

Inhibitory Control and the Resistance to Interference With dementia of the Alzheimer Type Patients of Different Degree of Severity.

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Abstract

Dementia of the Alzheimer type, which is going to be referred as DAT from now on this paper, is a neurodegenerative disease that produces memory disorders, along with other cognitive functions such as attention. The inhibitory control and the resistance to interference is defined as the ability to inhibit or suppress a behavioral tendency, which occurs automatically. The objective of the research was to analyze the inhibitory control and the resistance to interference in patients who were classified according to different degrees of severity. The sample consisted of 50 participants, 17 in mild phase, 17 in moderate phase, and 16 in moderately-severe phase and 60 subjects without cognitive impairment, which are to be referred as SWCI from now on in this paper. The results demonstrated that the subjects with moderately-severe and moderate DAT have worse yields in the inhibitory control than the subjects in mild phase. In addition, the results show that the inhibitory control follows a downward trend which affects in a greater way to severe and moderate DAT patients. The trend is constant in mild and moderate DAT patients in comparison to the SWCI. These results have not been affected by the age variable. In relation to the resistance to interference, this is greater in severe and moderate DAT patients while this decreases dramatically in moderate DAT patients, in comparison to those in mild phases and in the SWCI, and it has not been affected by the age variable.

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I. Introduction

Dementia is one of the medical challenges of the XIX century due to the socioeconomic problems that triggers. DAT is the first cause of dementia and affects 200,000 people under 65 years old and 5 million over 65 (Alzheimer's Association, 2015). The DAT rate in Europe was of 5,05%, being 3,31% in men and 7,13% in women in 2017 (Niu, Álvarez-Álvarez, Guillén-Grima, Aguinaga-Ontoso, 2017).

The DAT consists of a clinical pathological and neurodegenerative condition, which is irreversible and progressive, with an insidious start that affects

the episodic memory as the most common symptom along with severe alterations in the behavior (Merino, Sendin & Osorio, 2015; Muñoz-Neira, Slachevsky & López, 2016). In addition, the neuropsychological DAT profile is characterized by the alteration of the attentional procedures and the occurrence of executive dysfunctions (Weintraub, Wicklund, Salmon, 2012).

Attention can be defined as a neurocognitive ability that allows someone's concentration in a stimulus while other distractions or natural stimuli irrelevant for the task are ignored. The selective, sustained, alternating attention and other processes

related such as the inhibitory control and the resistance to interference, which is defined as the ability to inhibit or control deliberately a behavior, a thought or an automatic response according to the situation (Moraine, 2014).

This study took as a reference the Diamond (2013) executive functions model which states that the inhibitory control consists of the sensibility towards the interference, which includes two subprocesses: cognitive inhibition and selective attention (Figure 1).

The inhibitory control and the resistance to interference is one of the executive factors affected in the DAT (Collete, Van der Linden & Salmon, 1999). Some researchers have shown that DAT patients have more problems in the inhibitory of the main responses, increase in the reaction time and in the number of errors than people without cognitive decline (Belleville, Rouleau, & Van der Linden, 2006).

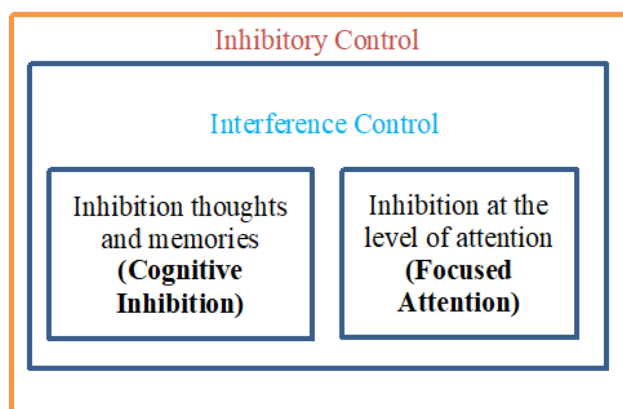


Fig. 1. Inhibitory control and the resistance to interference control model, based on the Diamond model (2013).

The Stroop test studies have displayed that DAT patients take more time doing it, make more mistakes and show inhibitory difficulties (Amieva, Lafont, Rouch-Leroy, Rainville, Dartigues, Orgogozo, & Fabrigoule, 2004; Bélanger, Belleville & Gauthier, 2010; Vasconcelos et al., 2014). It has been proved that the number of errors in the Stroop

test can predict from those who do the test who are likely to develop DAT (Balota, Tse, Hutchison, Spieler, Ducheck & Morris, 2010). Therefore, it can be a good reference in the DAT initial phases (Hutchison, Balota & Ducheck, 2010), although there are not studies that analyze and compare the inhibitory control and the interference resistance in DAT patients with different degrees of severity.

