NEUROPSYCHOLOGICAL CHARACTERIZATION IN CLINICAL SUBTYPES OF AN OBSESSIVE-COMPULSIVE DISORDER (OCD) SAMPLE OF PATIENTS[1]

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SUMMARY

Since the decade of the seventies, several neuropsychological abnormalities in very different cognitive domains have been described among patients with Obsessive-compulsive disorder (OCD). Due to the nature of these abnormalities, it was concluded that possibly the main dysfunction for this disorder was located in the right hemisphere, especially in the frontal cortex; nevertheless this particular brain region was found to be involved in other psychiatric disorders, so neuropsychological results were considered to be of limited precision and it was thought that the diversity in results was not due to the malfunction of one particular brain region.

So it became evident that a new research methodology based in the information processing model with highly specific neuropsychological paradigms of frontal functioning was needed; as well as considering a subtypology based in the cognitive characteristics in patients with the same disorder and similar phenomenology.

Regarding OCD it is well known that the dorsolateral prefrontal cortex is in charge of the regulation of complex actions, executive functions and the elaboration of logical strategies in a problem solving task; so its dysfunction causes a failure in the creation of response patterns and perseverations due to the inability to change a pattern when an alternative response is needed.

On the other hand, obsessions are associated mainly with the anterior cingulated cortex and the basal region of the corpus striatum and its connections with the limbic system, giving place to incapacity to select the relevant information from the environment, which makes the individual perceive irrelevant stimuli as threatening for physical integrity.

By the way, some clinical subtypes have also been identified: contamination/washing, aggressiveness/checking, hoarding, symmetry/order. There is also some evidence of different patterns of brain activation to several visual stimuli related to the obsessive or compulsive object in the clinical subtypes, as shown by functional magnetic resonance image in some regions of the frontal lobe, either dorsolateral, medial or basal and its connections with the basal ganglia, and in some cases thalamus or limbic system.

In the face of all this evidence, the goal of the present study was to find if within this disorder it was possible, through several neuropsychological paradigms of frontal functioning, to find different patterns of execution, considering the clinical subtype and the severity of obsessions and compulsions.

Fifty-eight patients with a diagnosis of OCD were studied; all patients were under treatment at the OCD clinic of the National Institute of Psychiatry Ramón de la Fuente in Mexico City.

Two neuropsychological tests were administered: 1) Trail Making Test (TMT) and 2) Wisconsin Card Sorting Test (WCST). From the Target Symptom List, the clinical subtype was obtained.

After the statistical analysis, we found no differences between the severity of obsessions and the severity of compulsions as measured by the Yale-Brown Scale. Also, we observed three factors concerning the neuropsychological tests, and patients were grouped in four different groups, each one with a distinct cognitive performance.

Through the interpretation of results it was concluded that in a sample of 58 patients with OCD, different groups of neuropsychological functioning where distinguished. In their own, these groups where associated with different clinical subtypes. These results are in accordance with the neurobiological modular organization model of OCD, which sustains the existence of independent systems of cognitive dysfunction that regulate different symptomatic expressions.

Key words: Obsessive-compulsive disorder, Wisconsin Card Sorting Test, Trail Making Test, OCD clinical subtypes, Yale-Brown Severity Scale.

RESUMEN

La metodología de investigación, a partir del modelo del procesamiento de información con paradigmas neuropsicológicos de funcionamiento del lóbulo frontal, permite un estudio más específico de los trastornos psiquiátricos con fenomenología parecida, lo que a su vez permite crear modelos basados en una subtipología de índole cognoscitiva y, por ende, lleva al

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conocimiento de los circuitos neurales involucrados en la manifestación clínica de estos padecimientos.

En el caso del trastorno obsesivo-compulsivo (TOC), la corteza prefrontal dorsolateral se encarga de regular las acciones complejas, las funciones ejecutivas y la elaboración de estrategias lógicas en la resolución de problemas, de tal manera que su mal funcionamiento ocasiona fallas en la creación de patrones de respuesta y perseveraciones por incapacidad de cambiar de patrón cuando se requiere otra alternativa de respuesta.

