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# Environmental and genetic factors associated with psychoactive medication use in adult females. A population-based twin study

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**Introduction**: Our objective is to determine the prevalence and factors associated to psychotropic medication consumption in a sample of adult females. Additionally, this study seeks to analyze the relative contribution of environmental and genetic factors to psychoactive medication use.

**Method**: Sample consists of a population-based cohort comprising 437 pairs of female twins born between 1940 and 1966. Information is collected through individual interviews, and it includes employment status, educational level, partner status, menopause, presence of mental disorders and psychoactive medication use. Logistic regression models are applied. The relative contribution of genetic and environmental factors to interindividual variation is analyzed through the classical twin design.

**Results**: In the past month, 34.0% of the women interviewed had consumed psychoactive medication. Consumption increases with age, in women out of the labor market, menopausal, and reporting a history of mental disorders. When controlling for age, all variables lost significance, except the presence of mental health problems. Heritability estimates for psychoactive medication use was 52%. This estimate is similar (46%) for consumption in the two categories studied.

**Conclusions**: There is a high prevalence of psychoactive medication use in this sample. This consumption is mainly associated with age and presence of mental disorders. About half of the interindividual variation in psychotropic medication use is attributable to genetic factors, while the rest of the variance would be due to environmental factors unique to each individual.

**Key words:** Pharmacoepidemiology, Psychopharmacology, Heritability, Twin studies

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## Factores ambientales y genéticos asociados al consumo de psicofármacos en mujeres adultas. Un estudio de gemelos de base poblacional

**Introducción**: Nuestro objetivo es determinar la prevalencia de consumo de psicofármacos, en una muestra de mujeres adultas, relacionándolo con variables sociodemográficas y con la presencia de trastornos mentales. Adicionalmente se pretende analizar la contribución relativa de factores ambientales y genéticos a dicho consumo.

**Método**: La muestra consiste en una cohorte, de base poblacional, formada por 437 parejas de gemelas nacidas entre 1940 y 1966. La información se recoge a través de entrevista individual que incluye situación laboral, nivel de estudios, situación de pareja, menopausia, presencia de trastorno mental y consumo de psicofármacos. Se utilizan modelos de regresión logística y se aplica el diseño clásico de estudios de gemelos para estimar la contribución relativa de factores genéticos y ambientales a la variación interindividual.

**Resultados**: En el último mes, el 34,0% de las mujeres entrevistadas habían consumido algún tipo de psicofármaco. El consumo aumenta con la edad, en mujeres inactivas laboralmente, menopáusicas, y que refieren haber padecido trastorno mental. Al controlar por edad, el efecto de todas las variables, a excepción de la presencia de patología, perdía significación. La heredabilidad estimada del consumo de psicofármacos es de un 52%. Esta estimación es similar (46%) para el consumo de las dos categorías estudiadas.

**Conclusiones**: El consumo de psicofármacos en la muestra analizada es elevado. Este consumo se asocia, principalmente a la presencia de trastornos mentales y a la edad. Aproximadamente la mitad de la variación interindividual en el consumo de psicofármacos es atribuible a factores genéticos, mientras que el resto se debería a factores ambientales exclusivos de cada individuo.

**Palabras clave:** Farmacoepidemiología, Psicofarmacología, Heredabilidad, Estudios de gemelos

## INTRODUCTION

In recent decades, there has been a significant increase in psychoactive drug consumption in our country, both in the medical practice and general population. This increase has mainly occurred in the consumption of anxiolytics and antidepressants.[1] This fact, which was not followed by a proportional increase of the state of health of the population, has stimulated interest in the investigation of epidemiological aspects of over-prescription and excessive consumption of said drugs.[2] In the National Health System, the tranquilizer group occupies the third place among those prescribed the most, this only being surpassed by analgesics and anti-inflammatory drugs.[1]

Furthermore, pharmaceutical cost in Spain makes up 18 to 20% of the total health care cost. This amount has undergone a continuous increase over recent years. Psychopharmaceuticals, especially antidepressants and benzodiazepines, account for a significant part of this cost. They are among those consumed the most in the general population. This confers to them an indubitable interest for public health and converts them into a challenge for health care planning.[3]