1. General Objective

Analyze the inhibitory control and the resistance to interference in DAT patients with different degrees of severity.

1.1. Specific Objective

- 1) To analyze inhibitory control in DAT patients with different degrees of severity, compared to SWCI.
- 2) To identify the resistance to interference in DAT patients with different degrees of severity, compared to SWCI.
- 3) To determine the influence of age on inhibitory control and the resistance to interference in DAT patients with different degrees of severity, compared to SWCI.

II. RESEARCH DESIGN

The methodological design of the non-experimental, cross-sectional study in this research follows different stages.

-Firstly, participants or their relatives when corresponding were asked for their consent by signature about the following information: the propose and the methodology to be used were described, participation is to be voluntary and the cost is free. The participants' right to refuse to take part of the study or to retire from it at any moment without having to give any explanation for it. Participants are not to be exposed to any physical harm nor to be economically compensated for their

participation. And the participants' personal information is to be confidential to which only researchers of this study are to have access. Whole process counted on the Ethic committees and the Psychobiology Psychology Department and the Behavioral Science Methodology Department at Universidad de Salamanca assessment and approval.

- Once the participants gave their consent, the DAT patients were selected from the Centro de Referencia Estatal de Atención a personas con Enfermedad de Alzheimer (Salamanca) and Centro San Rafael, Asociación de familiares de pacientes con Alzheimer (Ciudad Real).

- In order to register the biographic information, an anamnesis was carried out. Then the neurophysiological assessment process was applied beginning with the application of MMSE and CAMCOG to determine the cognitive level and the scale to determine the degree of severity in the dementia frame (Reisberg, Ferris, De Leon, & Crook, 1982).

The following evaluation tests were applied.

Frontal assessment battery- known as FAB

Brief assessment battery of the frontal lobe functions. The battery consists of six subtests: Similarities that measures the abstract reasoning; Lexical fluence that measures the cognitive flexibility; motor series that assess the motor programming; conflictive instructions value the interference sensibility; inhibitory control measures the Go/No Go ability and environmental autonomy that measures the context dependency.

The conflictive instructions subtest and inhibitory control subtest variables are the ones recorded in this study. In relation to the conflictive instructions subtest which measures the sensibility towards the interference and is characterized because the participant has to hit the table with his finger twice when the examiner hits the table once and the participant has to hit the table once when the examiner hits it twice. However, in the inhibitory

control subtest, the participant has to hit the table once when the examiner hits it once, and the participant does not have to hit the table when the examiner hits it twice, this task is called Go-No go. The battery shows a high accuracy among observers ($k = .87$; $p < .001$), an appropriate internal consistency ($\alpha = .78$) and an appropriate discriminative validity among frontal disfunction and average patients (89,1%)(Dubois, Slachevsky, Litvan & Pillon, 2000).

Stroop. The colors and words tests

This test is commonly used to assess the complex attention processes such as the inhibitory control and the resistance to the cognitive interference. The test consists of three subtests: the first one consists of the reading of colors names written in black ink (first subtest), the saying of the color of impression of some letters XXXX (second subtest) and saying the color of impression of the names of the colors, making obvious the verbal content when the verbal content with the verbal impression is never coherent (third subtest). The total number of the stimuli along the temporal interval of 45 seconds is recorded in each condition. Those in which the participants make an error are interrupted and a new execution of the element is carried out.

The interference of the third condition or “Stroop effect” is based on the premise that the lecture of words is an automatic verbal response that competes or interferes with the lecture of colors, so in an incongruous situation that automatic process should be inhibited or suppressed so as to favor the color denomination. A higher score in the third condition means lower interference susceptibility. For the study the following variables were studied: punctuation obtained in the relation word-color and the score in the Stroop interference condition (Golden, 1994).

A software IBM SPSS statistic, 22 version has been used to apply different technical and statistics

testssuch as the Kolmogorov-Smirnov (K-S) which determinates the model adjustment to the normal distribution; the Levene test which verifies the homogeneity of the variances; the difference of means in independent samples tests; T of Student and one-way Anova, Ancova and the non-parametrical alternative tests as U of the Mann Whitney and Kruskal-Wallis.