Por otra parte, las obsesiones se relacionan predominantemente con el cíngulo anterior y la parte basal del cuerpo estriado y de sus conexiones con el sistema límbico, dando lugar a la incapacidad para seleccionar la información relevante del entorno. Esto genera que el individuo perciba los estímulos inocuos como "amenazantes" para la integridad física.

También se han identificado subtipos clínicos de obsesiones y compulsiones, tales como contaminación, lavado, agresividad, comprobación, atesoramiento, simetría y de orden, entre otros, que se han relacionado con distintos patrones de transmisión genética, comorbilidad y respuesta a tratamiento. Además, se han documentado distintos patrones de aumento o disminución, ya sea de metabolismo cerebral o de flujo sanguíneo, en los circuitos fronto-estriados. Con la resonancia magnética funcional también se han encontrado distintos patrones de activación en los circuitos neuronales entre distintos subtipos clínicos, mediante la exposición de imágenes que se relacionan con el contenido de la obsesión o bien con la acción de la compulsión.

Ante esta evidencia, se decidió averiguar si en pacientes con este trastorno era posible encontrar, mediante distintos paradigmas neuropsicológicos de funcionamiento frontal, dichos patrones diferenciales, considerando tanto el subtipo clínico como la gravedad de las obsesiones y compulsiones.

En este estudio participaron 58 pacientes con este diagnóstico pertenecientes a la Clínica de TOC del Instituto Nacional de Psiquiatría Ramón de la Fuente, de los que 24 eran mujeres y 34, hombres. Una vez que los psiquiatras adscritos a dicha clínica confirmaban el diagnóstico obtenido en la cita de primera vez, referían a los pacientes al programa para computadora de Diagnóstico Neuropsicológico Automatizado (DIANA). Se aplicaron en una sola sesión las siguientes pruebas: 1) Trazado con Hitos (TH) y 2) Test de Categorización de Tarjetas de Wisconsin (TCTW).

Con posterioridad a la aplicación de las pruebas a todos los pacientes, se revisó cada uno de los expedientes de la clínica de TOC para obtener el subtipo clínico. En el análisis estadístico de los datos se realizó primero un análisis factorial para disminuir el número de variables y luego un análisis de conglomerados para ver si se formaban grupos conforme a la ejecución de los sujetos en las pruebas aplicadas.

De acuerdo con la ejecución de los pacientes se observó que los sujetos se agruparon en cuatro grupos distintos de desempeño cognoscitivo: el primero tuvo una ejecución muy deficiente en ambas pruebas. El segundo exhibió un desempeño regular en las dos pruebas pero fue mas rápido para terminar el TH. El tercero sólo estuvo constituido por dos pacientes que tuvieron un desempeño muy diferente al del resto, al presentar una ejecución sobresaliente en WCST pero con gran cantidad de errores en el TH. En tanto, en el cuarto de estos grupos, donde se concentraba la mayoría de la muestra, se consideró que su ejecución fue la más característica y su desempeño en ambas pruebas regular, pero más lento en TH. Cada uno de estos grupos de funcionamiento neuropsicológico se relacionó con los distintos subtipos de obsesiones y compulsiones, mas no con su gravedad.

Encontrar subtipos neuropsicológicos de TOC asociados a sintomatología clínica distinta presta apoyo al modelo de organización modular de los diferentes circuitos neurales que intervienen en la manifestación sintomática de este padecimiento.

Palabras clave: Trastorno obsesivo-compulsivo, Test de Clasificación de Tarjetas de Wisconsin, Trazado con Hitos, subtipos clínicos de TOC, Escala de severidad de Yale-Brown.

INTRODUCTION

Since l970, as a part of the neurosciences, neuropsychology has contributed to the study of cognitive alterations in obsessive-compulsive disorder (OCD), by proposing the frontal left region as the dysfunctional area in this entity (11).

