Development of a neuropsychological assessment in smoking

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Introduction. Smoking is one of the causes leading to the development of disease and mortality worldwide. One of the focuses of interest in this area is the impact of smoking on neuropsychological health. However, few studies provide instruments to assess executive functioning in smokers. The purpose of this study was to examine the viability of the internal structure of a neuropsychological battery for the assessment of executive function in smokers.

Subjects and methods. A total of 171 smokers (M_{age}= 47.44, SD_{age}= 8.48) were assessed. Executive functions were assessed at baseline with measures of inhibition (go/no go task and five digit test), updating (visual search and attention test and letter-number sequencing) and shifting (delay discounting task and Iowa gambling task).

Results. The exploratory factor analysis obtained a three-component solution of 59.6%. Establishing a first factor composed of visual search and attention test and letter-number sequencing, a second factor composed of delay discounting task and go/no go task and a third factor with Iowa gambling task and five digit test.

Conclusions. The analysis of the internal structure reflected three factors which are consistent with the structure proposed by Miyake (2000).

Key words. Executive functions. Flexibility. Inhibition. Neuropsychology. Smoking. Working memory.

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Introduction

The World Health Organization has highlighted the importance of studying the consequences of the nicotine dependence on mental health. Specifically, it is imperative to understand how the smoking population is suffering alterations in their cognitive abilities. Diverse findings have been described concerning the influence of nicotine on neuropsychological responses after a long history of smoking. In this sense, MRI studies show signs of structural deficiencies of the prefrontal cortex in chronic smokers [1-5] and poor performance on demanding executive process tasks [6-9]. Some data also emphasize the role of executive function (EF) deficits in tobacco consumption [9-11].

Executive function represent an 'umbrella term' that includes a series of higher-order cognitive processes which govern action towards a goal [12-14]. Executive functioning is distinguished by its ability to regulate cognitive, mental, behavioural and affective aspects that facilitate adaptive functioning [15].

The study of the structure and organization of executive mechanisms involves inherent difficulties due to the lack of a univocal and explicit operational definition [16]. Some theoretical proposals such as those of Miyake et al (2000) or Diamond (2013) [17,18] were postulated among the theoretical models most supported by the scientific literature [13,19]. Specifically, these approaches focus on three executive components which are independent but share a common underlying aspect. It should be noted that, despite the various theoretical paradigms that identify different components of EF, these proposals are not contradictory but rather complementary to each other [20].

However, the components and mechanisms which enable the operation of executive functions continue to be discussed [21]. According to Durazzo et al. (2010) many investigations only used measures of global cognitive function [9]. Other studies employed neuropsychological tests commonly used to evaluate the severity of cognitive dysfunction in a brain-damaged population [22]. This tendency strongly undermines the ecological validity of neuropsychological tests [18,23,24].

Taken together, it is essential to provide both guidelines and instruments for neuropsychological assessment in the context of nicotine addiction treatment. This assumption is in line with other au-

thors who refer to the importance of adapting the neuropsychological assessment to the assessment context, objectives and the population to whom it is addressed to [25]. Compared to other addictions, tobacco use disorder requires a novel therapeutic approach due to their peculiarities. In light of the above, further research is desirable to clarify the influence of smoking on executive function. Nevertheless, given the lack of a standardized instrument for assessing executive functions in smokers, we conducted a cross-sectional study to address this methodological gap. The purpose of this research is to create and validate a neuropsychological battery that allows the assessment of cognitive function in smoking. To this purpose, we shall examine the validity of the internal structure of the battery proposed. In this sense, we hypothesize that the different neuropsychological tests sensitive to the evaluation of executive components will be grouped into three components of 'update', 'flexibility/change' and 'inhibition' described by Miyake et al (2000). Furthermore, we expect the battery to have discriminant validity to differentiate executive performance based on smoking history. We consider that these results could favour the development of new neuropsychological tools in both clinical practice and research.