III. SAMPLEDESIGN

An intentional non-probability sampling was carried out. The DAT participants might accomplish several inclusion criteria: be from 50-99 years old, have at least 5 years of education, do not have neurological, neurosurgical and/or psychopathological proved dysfunctions, do not show level of previous drugs or alcohol consumption, have a dementia clinical diagnostic carried out by a specialist doctor in neurology; accomplish with the dementia criteria diagnosisestablished by the DSM-V (APA, 2013);

accomplish with the Alzheimer disease criteria diagnosis established by the NINCDS-ADRDA(McKhann et al., 2011); do not show an evolution of more than ten years, obtain a punctuation $24 <$ in the Cognitive mini mental exam Spanish adaptation MMSE (Lobo, Sanz, Marcos & ZARADEMP, 2002); obtain the score $=69 <$ in the Cognitive Cambridge Exam Spanish adaptation (López-Pousa, Llinás, Amiel, Vidal & Vilalta, 1990).

The DAT patients group consists of 50 participants, of whom 17 are in mild phase, 17 in moderate phase, 16 in moderately severe phase and 60 subjects without cognitive impairment, called SWCI. A comparison of the three groups in the sociodemographic variables has been carried out to state if there are internal differences among the subgroups. As it can be observed non-meaningful differences have been found ($P > .05$) (table 1)

Table 1. Comparative analysis. Sociodemographic characteristics of the DAT groups of different degree of severity.

Variable	Category	Mild (N=17)	Moderate (N=17)	Moderately severe (N=16)	Statistics	DF	P
GENDER	Woman	76.5%	70.6% (12)	75.0% (12)	$\chi^2 = 0.16$	2	.921 NM
	Man	23.5% (4)	29.4% (5)	25.0% (4)			
AGE		80.88 ± 5.75	79.24 ± 6.76	78.75 ± 9.43	$F = 0.38$	2;47	.687 NM
MARITAL STATUS	Married	47.1%	70.6% (12)	37.5% (6)	$\chi^2 = 3.87$	2	.145 NM
	Widower	(8) 52.9% (9)	29.4% (5)	62.5% (10)			
LEVEL OF EDUCATION	First studies	64.7% (11)	88.2% (15)	75.0% (12)	$\chi^2 = 4.62$	4	.329 NM
	Second studies	23.5% (4)	5.9% (1)	6.3% (1)			
	University studies	11.8% (2)	5.9% (1)	18.8% (3)			
YEARS OF		8.41	7.06 ± 3.27	8.31 ± 4.73	$F = 0.64$	2;47	.530

SCHOOLING		±3.48					NM
PROFESSION	Housewife	29.4% (5)	41.2% (7)	37.5% (6)			
	Worker	41.2% (7)	29.4% (5)	43.8% (7)			
	Skilled worker	11.8% (2)	11.8% (2)	6.3% (1)	Chi ² = 3.67	8	.886 NM
	Freelance worker	11.8% (2)	11.8% (2)	-			
	Specialist worker	5.9% (1)	5.9% (1)	12.5% (2)			
MANUAL DOMINANCE	Right-handed	100% (17)	88.2% (15)	100% (16)			
	Left-handed	-	5.9% (1)	-	Chi ² = 4.04	4	.400 NM
	left and right handed	-	5.9% (1)				

NM. = Non-Meaningful (P>.05)

Abbreviations: DAT = dementiaAlzheimerstype; DF, degree of freedom; N, Sample; P, p-value`sig

Therefore, the 110 participants are similar in all of the socio demographic variables. However, differences have come out in the age variable given the fact that the comparison group people are younger than the DAT group, difference that is estimated in 95% confidence interval between 5.6 and 11.64 years. Because of that it can be stated that the groups are not equivalent in this variable, so it does not modify the analyses carried out to study.

IV. RESULTS

The conflictive instructions subtest score (FAB).

In the comparison of the degree of severity cases meaningful differences are obtained in the effect size (F=29.30; P<.001) (table 2). In the multiple contrasts by pairs, the moderately-severe DAT cases have a minor mean than the mild DAT cases (P<.01). In the multiple contrasts by pairs, it is detected that the DAT cases of any phases always have a minor mean (P <.01) than the SWCI (Figure 2). Also, the moderatelysevere DAT cases have a minor mean
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that the mild DAT ones (P<.01).The age control shows that this is non-meaningful (P>.05) and it does not affect the previous analyses (F=21.72; P<.001) although it reduces the effect size (.383) (Table 3).

The Inhibitory Control subtest score (FAB).

When comparing the degree of severity with this test the statistical signification keeps the same (F=36.90; P<.001) and the magnitude of the effect size increases sensibly (.511) (table 2). The pair tests point out that the moderate and severely moderate DAT have a minor mean than the mild DAT ones (P<.01).

The pairs tests show that the any phases DAT cases always have a minor mean (P<.01) in relation to the SWCI, where a huge difference is obtained between the conflictive instructions subset and the inhibitory control in the moderate phase (Figure 2).