Following this particular finding, several researches were published which pointed out failures in different areas, such as motor and tactile functions, psychomotor coordination (16); visual information processing (5, 8, 12, 16); visuo-spatial perception (10, 25, 41), and handling of spatial information in relation to one's on body (5). On the other hand, it was found in the mnesic activity a deficit in visual memory regarding retention as well as recognition (8, 10, 12, 16), reasoning (25), intellectual processes (12), and performance of interference tasks that imply selective attention (21).

Due to the nature of the mentioned alterations, it was concluded that probably the dysfunction present in this disorder could be found in the right hemisphere with predominance in the frontal cortex. Nevertheless, this cerebral sector is also involved in other psychiatric diseases, and thus these findings were interpreted as scarcely accurate, and it was considered that the diversity of alterations was not caused by the ill-functioning of a particular structure (36, 39).

Therefore, it was needed to create another research methodology that would start from the model of the information process, with specific neuropsychological paradigms of frontal functioning that should include a series of subtypes based on the cognitive characteristics present in patients with the same psychiatric disorder and a similar phenomenology (19).

In the case of OCD, it is known that dorsal lateral prefrontal cortex (DLPC) is in charge of regulating complex actions and of elaborating logical strategies in problem solving, in a way that its dysfunction causes failures in creating response patterns, and also produces persistence due to the incapability to change patterns when another alternative for responding is required. Besides, its connection with the dorsal lateral part of the caudate nucleus -a region where behavioural fixed patterns are associated- causes this circuit to be related with certain compulsions of recurrent nature and with

the incapability to change a given response on behalf of another more adequate and adaptative (1-3, 35).

At the same time, obsessions are predominately associated to the anterior cingulum, the basal part of the striate body and its connections with the limbic system, giving place to incapability in selecting relevant surrounding information, a fact that causes the subject to perceive harmless stimuli as "threatening" to physical integrity (35, 40).

In this manner, it is proposed a model that may be applied to OCD, in which the anterior sector of the cingulum is in charge of detecting errors in the surroundings through selective attention, and at the same time, inhibits the behaviours taking place at that very moment and "indicates" to the dorsal lateral prefrontal cortex to participate in solving the problem that is present (2, 9).

Some clinic subtypes have also been identified, such as contamination/washing, aggressiveness/verification, accumulation, symmetry/order, which in turn have been related with different patterns of genetic transmission, co-morbidity and response to treatment. Different patterns of increase or decrease have also been found either of cerebral metabolism or blood stream, in the frontal striated circuits, according to the clinic subtype (33, 37).

On the other hand, using functional magnetic resonance in different clinic subtypes and through exposure to images related to the object of obsession or compulsion, different patterns of activation in the neural circuits have been reported, which involve different regions of the frontal lobe, either dorsal-lateral, median or basal and its connections with the basal ganglia, the thalamus or the limbic system. The former suggests that this disorder should be considered within a multiple and diverse scope of overlapping syndromes, instead of taking it as a unitary nosology entity (22, 23, 30).

Facing this evidence, the objective of our work was to investigate the probable existence of neuropsychological subtypes by using different paradigms of frontal functioning, in a group of patients with OCD, attending to their clinic subtype, as well as to the severity of their obsessions and compulsions.

MATERIAL AND METHOD

Subjects. The study was done with a sample of 58 patients with ODC diagnose, who attended the Clinic for this disorder of the Instituto Nacional de Psiquiatría Ramón de la Fuente. The sample was integrated by 24 women and 34 men, with an average age of ll.98 (SD=2.92). Two weeks before evaluation (average time for appointment), all patients had already started pharmacological treatment, mainly with inhibitors of serotonine recapture (N=46) and tricyclics (N=12). From the total of patients only 17 were taking benzodiazepines.

Procedure. After the diagnose received at the first time visit was confirmed by the psychiatrists assigned to the OCD clinic, patients were referred to a neuropsychologist experienced in computer evaluations, who applied to them the neuropsychological battery called Diagnóstico Neuropsicológico Automatizado (DIANA) (24), and who had no information either regarding the classification of OCD's subtype or of the severity of obsessions and compulsions, obtained through the Severity scale of Yale-Brown (13). These tests were done in one only session.