Subjects and methods

Participants

The sample comprised 171 smokers (59% females), whose age ranged between 27 and 69 years old (M = 47.44; SD = 8.48). Participants had requested treatment in the smoking cessation program of the Occupation Risk Prevention Service of the University of Granada. The average sample score in Fagerström Test for Nicotine Dependence (FTND) was 4.49 (SD = 2.32) and they smoked an average of 17.9 (SD = 8.94) cigarettes per day. Inclusion criteria were: 1) being a tobacco consumer (Fagerström > 3), 2) aged over 18 years, 3) having a work relationship with the University of Granada (Spain). Exclusion criteria were: 1) any illness or mental disorders suggesting possible difficulty in completing the different tasks and 2) current psychotropic medication for psychiatric symptoms, concurrent dependence on other substances (cocaine, heroin, alcohol, etc.). All the participants signed a written consent form. The study was approved by the Ethics Committee in Human Research of the University of Granada (Spain) and adhered to the tenets of the Declaration of Helsinki.

Instruments

- *Fagerström test for nicotine dependence* [26]. This test was designed to provide an ordinal measure of nicotine dependence related to cigarette smoking. It contains six items that assess the quantity of cigarette consumption, the compulsion to use and dependence.
- *Letter-number sequencing task (Wechsler adult intelligence scale, WAIS III, Spanish adaptation, TEA Editions)* [27]. In this test a combined sequence of letters and numbers is read to the participant. The task involves maintenance and manipulation of information from working memory. The total number of correct responses constitutes the variable score.
- *Visual search and attention test* [28]. In this visual search test, a target (a letter or coloured symbol) is identified in a matrix de- signed to explore sustained attention, understood as the ability to rapidly activate and inhibit motor responses. In this case, the total score of stimuli detected was used as an independent variable.
- *Go/no go task* [29]. This task assesses the ability to inhibit a simple motor response. It consisted of 60 trials. Responses were coded as hits (responding in presence the go trial), false alarms (responding in presence of the no go trial), misses (not responding in presence of the go trial), and correct rejections (not responding in presence of the no go trial). The main variable from this task was the false alarm rate, computed as the ratio between the number of false alarms and the total number of no go trials.
- *Delay discounting task* [30]. This is a 27-question monetary choice questionnaire that asks for preferences between smaller and immediate or larger but delayed rewards varying according to their value and time to be obtained. The area under the curve (AUC) was calculated using the Myerson et al. (2001) proposal. The AUC was estimated for the range of reward sizes covered in the questionnaire (small €5-35; medium €50-60; and large €75-85), according to the formula (x2-x1) [(y1-y2)/2], where x1 and x2 are successive delays, y1 and y2 are the subjective values associated with these delays [31]. The predictive variable was AUC, with lower AUC values indicating greater impulsivity.
- *Iowa gambling task* [32]. The task is a computerized measure of decision-making abilities. The participants attempt to win as much play money as possible by selecting cards from four decks (A, B, C and D). Each time a participant selects a

card, a specified amount of play money is awarded. The decisive dependent measure for this task was the difference in the number of cards selected from the advantageous versus disadvantageous decks across five blocks of 20 trials.

– *Five digit test* [33]. This test is a numerical Stroop task divided into four components. The first component demands participants to name numbers from 1 to 5 as fast as they can. On the second component, participants must describe quantities from 1 to 5. The third component involves a selective attention trial, they must not read the numbers but rather tell how many numbers are present in each stimulus. Finally, on the fourth component participants must read the stimulus numbers. The main dependent variable used in this test was the time required to complete each task.

Procedure

Participants were recruited as they engaged in an occupational health service that provides smoking cessation treatment including pharmacological (varenicline) and behavioral change components. The program begins with an initial session where a semi-structured interview for smokers is conducted as well as a neuropsychological assessment of all smokers, where the measures described above are administered.

On the other hand, the battery was administered with the order of task administration counterbalanced across 171 smokers along the natural course of a smoking cessation treatment. The fourth stage consisted of a dimensional analysis of the construct through a principal component analysis (PCA) from the sample of 171 smokers and the subsequent relevant model goodness-of-fit analyses. Finally, considering the variables with the highest factor loadings (> 0.40), we labelled each component taking into account the three executive functions proposed by Miyake (2000). In this sense, inhibition would involve those tasks that require the ability to inhibit an automatic or dominant response. On the other hand, updating would involve tasks that require manipulation of current information. Whereas, the shifting/flexibility component refers to tasks that require the ability to switch between different tasks or cognitive states [18].