Studies in this setting show significant variability of results, mainly because of their heterogeneity and extensive methodological diversity (sample, age, study population extension, temporality, information sources or consumption forms).[4] Thus, there are important differences in the consumption of psychopharmaceuticals, this varying from 4-12% according to the country analyzed.[5] In our setting, there is less information about real consumption.[2] According to the different studies, 10 to 20% of the general population take psychopharmaceuticals, this reaching almost 30% in the population over 65 years.[1,6-8] The ESEMeD study[3] analyzed the frequency of consumption of psychotropic drugs in the general Spanish population. It concluded that 16% consumed some psychopharmaceutical agent and that those consumed the most were benzodiazepines (11.4%) and antidepressants (4.7%). According to the National Health Survey (NHS) 2011-12[8], in the last 2 weeks, 16.9% of those interviewed had taken relaxants or hypnotic drugs and 7% antidepressants or stimulants. These percentages increased from 10.4% and 5.6%, respectively, in the 2006 edition of the NHS.[7] On the other hand, the data from the Home Survey on Alcohol and Drugs in Spain[9] reflect a prevalence of hypnosedative consumption in the adult population (tranquilizers and/or sedatives) in the year 2009 of 13.4 % (11 % tranquilizers and 6.3% sedatives) and 14.5% in 2011. This incidence clearly increases with age and is greater in women, reaching up to 27% in women aged 55 to 65.[10]

## FACTORS RELATED WITH PSYCHOPHARMACEUTICAL CONSUMPTION

Psychotropic consumption has been related to factors such as age, gender, civil status, educational level, occupational situation and social status.[1-5,11-20] A greater proportion of consumption of psychopharmaceuticals has been observed in different studies in older persons (≥ 55), this consumption increasing with age, and in women.[1-3,5,11-14,16,17,20-23] Age and gender are associated to consumption independently of mental health.[16] In regards to civil status, consumption seems to be greater among those who have been previously married (widow(ers) and divorced) and among single people.[3,20] However, these authors did not differentiate this effect according to gender. There is evidence that suggests that although marriage is a protective factor against mental disease in men, it is an important source of stress in women.[12] Consumption also varied based on type of family cohabitation. Persons who live alone consume more psychopharmaceuticals than those who live with family.[15,20] On the other hand, years of study show an inverse association with consumption of psychopharmaceuticals (e.g. less consumption with more education.[1,12,14,22] In regards to employment situation, greater likelihood of consumption is found among the retired, unemployed and housewives.[1,3,14,22]

There is an important percentage of presence of a friend or family member who are usual consumers of psychoactive drugs in those who self-medicate with psychoactive drugs.[18] The existence of severe familial dysfunction has also been associated to greater consumption,[22] as well as the presence of social problems or lack of social support.[12,24,25]

Psychoactive drugs are generally prescribed by the general practitioner[5,26,27] although some studies suggest high consumption of psychoactive drugs without medical control.[2] In regards to co-consumption, most of the studies have found a positive association between alcohol consumption and use of psychoactive drugs.[11,14,16,25,28,29] However, others have found a negative association. This would be explained by the fact that the subjects who drink obtain the desired effects from alcohol and would not need to consume psychoactive drugs.[14,16] A significant association has also been observed between women who smoke and consumption of psychoactive drugs. This may be derived from the relationship between smoking habit and anxiety or depression episodes.[14,16] In most of the studies, it was observed that the presence of physical and/or psychic disease significantly increases consumption of psychoactive drugs.[2,3,12,14,15,23,30] However, it has been seen that the presence of a psychic disease is associated to psychopharmaceutical treatment in a limited number of cases, that is, there is still a high percentage of individuals with mental disorder who do not consume psychoactive drugs.[2,3,6,31]