Then, the moderate DAT and the moderately severe DAT have a minor mean (P<.01) than the mild DAT cases. The Ancova results to control the age (table 3) show that it does not have a significant effect (P>.05),

Table 2. Differences in means test: Anova. Inhibitory control and resistance to the interference in patients with different degrees of severity

Variable / Severity		Anova 1 factor			POST-HOC: (meaningful pairs)	Size effect R ²	
		F	DF	P			
N.M. =	FAB – Conflictive Instructions	SWCI Mild Mod. M-G	29.30	3 ; 106	.000**	Mild <SWCI* Mod <SWCI** M-G <SWCI** M-G <Mild**	.453 Non-
	FAB – Inhibitory Control	SWCI Mild Mod. M-G	36.90	3 ; 106	.000**	Mild <SWCI** Mod <SWCI** M-G <SWCI** Mild < Mod** Mild < M-G**	.511
	STROOP – Word-Color	SWCI Mild Mod. M-G	21.94	3 ; 106	.000**	Mild <SWCI* Mod <SWCI** M-G <SWCI** M-G <Mild**	.385
	STROOP – Interference	SWCI Mild Mod. M-G	0.61	3 ; 106	.610 SM	NM	--

Meaningful (P>.05) *= Meaningful at 5% (P<.05) ** = Highly meaningful at 1% (P<.01).

Abbreviations, Snehdecor test; DF, degree of freedom; FAB, Frontal assessment battery; P, p-value `sig; SWCI, subjects without cognitive

impairment; R², Beta coefficient; Mod, moderate; M-S, moderately severe.

Fig. 2. Comparative means obtained between the conflictive instructions and the inhibitory control subtest in the study sample

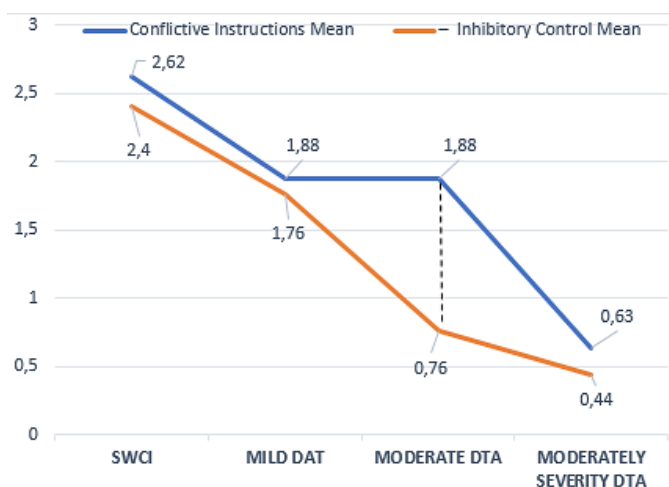


Table 3. Covariance analysis. Inhibitory control and resistance to the interference with patients of different degree of severity. controlling the age effect.

Variable	Factor	RMSE	F	DF	P	Beta ²
FAB –						
Conflictive Instructions	Severity	15.81	21.72	3 ; 105	.000**	.383
	Covariable: age	1.75	2.41	1 ; 105	.124 NS	--
FAB – Inhibitory Control	Severity	17.33	28.08	3 ; 105	.000**	.445
	Covariable: age	1.64	2.65	1 ; 105	.106 NS	--
STROOP – Word-Color	Severity	935.17	19.56	3 ; 105	.000**	.361
	Covariable: age	19.91	0.42	1 ; 105	.520 NS	--
STROOP – Interference	Severity	11.41	0.22	3 ; 105	.880 NS	--
	Covariable: age	261.79	5.14	1 ; 105	.025 *	.047

N.M. = Non-Meaningful ($P > .05$) * = Meaningful at 5% ($P < .05$) ** = Highly meaningful at 1% ($P < .01$).

Abbreviations: DF, degree of freedom; F, Sneath-decor test; FAB, Frontal assessment battery; P, value sig; RMSE, Root Mean Square. it does not disrupt the results ($F=17.33$; $P < .001$) and the size effect remains high (.445).

The condition word-color score (STROOP).

Significant differences ($F=21.94$; $P < .001$) with a superior size effect (.385) are found through the analysis according the degree of the severity (table

2). The post hoc tests shown that the moderately-severe DAT have a lower mean in relation to the mild DAT and moderate DAT ($P < .01$).