Data analysis

Before the analysis, an initial exploration of the data was carried out examining the pattern of missing values to estimate whether it corresponded to a random distribution. The analysis of the SPSS missing values showed that there were percentages of missing data greater than 5%. Consequently, the database was cleaned up by replacing the missing data through the estimation-maximization procedure.

We proposed a selection of new neuropsychological tasks to develop the battery, different from those used by the Miyake's model. For this reason, we analyzed the convergence between neuropsychological instruments based on the criterion of ecological validity and the executive components of the three-factor model, using principal components analysis (PCA). Multivariate principal component analysis allows a set of variables to be reduced to a set of linear combinations of factors capable of capturing the greatest variability of the original information. The choice of this dimensionality reduction method was based on the guarantees offered since the principal components obtained guarantee the maximum variance of X with the minimum loss of information and are orthogonal components, facilitating their subsequent independent processing.

The adequacy of the data was checked by the KaiserMeyer-Olkin (KMO) and Bartlett tests. Subsequently, we performed Principal Component Analysis with the Varimax extraction and rotation method [34]. The number of components extracted was determined following Cattel's criteria (extraction of components with own value greater than one) in order to find an acceptable solution with the least number of dimensions [35].

All statistical tests were performed using the software package SPSS version 25.0 [36]. We adopted a more conservative significance level ($p < 0.05$) and performed an analysis on all the participants simultaneously.

Results

The means and standard deviations of clinical aspects of smoking and neuropsychological measures are provided in Table I. The mean sample score on the Fagerström test for nicotine dependence (FTND) was moderate (M = 4.49, SD = 2.32). The sample had an average of 17.9 cigarettes per day (SD = 8.94) with an average nicotine level per cigarette of 0.99 mg (SD = 0.13). Besides, participants showed a low level of previous attempts to quit smoking (M = 1.27, SD = 1.35) during their years of addiction. Men smokers reported a significantly higher level of both nicotine dependence on the FTND overall (M = 5.05, SD = 2.51) and cigarettes per day (M = 20.96, SD = 10.02) that did woman smokers (M = 4.19, SD

Table I. Baseline demographic and smoking characteristics of the participants (*n* =171).

	Variables	Mean	SD	Range
	Age	47.3	8.31	27-69
	Years of schooling	17.13	5.40	8-25
Smoking characteristics	Fagerström Test for Nicotine Dependence	4.49	2.32	3-10
	Years of smoking addiction	28.43	9.84	4-57
	Number of daily cigarettes	17.9	8.94	2-60
	Level of nicotine	0.99	0.13	0.60-1.8
	Attempts to quit smoking	1.27	1.35	0-12
Neurocognitive variables	WAIS	8.64	2.98	0-15
	VSAT	228.13	58.26	18-383
	GNG	5.67	6.60	0-50
	DDT	.57	.22	0-1
	IGT	−0.882	26.11	−86-78
	FDT	14.49	8.76	−33-43

DDT: total score in the now or later test; GNG: go/no go task; FDT: total score in five digit test; IGT: Iowa gambling task; VSAT: total stimuli in the visual search and attention test; WAIS: total score in letters-numbers sequencing subtest of the Wechsler adult intelligence scale.

Table II. Correlation analysis between the instruments proposed.

	WAIS	VSAT	GNG	DDT	IGT	FDT
WAIS	1					
VSAT	0.177 [a]	1				
GNG	−0.029	−0.123 [a]	1			
DDT	−0.017	−0.045	−0.039	1		
IGT	0.020	0.039	−0.034	0.072	1	
FDT	−0.249 [a]	−0.152 [a]	0.165 [a]	−0.064	0.079	1

[a] $p < 0,05$. DDT: delay discounting task; FDT: five digit; GNG: go/no go task; IGT: Iowa gambling task; VSAT: visual search and attention test; WAIS: letter-number sequencing task.