The review made shows the need to continue carrying out pharmacoepidemiological studies in order to orient and facilitate the work of education for health and thus to avoid the possible risks derived from inappropriate use of this type of drugs.[1,14] Along this same line, identification of the con-

sumption patterns in the population must be identified in greater depth and their relationship with other sociodemographic and psychosocial type factors should be identified.[18] In addition, other factors that have not been sufficiently studied could be involved. Specifically, currently, not enough attention has been given to the possible influence of genetic factors. In accordance with the literature, it seems clear that the presence of mental disorder and consumption of psychopharmaceuticals are related but independent variables, and therefore they do not necessarily have to be influenced by exactly the same factors. While the analysis of genetic factors involved in mental disease has a long history and has produced an enormous amount of scientific information, the analysis of genetic factors involved in the consumption of psychopharmaceuticals has not followed a parallel road. There are very few studies along this line and the reports of these few studies have estimated the genetic contribution to consumption of psychopharmaceuticals to be 30% to 40%.[32,33] Significant effects of the environment shared with this phenotype have not been found. This would suggest that almost half of the interindividual variation in consumption of psychopharmaceuticals could be due to genetic causes while the rest would be explained by individual environmental factors of each subject.

Considering the questions noted, this work has a dual objective. On the one hand, it has aimed to analyze the incidence of consumption and characteristics associated to the use of psychopharmaceuticals in a population sample of adult women. On the other, it has aimed to carry out a classic study of twins in order to analyze the relative contribution of genetic and environmental factors to the phenotype of interest. To do so, we have analyzed the consumption of two large pharmacological groups: *tranquilizers, sedatives and hypnotic agents* (fundamentally benzodiazepines), and *antidepressants* in a cohort of 827 women born in multiple births.

## METHODS

### Participants

The sample comes from a cohort made up of pairs of female twins born between 1940 and 1966 who are included in the Registry of Twins of Murcia (RTM).[34,35]. The RTM is a registry of twins, both monozygotics (MZ) and dizygotics (DZ), of the population base managed by the University of Murcia and with the collaboration of the Ministry of Health and Social Policy of the Region of Murcia. The participants in the RTM were found through the database of the regional health system and were selected if they fulfilled the inclusion criteria: pairs with both members alive at the time of entering into the registry, administrative residency in the regional community, and absence of disorder or disability that could limit their voluntary and conscious participation in the registry. There are currently 2281 Recruited Participants in the entire RTM. The Registry itself as well as the research procedures derived from it were approved by the Ethics Committee of the University of Murcia.

For this work, the available data on female pairs registered in the RTM were selected. The women participating in the registry were contacted initially in 2007 by means of a telephone interview designed to establish a first contact to obtain their consent to participate in the registry and collect basic information on demographic, health and style of life aspects. On this occasion, information was gathered on 874 women. Afterwards (2009/2010), information was gathered again by a personal interview. A total of 827 women were included in this second gathering of data, 700 of whom had also participated in the first data gathering.

In order to optimize the information for analysis, the data collected in the second gathering were selected. Thus, the final sample used for this work was made up of 827 women distributed into 437 twin pairs: 217 MZ pairs (200 of them complete) and 200 DZ pairs (190 complete). Average age was 52.5 year (SD=7.4), the range being 43 to 70 years.

### Measurements

The measurement instrument used was an inventory specifically elaborated for this study. This was based on development and was validated for studies with similar samples from the Netherlands Twins Registry. It includes questions about health, morbidity and sociodemographic factors adapted to epidemiological surveys of our setting.[7] Specifically, data on the presence of mental disorders and consumption of psychopharmaceuticals were collected using the list of diseases (Have you ever suffered/in the last twenty four months *depression, anxiety or other mental disorders*?) and medications (Have you taken *tranquilizers, relaxants, sleeping pills or antidepressants, stimulants* in the last month?) contained in the NHS-2006.

The cygosity of twins was established by DNA markers and when this was not possible, a questionnaire was applied that was specifically elaborated for this registry through the adaptation of the 12-item questionnaire used by the Netherlands Twins Registry.

### *Statistical analysis*

Consumption of psychopharmaceuticals was taken into account as dependent variables (DV) of the study. These were considered in general and according to therapeutic type: tranquilizers, relaxants or hypnotics and antidepressants or stimulants. In order to simplify the logistic regression analysis, the independent variables (IV) analyzed, except age, were categorized binarily: having a current partner or not

having one; being an active (e.g. outside of the home) or inactive worker; primary studies or less and secondary studies or more; having initiated/passed menopause or not; and having suffered or not a recent mental disorder (last 24 months) or sustained one (both in 2007 and in 2009).

