of the working memory to retain the many sub-goals necessary in solving the task. This means that the subjects understand the strategies of reaching the goals, but due to their memory limitations, fail to execute them correctly.

4. Conclusions

The data shows:

1. Subjects with frontal lobe lesions are slow in all areas of cognitive processing. An increase in the level of difficulty shows a higher degree of inability in using strategies.
2. Frontal lesion patients show special difficulty beginning and maintaining certain perceptive abilities and their motor correlates.
3. They present impairment of their ability to formulate concepts, to sort and/or formulate categories in grouping different elements based on their physical characteristics, similarities and/or differences. These classifications, when achieved, are very poorly carried out.
4. Their problem solving abilities are diminished when there is a demand for planning, sequencing and/or performing different tasks directed towards a solution.
5. Frontal lesion subjects are not able to learn from errors they have made when reasoning and problem solving.
6. Frontal patients make perseverative errors due to their difficulty to ignore concepts, categories and/or strategies that have proven to be inefficient in solving the problems presented.
7. They show limited cognitive flexibility.
8. Frontal lobe patients present problems of working memory.
9. Non-frontal lesion patients also show deficiencies in executive functioning, perhaps related to impaired connections with the frontal lobe.
10. Deficits presented by non-frontal lobe are less handicapping than those presented in

frontal patients, and are probably easier to rehabilitate.

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