= 2.05; M = 16.20, SD = 7.92). On the other hand, the correlation analyzes between the proposed instruments are shown in Table II.

In the first step, in order to explore the internal structure, the suitability of the data for a Principal Component Analysis was examined. For this purpose, both the Kaiser-Meyer-Olkin test (0.541) and Bartlett's sphericity test ($X^2_{(15)} = 30.344$, $p < 0.001$) indicate that the ACP is a statistical test that could be carried out with these data.

After carrying out the analysis with six neuropsychological tasks, a structure of three components was obtained which explains the total variance of 59.6%. From the three-components structure, component 1 explains 23.33%, 18.71% corresponds to component 2 and 17.58% concerns component 3. Taking as reference the variables with the highest factorial loads (> 0.40) considering our sample size [37] labels each factor according to the structure of the correlations. Labeling component 1 as updating, component 2 as inhibition and component 3 as flexibility (Table III).

On the other hand, the goodness-of-fit index (CFI) is 0.62 while the Tucker-Lewis index (TLI) was 0.52 and the root mean square error of approximation (RMSEA) was 0.048 with a 95% confidence interval indicating that it is within the recommended acceptance limits.

To assess discriminant validity, a t-Student hypothesis test was performed to examine whether there were differences between smokers with a long history of addiction and those with a shorter history of addiction. The results were statistically significant [t (172) = 1.938; $p < 0.000$; MS = 54.367). The overall score of the group with a long history of addiction is significantly lower than the group with a shorter history of addiction (Table IV).

Finally, ANOVA analyses were calculated to test the influence of socio-demographic variables on performance on the executive components. The results showed that the performances in the different components did not differ significantly according to gender for updating [F (3, 170) = 1.880, MS = 6735.07; $p = 0.17$], flexibility [F(3 , 170) = 0.944, MS = 781.59; $p = 0.33$] and inhibition [F(3 , 170) = 0.150, MS = 7.001; $p = 0.69$]. On the other hand, the updating [F (3, 168) = 0.905, MS = 3262.01; $p = 0.44$], inhibition [F(3, 168) = 2.13, MS = 96.82; $p = 0.098$] and flexibility [F(3, 168) = 0.526, MS = 438.63; $p = 0.66$] components did not show statistically significant differences according to socioeconomic status either.

Discussion

The purpose of this study was to explore the validi-

Table III. Principal component analysis (n = 171).

	Components			Total variance (%)
	Component 1 'Updating'	*Component 2 'Inhibition'*	*Component 3 'Flexibility'*	
VSAT	0.707	0.053	0.194	
WAIS	0.673	–0.028	–0.069	23.33%
FDT	–0.519	0.434	0.405	
DDT	–0.272	–0.809	0.087	18.71%
GNG	–0.296	0.495	–0.045	
IGT	0.076	–0.116	0.915	17.58%
Total				59.6%

DDT= total score in the now or later test; FDT= total score in five digit test; GNG= go/no go task; IGT= Iowa gambling task; VSAT= total stimuli in the visual search and attention test; WAIS: total score in letters-numbers sequencing subtest of the Wechsler adult intelligence scale. p<0.05.

Table IV. Discriminant Validity.

	Long history		Low history				
	Mean	SD	Mean	SD	T value	df	p value
Total EF	223.00	56.8	277.37	62.5	5.81	172	0.000

Long smoking history (≥ 25 years); low smoking history (0-24 years). p < 0.05.

ty of the internal structure of a neuropsychological battery to assess executive function in smokers. Through the multivariate technique denominated factorial analysis, the common factors that best explained the total variability of the study variables would be obtained.

In our study, the first stage of the analysis verifies that all the analyses regarding the relevance and validity of the data matrix have been satisfactorily passed. In the matrix of rotated components there is a clear grouping of patterns where variables that define the components prevail. However, the VARIMAX rotation method was applied to reduce ambiguities in the factor loads of the variables and a total three-component variation solution of 59.6% was obtained. Establishing a first component composed of VSAT and WAIS, a second component composed of DDT and GNG and a third component with IGT and 5DT. Consequently, six variables are reduced to three factors representing three components frequently valued in the executive function.