Instruments applied. Two paradigms were applied to confirm the research objective: Trail Making Test B (TMTB) and the Wisconsin Card Sorting Test (WCST).

1. The TMTB explores the frontal-striated system functioning. Specifically, it evaluates visual search, mental flexibility and motor function. In this paradigm are shown diverse circles with letters and numbers in the inner part, and the task consists in joining these circles with lines, in such a way that the alternating sequence continues successively between number and letter: 1, A, 2, B, 3, C… etc., until ending with the circles that appear on the screen, during a time limit of three minutes. The following variables are considered: time of performance, number of wrong answers and number of asserts (20, 24).
2. The WCST, created by Berg and Grant in l948 (15) to evaluate abstract reasoning, is composed by a set of cards that have three characteristics which, in turn, have four values each: a) type of image (triangle, star, cross and circle); b) colour (red, yellow, green and blue); number of figures (from one to four). Each card must be assigned by the subject to one of the four "model" cards represented by a red triangle, two green stars, three yellow crosses and four blue circles (20). The subject must complete successfully ten items, according to either one of the three finished categories: colour, form and number. This sequence is repeated twice in this order. From this test the following results were taken: cards presented, concluded categories, preseverative errors, number of errors and errors to maintain category. Two specific measurements were also considered in the same test: the number of perseverative errors and the errors to maintain category. The first one is a cognitive flexibility measure realized by the dorsal-lateral prefrontal sector, and the second is useful to explore working

memory, associated with the anterior part of the cingulum (15, 20).

Following the application of tests, the files of all the patients in the OCD Clinic were revised in order to obtain the clinic subtype. We used the "Target symptoms list" where the patient informs verbally which are the three obsessions and the three compulsions most important to him or her. Obsessions are classified as aggression, contamination, sexual, accumulation, religious, symmetry and somatic. Compulsions could be cleanliness and washing, revision, counting, arrangement, keeping or collecting, mental rituals, motor rituals and means to avoid damage.

The punctuations of the Yale-Brown scale were obtained also. This scale was applied once the patient was considered as part of the OCD Clinic.

Data analysis

To explore if there were significant differences between the different punctuations (obsessions and compulsions) in the Severity scale of Yale-Brown, the *t* test for related samples was employed.

Through the Statistics package for social sciences (SPSS) (38), a factorial analysis was done with the variables selected in the WCST and in the TMTB, with the purpose to decrease them. Afterwards, a conglomerates analysis was done to find out if, from the factors found, the groups were formed according to the subjects' performance in the tests applied.

The Kruskal-Wallis test was used to find out if there were differences regarding age and schooling in the groups that were formed.

Finally, to find out if there was an association between perseverative answers and errors to maintain the category of WCST, and the severity of obsessions and compulsions obtained by the Yale-Brown scale, the Pearson correlation coefficient was calculated.

RESULTS

No differences were found as to age and schooling by applying the Kruskal-Wallis test. Besides, ages of evolution as well as gender were distributed equally in the four groups.

Figure l shows percentages of each symptom subtypes, either for obsessions (part A) or compulsions (part B). As the same patient could present three subtypes of obsessions and compulsions, percentages were calculated based on the frequency of each subtype in respect to the total sample.

On the other hand, no significant differences were found between punctuations (obsessions and compulsions) with the Severity scale of Yale-Brown.

