Clinical and psychophysiological features of smoking and depression (preliminary results)

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Abstract

Objective: *Smoking and depression are two mental health problems that can have a negative effect on a person's overall health. Studies have shown that smoking and mayor depressive disorder (MDD) have a bidirectional relationship. The objective of this study was to deepen the knowledge of the clinical features and psychophysiological bases of heart rate variability (HRV).* **Methods:** *Eighty participants (40% females, 18 and 45 years old) were included and represent a subsample of a randomized clinical trial that explored the therapeutic effects of transcranial magnetic stimulation in patients with depression, suicidal ideation, and smoking. Clinical features were measured in smokers n = 20, MDD n = 20, smokers + MDD n = 20, and controls n = 20 using MINI-plus, the Beck Depression Inventory, the Hamilton Anxiety Scale, the Hamilton Depression Scale, the Fagerström test (FT), the Nicotine Craving Questionnaire (NCQ), co-oximetry and a signal reactivity paradigm with HRV for psychophysiological measures, and the Marlow and Crowne Scale.* **Results:** *Comparison between groups demonstrated that participants with MDD and smokers + MDD had higher scores than the other groups on the depression (p < 0.001) and anxiety scales (p < 0.001). In the FT, smokers present higher consumption compared to all the groups (p < 0.001). In the NCQ, smokers and smokers + MDD had similar behavior with higher scores (p < 0.001).* **Conclusions:** *The MDD group had HRV values below the references; smokers and smokers + MDD presented a greater psychophysiological reaction when exposed to the signal reactivity paradigm, and this was reflected in the HRV as they had values below the references.*

Keywords: *Depression. Smoking. Heart rate. Psychophysiology.*

Características clínicas y psicofisiológicas del tabaquismo y la depresión (resultados preliminares)

Resumen

Objetivo: *El tabaquismo y la depresión son dos problemas de salud mental que pueden tener un efecto negativo en la salud general de una persona. Los estudios han demostrado que el tabaquismo y la depresión (TDM) tienen una relación bidireccional. El objetivo de este estudio fue profundizar en el conocimiento de las características clínicas y las bases psicofisiológicas de la variabilidad de la frecuencia cardíaca (VFC).* **Métodos:** *Se incluyeron 80 participantes (40% mujeres,*

18 y 45 años). Las características clínicas se midieron en fumadores n = 20, TDM n = 20, fumadores + TDM n = 20 y controles n = 20 utilizando el Inventario de Depresión de Beck (BDI), la Escala de Ansiedad de Hamilton (HAS), la Escala de Depresión de Hamilton (HDS), la prueba de Fagerström. (FT), Cuestionario de ansia de nicotina (NCQ), Cooximetría y paradigma de reactividad de señales y VFC. **Resultados:** *La comparación entre grupos demostró que los participantes con TDM y fumadores + TDM tuvieron puntuaciones más altas que los otros grupos en la escala de depresión (p < 0,001) y ansiedad (p < 0,001), en el FT los fumadores presentan mayor consumo en comparación con todos los grupos (p < 0,001), en el NCQ los fumadores y fumadores + TDM tuvieron un comportamiento similar con puntuaciones más altas (p < 0,001).* **Conclusiones:** *El grupo TDM tuvo valores de VFC por debajo de las referencias, los fumadores y fumadores + TDM presentaron una mayor reacción psicofisiológica al exponerse al paradigma de reactividad de señales y esto se reflejó en la VFC al tener valores por debajo de las referencias.*