Comparing scores on the battery between smokers with a long history of addiction and smokers with a shorter history of addiction, the results showed that there were significant differences, thus demonstrating the discriminant validity of the instrument. In conjunction, ANOVA tests confirmed that these differences were not explained by relevant socio-demographic variables such as gender or socio-economic status. Therefore, these results allow us to corroborate the hypothesis previously put forward, which alluded to the ability of the battery to differentiate executive performance according to smoking history.

In agreement with previous research [17,18], in our study the analysis of the internal structure reflected the existence of three components revealing a structure consistent with Miyake's (2000) proposal. Therefore, the instrument that we have presented offers an opportunity to be able to approach the study of the executive function in smokers. Optimization in data acquisition combined with a wide range of measures to efficiently obtain a global vision of executive behavior allows this battery to be considered an adequate and plausible approach for clinical practice.

Conclusion

As a result of the standardisation of the test, the collection of normative data should become more feasible [25]. In particular, developing an Executive Functioning Profile in smokers represents a way of achieving parsimony and standardisation in the way data is recorded in this group. This is because cognitive assessment in smokers could be a complex process due to the fact that they frequently ignore the impact of tobacco on their health [38]. Furthermore, a battery based on ecological validity also prevents the inflexibility of certain neuropsychological assessment tasks which are commonly employed in the clinical context.

On the other hand, the lack of accessibility as well as the inconsistency for evaluating neuropsychological variables in addictive disorders complicate the comparison and generalizability [24]. Despite their usefulness in detecting disorders, many of the neuropsychological tests frequently used in clinical practice have been criticised for being unrepresentative of the real world. This fact notably limits their ability to generalise the results [24,25,

29,39]. A commitment to ecological orientation in neuropsychological assessment highlights the importance of identifying the cognitive processes implicated as well as the impact of these deficits on everyday functional aspects. The results of the study indicate that it has been possible to design a viable evaluation battery with adequate internal consistency. To our knowledge, few studies have provided specific tools for executive assessment in tobacco. The advantage of this type of standardised assessment would be to provide clinical psychologists with an accessible and useful methodology for evaluation and treatment. From a methodological point of view, consistency in the operationalization and evaluation of the EF will allow to mitigate the problem of task impurity [40].

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Desarrollo de una batería de evaluación neuropsicológica en fumadores

Introducción. El tabaquismo es una de las causas que conducen al desarrollo de enfermedades y a la mortalidad en todo el mundo. Uno de los focos de interés en esta área es el impacto del tabaquismo en la salud neuropsicológica. Sin embargo, son pocos los estudios que proporcionan instrumentos para evaluar el funcionamiento ejecutivo en los fumadores. El propósito de este estudio fue examinar la viabilidad de la estructura interna de una batería neuropsicológica para la evaluación de la función ejecutiva en fumadores**.**

Sujetos y métodos. Se evaluó a un total de 171 fumadores ($media_{edad}$ = 47,44; $desviación\ estándar_{edad}$ = 8,48). Las funciones ejecutivas se evaluaron en la línea de base con medidas de inhibición (tarea *go/no go* y prueba de los cinco dígitos), actualización (prueba de búsqueda y atención visual, y escala de inteligencia de Wechsler para adultos) y cambio (tarea de descuento por demora y tarea de juego de Iowa).

Resultados. El análisis factorial exploratorio obtuvo una solución de tres componentes del 59,6%, y se estableció un primer factor compuesto por la prueba de búsqueda y atención visual y la escala de inteligencia de Wechsler para adultos; un segundo factor, por la tarea de descuento por demora y la tarea *go/no go;* y un tercer factor, por la tarea de juego de Iowa y la prueba de los cinco dígitos.

Conclusiones. El análisis de la estructura interna reflejó tres factores que son consistentes con la estructura propuesta por Miyake (2000).

Palabras clave. Flexibilidad. Funciones ejecutivas. Inhibición. Memoria de trabajo. Neuropsicología. Tabaquismo.