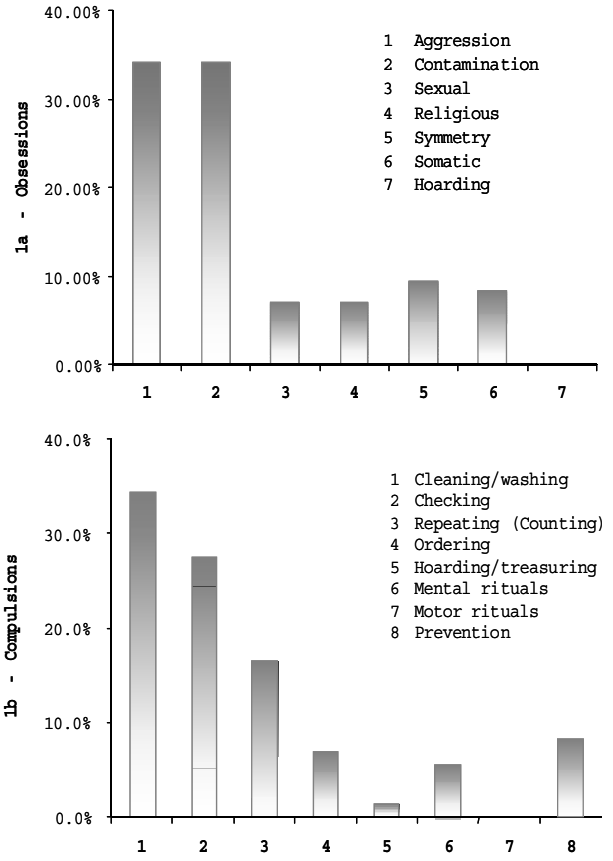

Fig. 1. Percentage, with respect to total, of the main obsessions and compulsions obtain through the Target Symptoms List of the patients in sample.

Through the factorial analysis three factors were obtained which explained 80% of the variance; the first corresponded to the WCST and included the following variables: number of cards presented, perserverative errors, number of errors, and errors to maintain category. From the TMTB, two factors were obtained: one for the number of wrong answers and the other for the time of execution (fig. 2).

According to the patients' performance and through the analysis of conglomerates, it was observed that subjects formed four groups, and according to the factorial values obtained, it was considered that their performance had been deficient, regular and adequate (fig. 3).

GROUP 1 (N=8) represented 14% of patients. In six of these eight patients, contamination obsessions were prevalent (75%), while in four (50%) washing compulsions prevailed. This group performed erroneously in the WCST; at the same time had more errors in TMTB and took longer to perform. In short, performance was deficient in both tests.

GROUP 2 (N=11) constituted l9% of the sample and showed dominance of obsessions of aggressive type in 55%. This group had a regular performance in