Palabras clave: *Depresión. Tabaquismo. Frecuencia cardíaca. Psicofisiología.*

Introduction

Smoking and depression are two mental health problems that can have a negative effect on a person's overall health. Studies have shown that smoking and depression have a bidirectional relationship, where smoking increases the risk of developing depression and depression increases the risk of becoming a smoker[1-3]. At present, there are several hypotheses that are proposed to explain the high rates of smoking in people with depression; for example, the work of Boden et al. proposes that people turn to tobacco to relieve their symptoms of depression and anxiety. It is suggested that the association between smoking and depression may also be bidirectional, and the comorbidity of both arises from two pathways: (1) common factors of risk and (2) smoking withdrawal symptoms increased anxiety and negative affect may be mistakenly attributed to reflecting genuine mood symptoms, leading to the impression that smoking improves mood[4,5]. As the neurobiological relationship between smoking and depression, different evidence has shown that nicotine facilitates the release of three major monoamines (dopamine, norepinephrine, and serotonin) implicated in the etiology of clinical depression. Furthermore, chronic nicotine treatment has been shown to increase the expression of brain-derived neurotrophic factor and fibroblast growth factor. Positive modulation of these trophic factors by monamines and cyclic adenosine monophosphate is now thought to play a role in the actions of antidepressants and mood stabilizers. The nicotinic receptors are localized in different structures relevant to depression (i.e., cingulate cortex, prefrontal cortex, amygdala, and dorsal raphe nucleus). On the other hand, nicotine has complex effects on the hypothalamic-pituitary-adrenal axis, inducing its activation, and this is associated with the hypercortisolemic state observed in some depressed patients[6-8].

In addition, recent research has shown that smokers have decreased heart rate variability (HRV), which could be related to increased depression[9-13]. HRV refers to the natural variation of the frequency, that is, the difference in the interval between successive cardiac contractions[14,15]. This relationship between smoking, depression, and HRV is an emerging area of research that may have significant implications for the prevention and treatment of these diseases.

HRV can be analyzed through several methods that are based on time domain, frequency domain, geometric measurements, and non-linear variables[15]. Within the temporal domain variables, we can find the standard deviation of RR intervals (RRSD), percentage of successive RR intervals that differ by more than 50 ms (PNN50), SD of the average NN intervals for each 5-min segment of a 24-h HRV recording (SDAN), and RMSSD[15]. The most commonly used is the RMSSD, which is the square root of the mean value of the sum of the squared differences of all successive RR intervals in the measured time. This measure is a cardiac vagal modulation index that is suggested as a method superior to spectral measures because it presents less sensitivity to variations in respiratory patterns and, in turn, is the most appropriate procedure for evaluating short periods in the HRV[16].

The objective of this study was to deepen the knowledge of the psychophysiological bases of HRV in participants who were smokers and had been diagnosed with depression, or both.

The data presented in this article represent a subsample of a randomized clinical trial that explored the therapeutic effects of transcranial magnetic stimulation in patients with depression, suicidal ideation, and smoking. In this article, we show the preliminary results of the influence of depression with and without comorbidity with smoking on HRV and whether said comorbidity affects tobacco consumption.

Methodology

Participants: a total of 80 participants, between 18 and 45 years of age, of both sexes were included, 20 of whom had a diagnosis of depression, 20 were smokers, 20 were both smokers and had a diagnosis of depression, and 20 were control participants. All of them attended the Neurodiagnostic and Neurorehabilitation Unit[1] of "Dr. Moisés López González", which is part of the University Health System of the Autonomous University of Querétaro (UAQ), and agreed to sign an informed consent letter, which was previously explained to them. All participants were diagnosed according to the DSM-5 criteria (APA 2013). This study was approved by the bioethics committee of the UAQ's Faculty of Medicine under number 11343. The clinical trial registration number is NCT05694754 (ClinicalTrials.gov PRS).

Instruments

Mini International Neuropsychiatric Interview (MINI Plus): a brief and highly structured interview of the main psychiatric disorders of the ICD-10 and DSM IV; it is structured in formats and algorithms and is modular by diagnostic categories[17]. Used in this work as a support instrument for the diagnosis of depression and the exclusion of other psychiatric disorders.

Marlow and Crowne Social Desirability Scale: a 33-item self-applied scale that allows us to evaluate the participants need to respond in a culturally accepted way. It produces values between 0 and 33, in which a higher score indicates greater desirability, understood as response bias[17,18].

Beck depression inventory (BDI): a self-applicable test consisting of 21 items for the evaluation of depressive clinical symptoms. The cutoff points range from 0 to 9 (absent or minimal), 10 to 16 (mild), 17 to 29 (moderate), and 30 to 36 (severe)[19].

Hamilton anxiety scale (HAS): a hetero-applicable instrument consisting of 14 items for the assessment of the severity of symptoms of anxiety states; it is divided into two subscales: psychic anxiety and somatic anxiety. A higher score indicates a higher intensity[20].