Binary logistic regression models were applied with every DV to evaluate the association between the sociodemographic and clinical characteristics of the women of the sample with the use of psychotropic drugs. First, the simple logistic regression models were used to verify the capacity of the statistical association of each predictor separately. After, the multiple logistic regression was applied in order to select the combination of factors having the greatest predictive capacity. Reference categories used were as following: active employment status, having a partner, secondary studies or higher, not having begun menopause yet and not having suffered a mental disorder. The analysis of subjects from the same family produces dependency in the data. Therefore, the regression analyses were performed with adjustment of the standard error estimations to take said dependency into account. This method provides robust statistical estimations for the characteristics of the model. The analyses were performed using the STATA 12.0 statistical program.[36] Statistical significant level was established at $\alpha$=0.05 and confidence interval (CI) at 95%.

### *Genetic analysis*

Heritability was estimated with the classical study of twins, using the Mx statistical program.[37] This design basically consists in comparing the degree of similarity regarding a selected character between MZ and CZ twins. The MZ twins are genetically equal while the DZs share an average of half of their genoma. When there is phenotypal information of both twin types, the total variance of a trait can be broken down into variance due to additive genetic factors (A ), common environment (C) and unique environment. Greater similarity between MZ than DZ twins is interpreted as the result of a genetic influence on the individual differences in the trait studied. If the DZ twins show more than half of the similarity found among the MZs, this would be interpreted as an indication of the presence of common environmental effects. These effects refer to intra-familial factors that contribute to greater similarity between individuals who have lived within the same familial setting. Finally, unique environmental factors are those that specifically affect each individual and therefore contribute to differentiate the members of a couple, independently of their cygosity.

As they were categorical, the dependent variables were analyzed using the Threshold liability model. This analysis model assumes that the categories reflect an inexact measurement of an underlying liability distribution that would have one or more thresholds to discriminate between categories. This liability may be influenced by genetic as well as environmental factors and is normally distributed, with a mean equal to 0 and a variance equal to 1. The similarity of the twin pairs may therefore be estimated by the correlation on this liability scale. Said correlation is called tetrachoric or polychoric and has the classical values of this type of analysis.

To be able to use all the data, independently of whether the pair is or is not complete, the Full Information Maximum Likelihood – FIML was used in raw data. In this method, the negative likelihood logarithm (-LL) and parameters are estimated so that the likelihood of the raw data is maximized. The correlation between twins was estimated in a saturated model. The nested models were compared using the Likelihood Ratio Test - LRT, obtained from the difference between the model more and less restrictive model ($\chi^2=(-2LL_0)-(-2LL_1)$). The resulting statistics has a $\chi^2$ distribution with degrees of freedom (*df*) equivalent to the difference in *df* between both models. When the adjustment of a more restricted model significantly differs from another less restricted one, it is understood that the restriction imposed in the nested model is not adequate for the data. A non-significant change suggests that the reduction in parameters is acceptable. The best fit model, more parsimonious, is selected based on the LRT and comparing the Akaike's Information Criterion – (AIC), whose value is less as the adjustment becomes greater.[38]

## RESULTS

### Prevalence of consumption and mental disorders

The sociodemographic characteristics of the sample are summarized in Table 1. In the last month, 34.0% of the women interviewed reported that they had consumed some type of psychopharmaceuticals, relaxants or hypnotics and 15.0% antidepressants or stimulants. Analyzing the sustained consumption, 12.7% of the women reported having consumed some type of psychopharmaceutical agent in the two points in time of data collection (both in 2007 and in 2009), with 9.7% for tranquilizers, relaxants or hypnotics and 4.5% antidepressants or stimulants.

Regarding the prevalence of mental disease, 34.9% reported having recently suffered some type of mental disorder. Of these, 26 % already mentioned the presence of some disorder two years earlier.