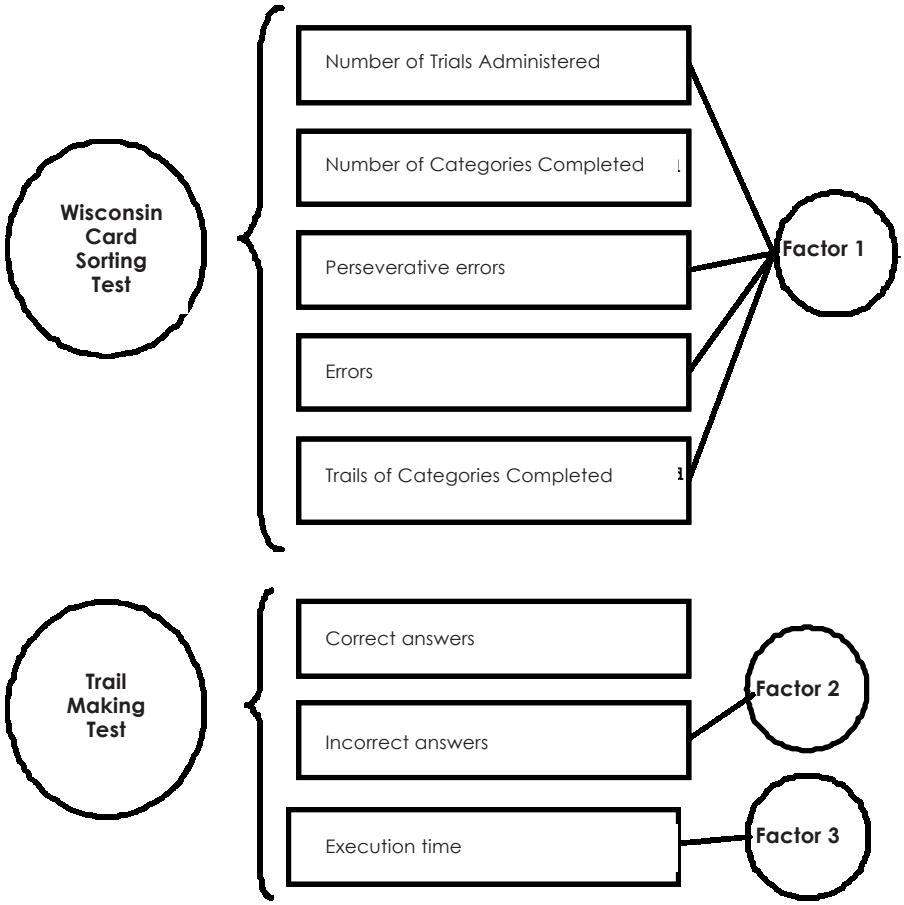

Fig. 2. Evaluated variables in each test and how they were grouped afterwards in a factor analysis.

both tests in comparison to the rest; nevertheless, it was the faster to finish the TMTB.

GROUP 3 (N=2) included 3% of the patients. Apparently, these two patients did not have common characteristics, but were quite different from the rest of the sample in the sense that they obtained an outstanding performance in the WCST, although they were slow and made more mistakes in the TMTB.

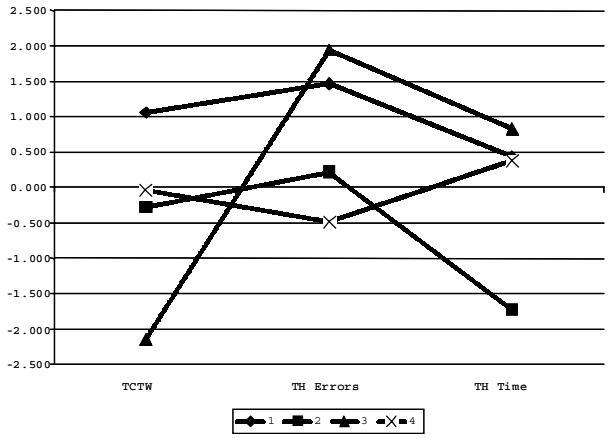

Fig. 3. Execution, as according to factorial punctuation, of each one of the for groups in each one of the three factors.

GROUP 4 (N=37) represented 64% of the sample. In these 37 patients it was found that 54% showed obsessions and aggression as prevalent, while 41% presented washing compulsions. Surprisingly, the former were combined in 20% with washing compulsion, while the latter were combined with different kinds of obsessions. The four patients who were strictly obsessive were placed in this group. Data suggests that independently from clinic characteristics and subtype, this would be the typical execution pattern of this sample of OCD. Performance shows that in both tests their execution was regular but slower in the TMTB.

Table 1 shows for each group the average values of punctuations in obsessions and compulsions obtained through the Yale-Brown scale. This scale also shows the outstanding similarity of severity present in obsessions as well as in compulsions in the four groups. In group 3, apparently, compulsions are dominant although it must be remembered that only two subjects integrated this group.

No relevant correlations were found, when the coefficient of correlation of Pearson was used to find out if there was an association between perseverative answers and errors to maintain category of the WCST,

TABLE 1. Average values of the obsessions and compulsions punctuations (Yale-Brown Scale) obtain in each group

Group	*Yale-O*	*Yale-C*
1	11.6	12.1
2	12.6	11.4
3	8.5	11.5
4	12.9	12.8

TABLE 2. Pearson's correlation coefficient values obtain between obsessions and compulsions' severity (Yale-Brown Scale) and the number of perseverative errors and failures to maintain set (Wisconsin Card Sorting Tests)

	Obsessions	*Compulsions*
Perseverative errors	0.171	0.206
Failures to maintain set	-0.076	-0.013

with the severity of obsessions and compulsions obtained through the Yale-Brown scale (table 2).

DISCUSSION

First of all, it is concluded that in a sample of 58 patients with OCD, different groups of neuropsychological deficit were found, a fact that, in turn, indicates a neurobiological dysfunction which is different within the same psychopathological entity.