The posteriori tests point out that the DAT cases means are minor ($P < .01$) than the SWCI; in addition, the moderately-severe DAT have a minor mean ($P < .01$) than the mild DAT and the moderate DAT. When controlling the age (table 3), it is proved that it does not have effect ($P > .05$) and so that it does not modify the previous results ($F=19.56$; $P < .001$)

which keep a high effect size (.361).

The interference condition score (STROOP).

It is observed that when comparing among the different groups, the means, the differences that can be considered significant do not turn up ($P < .05$) (table 2).

When controlling the age although an effect of it is noticed, the previous results are not affected by it ($P < .05$).

Discussion

Taking into consideration the selected variables “conflictive instructions” and “inhibitory control” from the FAB test, the moderately-severe DAT patients have obtained lower performances than the mild and moderate DAT patients.

Also, as it has been observed in the moderate phase, there is a great difference between the inhibitory control and the conflictive instructions performances. This data indicates that in the mild and moderate phases the capacity to resist an interference keeps stable and there is a significant decrease in the inhibitory control (FAB), what could point out a possible differential progression rate.

In relation to the Stroop test the word-color variables, the moderately-severe DAT have obtained lower means than the ones with the moderate (Fisher, Freed & Corkin, 1990; Hutchison, Balota, Ducheck, 2010) and mild DAT (Balota, Tse, Hutchison, Spieler, Duchek & Morris, 2010; Bélanger, Belleville, Gauthier, 2010), what shows a higher affection in relation to the dementia severity.

Other studies which have applied the Stroop paradigm have shown the DAT patients take longer when doing it, make more mistakes and show more inhibitory difficulties in their execution (Vasconcelos et al., 2014). These results indicate that DAT patients show some alterations in their inhibitory control and their interference resistance.

The anatomical correlates show that the deficient execution of the Stroop test in DAT patients is

related to the implication of the temporal superior, parietal inferior and frontal medial structures (Bondi et al., 2002).

Taking into account the visual recording and the saccadic movements against Go-no Go stimuli in DAT patients, it is evident the slowing down at the beginning of the ocular movement (Crawford, Higham, Mayes, Dale, Shaunak & Lekwuwa, 2013). high distraction levels in the eye's movements, what suggests the presence of an inhibition deficit (Crawford & Higham, 2016).

However, the interference variable of the Stroop test has not found significant differences among the DAT cases with different degrees of severity, what is different to most of the research studies. This fact can be due to a different Stroop test paradigm applied in the research studies. Other researchers used the 100 items in 3 subtests with time of 45 seconds Stroop test and found out that the interference effect did not vary among groups, it was inconsistent, dependent of the dementia severity and could be explained by a visual level of affection (Fisher, Freed & Corkin, 1990).

In the Stroop test computing version of the 100 items in 3 subtests with time of 45 seconds has been found that this effect took place even in DAT patients in mild-moderate stages and it is thought that could happen a subsequent problem in the decrease of the processing speed (Bondi et al., 2002).

In another experimental paradigm in which the interference task was managed after an inverse task, the DAT patients showed worse execution to this task and a higher Stroop effect showing an inherent difficulty in the patients to eliminate or inhibit learnt responses previously so as to learn a new strategy (Amieva et al., 2004).

Therefore, it can be confirmed the hypothesis that the higher the DAT severity higher the affection of the inhibitory control, given the fact that the moderately-severe DAT patients show lower values than the mild DAT, moderate DAT and compared to SWCI.

V. CONCLUSION

In the inhibition, it resulted that its application to DAT patients is not related to the age variable, it follows a descending progression of greater affectation in patients with moderately-severe DAT, observing maintenance in the mild and moderate phases, compared to SWCI.

In relation to the resistance to interference, it resulted that its application to DAT patients is not related to the age variable, which is higher in moderate and severe DAT patients, and decreases dramatically in the moderate phase in comparison to the mild phases and to the SWCI.

VI. Limitations of the Study

A fundamental limitation of the study is the small size of patients sample with different degrees of severity, so that the results cannot be extrapolated to the population.

VII. Scope for future research

A future research could consist of carrying out longitudinal studies so as to predict the DAT evolutionary state from the application of these kind of analyses. Because of that, the inhibitory control and the resistance to interference can work as a neuropsychological differentiation of the conversion and progression of some of the Alzheimer phases (Cervera-Crespo, González-Álvarez, Rosell-Clarí, 2019), in comparison to measures such as the episodic memory alteration, which is the most significant signal of replication to determine the DAT appearance.

It would be convenient to carry out cognitive stimulation programs that let develop the inhibitory capacity and strengthen the resistance to interference with the aim of slowing down the cognitive deterioration progression.

Declaration of interest

The researches state not having any personal, financial, intellectual, economic or corporative interest when carrying out the research.

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