### Factors related with consumption

#### *Sociodemographic variables and consumption of psychopharmaceuticals*

Table 2 shows the relationship of psychopharmaceutical consumption with the different sociodemographic characteristics of the sample. All the sociodemographic variables analyzed, except for the partner situation ($p$ >0.05), showed a statistically significant relationship with consumption of

**Tabla 1** Sociodemographic characteristics of the sample

| | N | % |
|---|---|---|
| Total | 827 | 100.0 |
| Employment status | | |
| Not employed | 418 | 50.6 |
| Working | 398 | 48.1 |
| NK/NA | 11 | 1.3 |
| Partnership status | | |
| Without current partner | 172 | 20.8 |
| With current partner | 647 | 78.2 |
| NK/NA | 8 | 1.0 |
| Educational level | | |
| Primary studies or less | 417 | 50.4 |
| Secondary studies or more | 387 | 46.8 |
| NK/NA | 23 | 2.8 |
| Menopause | | |
| No menopause | 295 | 35.7 |
| Menopause | 520 | 62.9 |
| NK/NA | 12 | 1.4 |

NK=does not know; NA=does not answer

psychopharmaceuticals in all the categories evaluated. Said consumption seems to increase as age increases and when the educational level is of elementary level. Thus, 40.0% of the women who manifested having only primary studies had consumed some psychopharmaceutical in the last month compared to 27.6% among those who had at least secondary studies. To be more specific, these percentages are 18.9% for antidepressants and 35.3% for tranquilizers (10.9% and 27,0%, respectively, in women with secondary school studies).

In relation to the employment situation, the likelihood of consumption was greater among those women who had no activity outside of the home (unemployed, retired or those who dedicated their time of housework) than among women who were occupationally active. The prevalences were, for general consumption: 42.4% versus 25.5%; for antidepressants: 20.7% versus 9.3%; and for consumption of tranquilizers: 39.2% versus 23.2%.

Finally, women who stated they had initiated/completed menopause showed greater consumption of psychodrugs than those who had not initiated the process. Specifically, psychodrug consumption in general was 38.5% versus 26.4%; antidepressant consumption of 18.0% versus 9.6%; and tranquilizers 34.9% versus 25.6%.

### *Mental disorder and consumption of psychodrugs*

In regards to having suffered a recent mental disorder, the data have established a clear association with the 3 categories analyzed ($p<0.001$). A total of 69.8% of the women who reported having suffered disorders of this type currently consume some type of psychodrug (61.9% tranquilizers and 39.2% antidepressants). When the disorder was sustained over time (it was already present in 2007), these percentages increased so that 84.9% of these women stated they currently consumed some psychodrug (74.3% tranquilizers and 63% antidepressants).

### *Multivariate analysis*

The multiple logistic regression analysis showed that the predictors selected for the multiple regression model three DVs analyzed were exclusively age and having suffered a previous mental disorder, both recent and sustained (Table 3). Thus, age significantly affected consumption of psychodrugs in general (OR:1.05; 95% CI:1.03-1.08) and in a similar degree, the two categories of drugs analyzed. On the other hand, having suffered a previous mental disorder significantly increased the likelihood of consumption (OR:9.63; 95% CI:6.36-14.60), especially in the case of antidepressants (OR:29.46; 95% CI:13.14-66.03). Independently, the disorder maintained over time also showed a positive association, although less, with the likelihood of consumption (OR:3.43; 95% CI:1.69-6.95). Said association was maintained for both types of psychodrugs.

## Influence regarding genetic and environmental factors

The type of sample used makes it possible to perform a classical design of twins to estimate distribution of the phenotypal variance between its genetic and environmental components. As could be expected, the tetrachoric correlations obtained were consistently greater among MZ twins than among DZ ones (Table 4). This greater similarity of the MZ points towards the presence of genetic factors involved in the phenotype of interest.

The results of the adjustment of the genetic models are shown in Table 5. In the saturated models, the thresholds could be restricted to the same values in all the groups although the fit was not significantly worse ($p > 0.05$). Thus, as expected, it is assumed that there are no differences by order between partners or by cygosity. In every case, the ACE model presented an adequate fit, without presenting significant differences with the saturated models. Thus, the nested models were adjusted, successively analyzing if the AE, CE or E models could explain the data with significant loss of adjustment. The models that best adjusted, in the