Of the four groups that were formed, the first one showed relevant difficulties to execute both tasks, as compared to the other three groups. This could be related to the fact that this pattern may be due to failures in operation of the prefrontal dorsal-lateral sector as well as of the frontal-striated circuit. It must be stressed that this group had a larger percentage of individuals with contamination obsessions (75%) and washing compulsions (50%). Probably, this coexistence of cognitive deficit is related with the incapability to respond to these tasks, and denotes a greater dysfunction that implies an alteration in self-regulation combined with incapability for premise reasoning, and gives place for associated compulsion and obsession. Still, this can be related to the fact that some actions that are partly automatic -such as cleaning- are not inhibited, and the subject is unable to regulate them.

The second group attained a regular performance in both paradigms, comparable to the last group's, although it was faster at the task of tracing lines from target to target, thus implying motor response and visual following in a partly automatic sequence. In this sense, there was more evidence of a dysfunction at a prefrontal dorsal-lateral level, due to the failure in self-regulation of which this sector is in charge, which is associated with a greater impulsivity to carry out the task.

Besides, it was found that 55% of the patients had obsessions of aggressiveness, which leads us to think that this dysfunction could also be related with the attempts of such sector to inhibit the operation of these impulses (17, 18).

The third group was formed by two patients with a very different performance from that attained by the other three groups, in such a way that it would be difficult to draw conclusions.

In contrast, the last group, which included the majority of patients, had a regular performance in both tests though it was slower in carrying out the TMTB, a fact that would involve a greater commitment of the frontal striated circuit. This agrees with what has been mentioned in different researches which constantly have found deficiencies in this cortical-subcortical circuit (1, 4, 6, 7, 17, 27-29, 32, 33, 37), where the striated body appears as a structure related with habits or semiautomatic actions that allow the species survival, as would be the case of personal hygiene (7, 17).

In patients of this group, 41% of washing compulsions were observed, in such a way that the action of cleaning would appear as uninhibited and pathological, resulting from a dysfunction in this area. The fact that this group is the largest of the sample suggests that, independently from any clinical characteristic or subtype, that would be the execution pattern more representative of this OCD sample.

On the other hand, at first it was considered also the possibility of finding the relationship between the disorder's severity and the different kinds of neuropsychological failures. Nevertheless, when analyzing the results it was found that most of the sample had been formed by patients with similar severity for both symptoms; only 4 of the 58 patients (3%) were exclusively obsessive, and thus it is not possible to establish such relationship.

Besides the fact that in this type of patients the WCST variables form only one factor -that is, they do not discriminate between processes associated with the cingulum and with the dorsal-lateral cortex- may also be attributed to the sample being formed by patients who had obsessions as well as compulsions whose severity was similar. This would explain the absence of a significant correlation between these WCST variables and the values in the severity scale of Yale-Brown.

The findings in this sample, in a neuropsychological sense, are similar to those of Prichep, who demonstrated the existence of two electroencephalographic subgroups in a sample of patients with OCD, homogeneous from the clinic point of view: one is typified by an excess of theta relative potency, particularly in frontal and frontal-temporal regions, and the other by an increase of alpha relative potency (31).

In this manner, our findings acquire relevance by considering the type of dysfunction prevailing in each patient, either in prefrontal (PFDL) or orbit-frontal (OF) regions, as a means for selecting the more convenient pharmacological treatment, making an accurate prognosis, and considering therapeutic alternatives within a cognitive-behavioural approach. In this sense it has been observed that inhibitors of serotonine recapture (ISR) have a better effect in patients with a dysfunction in sector PFDL, differently from those with OF alteration (26).

These results are not due to pharmacological effects, as it has been possible to confirm that neuropsychological alterations appear with or without pharmacological handling, and, on the other hand, are not secondary to symptoms. Therefore, they are considered as a trait of the disorder or as a phenotypic characteristic (23, 26). Besides, on average, patients had initiated treatment two weeks before the application of DIANA; therefore, it is more difficult to attribute such failures to medical therapy.

Finally, to typify cognitive deficits may shed light on neuroanatomic localization and on therapeutic approach and, if combined with functional images, it can contribute to attain more accuracy in regard to the brain's topography through an adequate selection of frontal paradigms, and of their correlation with other studies of paraclinic nature.

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