Hamilton Depression Scale (HDS): consisting of 21 items for the assessment of the severity of depressive symptoms. It provides a global score for the severity of the depressive symptoms and a score for three indexes, which are melancholy, anxiety, and sleep. The cutoff points range from 0 to 7 (without depression), 8 to 13 (mild depression), 14 to 18 (moderate depression),

19 to 22 (severe depression), and higher than 23 (very severe depression)[20].

Fagerström test: a short and simple test consisting of six questions that assess dependence on tobacco users. The score ranges from 0 to 10 in such a way that the higher the score, the greater the dependence[21].

Nicotine Craving Questionnaire (NCQ): a 12-item questionnaire to assess the degree of craving, with five response options ranging from 1 (completely disagree) to 5 (completely agree)[22].

Co-oximetry: it is a spectrophotometric technique to detect the loss in the oxygenation capacity of hemoglobin, which consists of determining the level of carbon monoxide (CO) in the air exhaled by an individual. The device used to perform this test is called a co-oximeter, a high-precision monitor that measures the concentration of CO in parts per million (ppm).

The co-oximeter indicator stabilizes and marks the exact number of ppm of CO in the subject's exhaled air.

HRV: it performed using the signal reactivity paradigm, which consists of presenting blocks of images that were chosen from the International Smoking Imaging Series (with neutral counterparts), Version 1.2. In this test, the participant is subjected to a series of visual stimuli while wearing a Polar H10 chest strap sensor and a Bluetooth transmitter used for HRV measurement. The test consists of four blocks of images: two blocks of tobacco images and two blocks of neutral images, which in turn are interspersed. Each block of images consisted of 25 images; each image appeared for 6 s on the screen, for a total of 150 s per block.

Statistical analysis

A statistical analysis was performed using the IBM SPSS Statistics 25 software as well as the GraphPad Prism 6 software. The mean of the clinical and psychophysiological scores was compared between various groups of the tested variables using a one-way ANOVA. For *post hoc* analysis, the Fisher's LDS method was employed, and the significance level was set at p < 0.05.

Results

Table 1 shows the sociodemographic data of the four groups and the clinical results. It was found in the BDI that the major depressive disorder (MDD) group had a higher score than the other groups (p < 0.001); likewise, the smokers + MDD group showed differences in regard to the other groups (p < 0.001). Furthermore, it