**Table 2** **Consumption of psychotropic drugs according to therapeutic class and sociodemographic and mental disease variables. Simple logistic regression**

| | General consumption with psychopharmaceuticals | | | | Tranquilizers, relaxants or hypnotics | | | | Antidepressants or stimulants | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *n* | OR | 95% CI | *p* | *n* | OR | 95% CI | *p* | *n* | OR | 95% CI | *p* |
| Age | 820 | 1.05 | 1.03-1.07 | <0.001 | 822 | 1.05 | 1.03-1.07 | <0.001 | 820 | 1.06 | 1.03-1.09 | <0.001 |
| Partner | 814 | 1.07 | 0.74-1.54 | 0.340 | 816 | 1.08 | 0.74-1.58 | 0.700 | 814 | 1.12 | 0.71-1.77 | 0.615 |
| Educational L. | 797 | 1.74 | 1.27-2.39 | 0.001 | 799 | 1.47 | 1.07-2.03 | 0.018 | 797 | 1.89 | 1.23-2.92 | 0.004 |
| Employment status | 811 | 2.15 | 1.57-2.94 | <0.001 | 813 | 2.14 | 1.55-2.95 | <0.001 | 811 | 2.54 | 1.69-3.81 | <0.001 |
| Menopause | 809 | 1.75 | 1.25-2.45 | 0.001 | 809 | 1.56 | 1.12-2.18 | 0.009 | 809 | 2.07 | 1.29-3.32 | 0.003 |
| Recent MD | 816 | 13.13 | 9.24-18.66 | <0.001 | 818 | 9.27 | 6.59-13.03 | <0.001 | 816 | 33.45 | 17.04-65.64 | <0.001 |
| Sustained MD | 696 | 14.32 | 7.35-27.86 | <0.001 | 698 | 8.12 | 4.64-14.20 | <0.001 | 696 | 15.69 | 8.70-28.32 | <0.001 |

OR: Odds ratio; CI: confidence interval. MD: mental disorder L. Level

**Table 3** **Consumption of psychotropic drugs according to therapeutic class and sociodemographic and mental disease variables. Multiple logistic regression**

| | General consumption with psychopharmaceuticals (n = 680) 82.2% | | | Tranquilizers, relaxants or hypnotics (n = 682) 82.5% | | | Antidepressants or stimulants (n = 680) 82.2% | | |
|---|---|---|---|---|---|---|---|---|---|
| | OR | 95% CI | *p* | OR | 95% CI | *p* | OR | 95% CI | *p* |
| Age | 1.05 | 1.03-1.08 | <0.001 | 1.05 | 1.02-1.07 | 0.001 | 1.07 | 1.03-1.11 | <0.001 |
| Recent MD | 9.63 | 6.36-14.60 | <0.001 | 7.06 | 4.72-10.56 | <0.001 | 29.46 | 13.14-66.03 | <0.001 |
| Sustained MD | 3.43 | 1.69-6.95 | 0.001 | 2.32 | 1.26-4.25 | 0.007 | 4.01 | 2.21-7.28 | <0.001 |

OR: *Odds ratio;* IC: intervalo de confianza

**Table 4** **Tetrachoric correlations between monozygotic twins (rMZ) and dicygotic twins (rDZ). Confidence interval (CI) 95%**

| | rMZ (n=200 pairs) | rDZ (n=190 pairs) |
|---|---|---|
| Consumption of psychoactive medication (Any) | 0.54 (0.341. 0.701) | 0.21 (-0.022. 0.426) |
| Tranquilizers, relaxants or hypnotics | 0.45 (0.247. 0.638) | 0.22 (-0.019. 0.439) |
| Antidepressants or stimulants | 0.43 (0.130. 0.668) | 0.31 (0.012. 0.564) |

three cases, were those that distribute the variance between the additive genetic (A ) and unique environment (E) of each individual (AE). No evidence was detected on the presence of common environmental (C) factors in any of the three phenotypes studied.

The estimations of the distribution of the variance are shown on the right side of Table 5. As can be observed, estimations of heritability indicate that approximately half of the variance observed in the consumption of psychoactive medication (e.g. 0.52 for consumption in general, 0.46 therefore for consumption of tranquilizers and antidepressants) is due to genetic factors, while the rest would be due to environmental factors of each individual.

## DISCUSSION AND CONCLUSIONS

This study was proposed with two complementary objectives: to analyze the prevalence of factors associated to consumption of psychopharmaceuticals in a population group (e.g., adult women) with specific traits and special interest; and to estimate the heritability of said consumption in the general population, as a phenotype with its own characteristics.

The consumption prevalence levels obtained were elevated (34.4% for consumption in general; 31.2%

**Table 5** **Results of the genetic models**

| | | Goodness of fit | | | | | | Estimations of the parameters | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Model | Components | -2LL | gl | AIC | $\Delta\chi^2$ | $\Delta$gl | P | A | C | E |
| Consumption of psychoactive medication (any) | | | | | | | | | | |
| 1 | ACE | 1027.1 | 817 | -606.8 | -- | | | 0.52 | 0 | 0.48 |
| **2** | **AE** | **1027.1** | **818** | **-608.9** | **0** | **1** | **1.00** | **0.52** | **--** | **0.48** |
| 3 | CE | 1031.8 | 818 | -604.2 | 4.67 | 1 | 0.03 | -- | 0.38 | 0.62 |
| 4 | E | 1054.2 | 819 | -583.8 | 27.06 | 2 | <0.001 | -- | -- | 1 |
| Tranquilizers, relaxants or hypnotics | | | | | | | | | | |
| 1 | ACE | 1003.09 | 819 | -634.9 | -- | | | 0.46 | 0 | 0.54 |
| **2** | **AE** | **1003.09** | **820** | **-636.9** | **0** | **1** | **1.00** | **0.46** | **--** | **0.54** |
| 3 | CE | 1005.48 | 820 | -634.5 | 2.38 | 1 | 0.12 | -- | 0.34 | 0.65 |
| 4 | E | 1022.83 | 821 | -619.2 | 19.73 | 2 | <0.001 | -- | -- | 1 |
| Antidepressants or stimulants | | | | | | | | | | |
| 1 | ACE | 684.75 | 817 | -949.25 | | | | 0.24 | 0.19 | 0.57 |
| **2** | **AE** | **685.08** | **818** | **-950.92** | **0.33** | **1** | **0.56** | **0.46** | **--** | **0.54** |
| 3 | CE | 685.11 | 818 | -950.88 | 0.37 | 1 | 0.54 | -- | 0.37 | 0.63 |
| 4 | E | 696.71 | 819 | -941.29 | 11.96 | 2 | <0.001 | - | - | 1 |

The models with best fit are shown in bold. AIC: Akaike Information Criterion. Proportion of variance explained by: Factores: additive genetics (A); presence of common environment (C); and unique environment (E) factors.

tranquilizers and 15% antidepressants). This fact can be explained by the sample composition that was only made up of adult women. It is a constant finding in the literature that this group consumes more psychopharmaceuticals than the male and younger population[1-3]. In fact, the last National Health Survey published (NHS-11/12) showed very similar figures for a population of these characteristics (Tranquilizers: 24.7% and 36.5% for women aged 45 to 64 years and 65 or more, respectively; Antidepressants: 13% and 14.5% for the age groups mentioned).] Furthermore, we found that the most commonly consumed psychopharmaceutical group is that of benzodiazepines, above the group of antidepressants. This also agrees with the studies reviewed.[3,20,22]

In the literature, psychopharmaceutical consumption is related not only to female gender and elderly age but also physical (above all chronic) and psychiatric condition, consumption of another medication, loss of social support, urban area, living alone (separated, divorced or widowed), not working outside of the home and low education level.[3,20,22,31] Our data coincide initially with part of these results. Thus, it is seen that as age increases, the consumption levels increase, that said consumption is greater among women who are not working (mainly housewives and retired), when they have initiated and completed menopause and that as the level of studies increases, consumption decreases. However, we did not find a relation between consumption and status of having a significant other. In this sense, it should be stated that a complementary analysis also showed that there were no significant differences in consumption among the different situations that occurred regarding living with a significant other (being single, separated/divorced or widowed). On the other hand, as is obvious, there is greater consumption among women who have suffered some type of mental disorder.

The multivariate analysis, however, shows the limitation of the effects of these variables in this population group. Only age and having suffered a mental disorder, both recent and sustained, maintain significance in this model. Again, the interpretation of this loss of significance is found on the characteristics of the sample. The sociodemographic variables analyzed are closely related with age. As this increases, the likelihood of belonging to the group of women who do not work (e.g. retired, housewives) and have a lower level of studies grows parallelly. Obviously, the likelihood of having begun menopause is also greater. Because of this close relationship, age is finally that which is most important for the predictive value on the consumption of psychopharmaceuticals.