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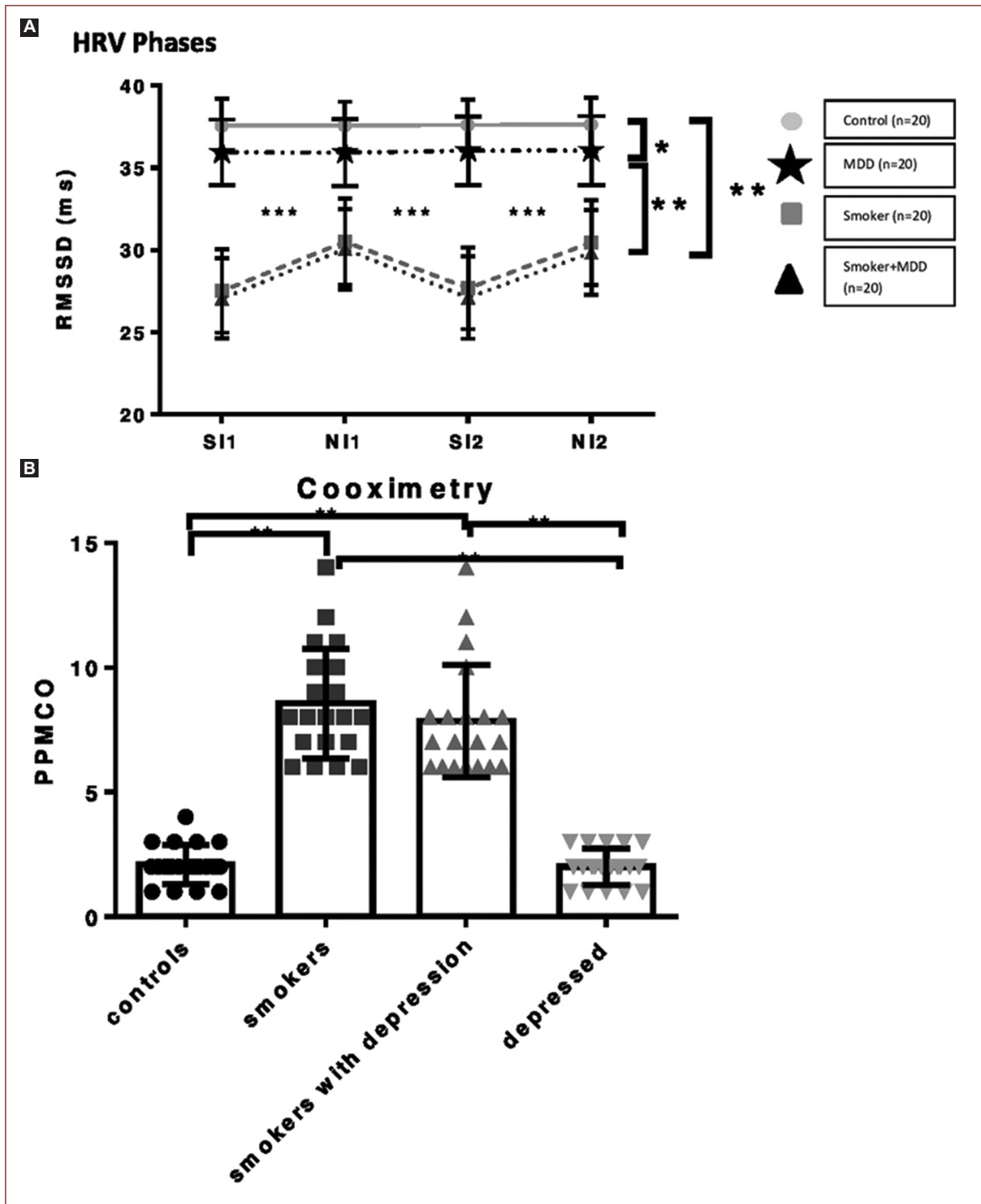1 In Spanish: *Unidad de Neurodiagnóstico y Neurorehabilitación.*

Figure 1. A: in this figure, we can see the comparison between HRV groups throughout the four phases of the signal reactivity paradigm. On the X-axis, we can see the four blocks of the reactivity signal paradigm and on the Y-axis, we can observe the media of the RMSSD (ms). **B:** the comparison between the groups of the values obtained in the co-oximetry test is shown. On the X-axis, we can observe the four groups and on the Y-axis, we can see the PPMCO. SI1 (smoking images 1), NI1 (Neutral images 1), SI2 (smoking images 2), NI2 (Neutral images 2), RMSSD ms (square root of the mean value of the sum of the squared differences of all successive RR intervals in the measured time expressed in milliseconds) PPMCO (particles per million of carbon monoxide); * = $p < 0.05$, ** = $p < 0.001$, *** = $p < 0.0001$.

Table 1. Sociodemographics and clinical results

Variables	Groups			
	Control (n = 20)	**Smokers (n = 20)**	**Smokers+MDD (n = 20)**	**MDD (n = 20)**
Gender	♂ = *38%* ♀ = *62%*	♂ = 35% ♀ = 65%	♂ = 45% ♀ = 55%	♂ = 33% ♀ = 67%
Age	$\bar{X}$ = 37.66 ± 6.39	$\bar{X}$ = 36.26 ± 8.02	$\bar{X}$ = 35.83 ± 8.41	$\bar{X}$ = 34.93 ± 7.24
Years of study	$\bar{X}$ = 18.08 ± 2.42	$\bar{X}$ = 17.3 ± 3.17	$\bar{X}$ = 17.66 ± 2.62	$\bar{X}$ = 16.85 ± 2.06
Depressive episodes throughout life	$\bar{X}$ = 0	$\bar{X}$ = 0	$\bar{X}$ = 7.08 ± 3.39	$\bar{X}$ = 6.38 ± 1.83
Duration of most recent depressive episode (months)	$\bar{X}$ = 0	$\bar{X}$ = 0	$\bar{X}$ = 8.49 ± 5.59	$\bar{X}$ = 5.38 ± 3.04