On the other hand, the other variable that seems to be a risk factor for this consumption is having suffered a mental disorder, either whether because it occurred in the previous

24 months or sustained over time. The influence of this factor is so great that both categories are maintained as independent risk factors for the consumption of psychopharmaceuticals. On the other hand, it must be taken into account that in spite of the important effect recorded, there is no perfect correspondence between suffering mental disorder and consuming psychopharmaceuticals. Thus, 28.2% of those women who had taken psychoactive drugs in the last month stated they have not had any recent mental disorder. This high percentage could be partially explained by the existence of other approved indication for these drugs such as the muscle relaxant effect provided by benzodiazepines, or the use of some types of antidepressants in migraines and other diseases.[27,39] However, on the other hand, it could be suggested that a relevant percentage of subjects may be inadequately taking psychopharmaceuticals.[27,40] This would have important implications for public health that are worthwhile analyzing. These aspects should probably be studied in greater depth, placing greater attention on the analysis of the complex mechanism that conditions the prescription and use of psychopharmaceuticals in the population and to develop intervention strategies in health aimed at improving these results.

The other principal objective of this study consisted in analyzing the relative contribution of genetic and environmental factors to the consumption of psychopharmaceuticals. The estimation of the heritability obtained through the models applied indicates that approximately half of the variance of this sample would be attributable to genetic factors and the other half to individual environmental factors. This estimation is similar for all types of consumption, which supports the reliability of the results. Although there is a considerable literature on the genetic influence on the onset and frequency of consumption of illegal drugs and similar areas, such as alcohol or tobacco consumption,[41,42] we have found few comparable works. For example, Allgulander et al.[32] estimated 0.49 heritability of treatment with psychoactive medication in Swedish twins, independently of gender. Another study reported 0.28 heritability for the use of self-reported tranquilizers.[33] Although it is not directly comparable, our estimate in this sample has a similar range. That is, our data confirm that genetic factors play an important role in this phenotype. Said factors could be partially shared with an underlying mental disorder and be partially specific for the consumption of psychoactive drugs. This is especially true is we take into account the high percentage of consumers who state they have not recently suffered a mental disorder. The presence of mild psychological morbidity or personality traits (e.g. neuroticism) could act as mediators of such specific influences. On the other hand, we have not found any impact of common environmental factors. That is, the intra-familial environment, if it at one time had had an effect on this phenotype, stopped having it with the increase of age and the concomitant individual experiences.

## Limitations of the study

The type of population used, although it is a strength, can also be seen as a limitation of our study since it prevents comparison with other age groups and with males. The data collected also have some limitations. First of all, the time reference of consumption of psychopharmaceuticals was adapted and therefore it is not exactly the same as in other epidemiological studies. Although this adaptation may introduce some differences regarding comparison with surveys of Spanish reference, we understand that these differences should be very small. On the other hand, this does not invalidate the results or affect, in any way, the estimation of the distribution of variance. Along a similar line, the time reference of the consumption of the medication and having suffered mental disorder are not the same, a common fact in surveys of this type. Another limitation is that the recall bias and error could not be totally eliminated as the data were self-reported. This implies that the results should be considered conservatively. The data on the presence of mental disorders were collected using the list of diseases contained in the NHS-2006. However, the diagnosis of mental disease was not clinically confirmed with diagnostic criteria (DSM-IV-R/ ICD-10). In addition, data on frequency of consumption, dose or duration of the treatment were not collected. These data would have provided greater depth to the analysis. Finally, hormonal changes that occur during menopause may cause modifications in the mood state that could be related with the consumption, independently of age. However, our study was not designed to identify such changes adequately.

## Implications

This is one of the few population studies on the use of psychoactive medication performed by direct interview in Spain and it is the only one that permits an estimation of heritability of this phenotype. Thus, in spite of the limitations mentioned, we believe that it could be a reference point for future studies. The results achieved are useful, on the one hand, as a starting point of information for the analysis and planning of health care policies and for interventions for improvement of prescription and habits of consumption of psychopharmaceuticals. On the other hand, they represent a necessary base for the subsequent development of more specific analyses that attempt to dissect the role of the genetic factors in the consumption of psychoactive medication, independently of the presence of psychiatric disease.

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