Clinical variables	Groups					
	Control	**Smokers**	**Smokers + MDD**	**MDD**	**F**	**p-value**
	M (SD)	M (SD)	M (SD)	M (SD)		
BDI	#^1.6 (0.82)	#^1.8 (1.2)	#35 (5.2)	30.8 (3.3)	648.601	< 0.001
HDS	#^1.35 (1.30)	#^1.7 (1.7)	30.8 (3.4)	30.4 (8.1)	273.716	< 0.001
HAS	#^2 (0.97)	#^2.2 (1.2)	*25.2 (3.7)	28.1 (4.8)	399.212	< 0.001
Fageström	***^0 (0)	#^9.3 (2.4)	7.4 (1.9)	***^0 (0)	191.462	< 0.001
Craving	***^0 (0)	#37.4 (4.8)	37.3 (4.6)	***^0 (0)	820.738	< 0.001

MDD: mayor depressive disorder; M: media; SD: standard deviation; $\bar{X}$: mean.
* = $p < 0.05$ compared with MDD group.
*** = $p < 0.0001$ compared with smokers group.
^ = $p < 0.0001$ compared with smokers + MDD group.
\# = $p < 0.0001$ compared with MDD group.

was observed in the HDS that the MDD and smokers + MDD groups had a higher score than the other groups ($p < 0.001$).

As for the HAS, the MDD and smokers + MDD show differences with higher scores ($p < 0.0001$) compared with the other groups, and MDD shows higher scores than smokers + MDD ($p < 0.05$).

However, in the Fagerström test, smokers presented a higher consumption compared to all the groups ($p < 0.001$).

In the NCQ, both smoker and smokers + MDD groups showed similar behavior in the scores, which were higher than the other groups ($p < 0.001$).

Fig. 1A shows that both the smokers and smokers + MDD groups have below-reference HRV values and significant differences with the control and MDD groups ($p < 0.001$ in both cases); the MDD group shows a reference value lower than the control group ($p = 0.023$). The within intragroup analysis shows that smokers and smokers + MDD have differences in the HRV along the signal reactivity paradigm, with lower values in the blocks of smoking images in comparison with the neutral image blocks ($p < 0.001$ for both groups).

Fig. 1B shows that the smokers and smokers + MDD groups show a higher concentration of PPMCO in co-oximetry ($p < 0.001$) compared with the other groups.

Discussion, Conclusions, and Limitations

To the best of our knowledge, this is the first study carried out in a Mexican population in which the psychophysiological component of HRV was evaluated in these groups of patients. The results of this study are consistent with the reports of Schiweck, Sgoifo, Kircansky, and Kindwell, where they found a reduction in HRV in subjects with depression[13,23,24]. Based on the results of this study, we can observe that participants in the smokers and smokers + MDD groups, who presented a significant reduction in HRV during all phases of the signal reactivity paradigm (neutral images and smoking imaging blocks) compared with the control and MDD groups, had a psychophysiological reaction that has been described by Ashare, Soares, and Erblich[11,25,26].

Having carried out the analyses, we can conclude that the participants with MDD showed below-reference HRV values. In a similar manner, participants in the

smokers and smokers + MDD groups presented a greater psychophysiological reaction when exposed to the signal reactivity paradigm, which was a below-reference HRV value. These findings are similar to those reported by Kroczek et al. who show changes in spectral measures of HRV during smoking cue exposition[27].

Our results have potential clinical importance since exploring the different dimensions in which smoking and depression can manifest themselves allows us to search for new and better diagnostic and evaluation alternatives for the different dimensions that may be affected. For example, the associations between some symptoms of MDD measured by HDS and HRV have already been reported. In this sense, melancholic features of MDD were related to HRV parameters using frequency methods[28] and temporal parameters (SDNN and RMSSD)[29]. The existent evidence shows a relationship between HRV and the severity of depression; for example, patients with more severe depression tend to have a lower HRV than those with less severe depression[29,30].

Some limitations should be noted, especially the sample sizes; had they been larger, we could have formed subgroups based on cigarette consumption. In the same way, we need to deepen the analysis of the HRV by including more variables.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality of data. The authors declare that no patient data appear in this article.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

Use of artificial intelligence for generating text. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript or for the creation of images, graphics, tables, or their corresponding captions.

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