ORIGINAL ARTICLE

An evolutionary approach to mania studying Sardinian immigrants to Argentina

Mauro G. Carta,¹ Alessandra Perra,¹ Michela Atzeni,¹ Silvia D'Oca,¹ Maria F. Moro,^{1,2} Peter K. Kurotschka,¹ Daniela Moro,¹ Federica Sancassiani,¹ Luigi Minerba,¹ Maria V. Brasesco,³ Gustavo Mausel,³ Antonio E. Nardi,⁴ Leonardo Tondo^{5,6}

¹Dipartimento di Scienze Mediche e Sanitè Pubblica, Universitè degli studi di Cagliari, Cagliari, Italy. ²Mailman School of Public Health, Columbia University, New York, NY, USA. ³Facultad de Humanidades, Universidad del Museo Social Argentino, Buenos Aires, Argentina. ⁴Instituto de Psiquiatria (IPUB), Universidade Federal do Rio de Janeiro (UFRJ), Rio de Janeiro, RJ, Brazil. ⁵Centro Lucio Bini Cagliari and Centro Lucio Bini Roma, Italy. ⁶Harvard Medical School, McLean Hospital, Boston, MA, USA.

Objective: To ascertain lifetime prevalence of positivity to a screening questionnaire for bipolar disorders (BD) in Sardinian immigrants to Argentina and residents of Sardinia and assess whether such positivity affects quality of life (QoL) in either group. Our hypothesis is that screen positivity for BD may be more frequent in immigrants.

Methods: Observational study. Subjects were randomly selected from the membership lists of associations of Sardinian immigrants in Argentina. A study carried out in Sardinia using the same methodology was used for comparison. The Mood Disorder Questionnaire was used to screen for mania/hypomania and the Short-Form Health Survey-12 to measure QoL.

Results: A higher prevalence of manic/hypomanic episodes was found in Sardinian immigrants to Argentina (p < 0.0001; odds ratio = 3.0, 95% confidence interval 1.87-4.77). Positivity at screening was associated with a lower QoL both in Sardinian immigrants to Argentina and in residents of Sardinia. **Conclusions:** To the best of our knowledge, this is the first study to show a higher lifetime prevalence of manic/hypomanic episodes in a general-population sample of individuals who migrated to a foreign country. Our results are in agreement with the hypothesis that hyperactive/novelty-seeking features may represent an adaptive substrate in certain conditions of social change.

Keywords: Epidemiology; mood disorders, bipolar; models/theories of psychiatry; social and political issues

Introduction

The study of social determinants associated with psychopathological risk in migrant populations has historically been opposed to the search for genetic-biological factors that would determine the choice to migrate in "constitutionally predisposed" individuals. The latter line of research was opened in the second half of the 19th century by the work of French psychiatrist Achille-Louis-François Foville,¹ who stated that a mental disorder might be the reason for migration. In this reformulated conception, Foville attributed a sort of "constitutional instability" to migrants. This hypothesis, which could be considered positivistic because of its outdated evolutionary perspective, was resumed by subsequent studies in Norwegian immigrants to Minnesota by Ødegaard,² who advanced the hypothesis of "selective migration." This view, later abandoned because of the stigma that it attached to migrant populations

Correspondence: Mauro Giovanni Carta, Dipartimento di sanitè pubblica, medicina clinica e molecolare, Universitè degli studi di Cagliari, Cittadella Universitaria, 09042 SS554, Monserrato, Cagliari, Italy.

as being characterized by a kind of debility compared to the populations that remained in the country of origin and those of the host country, was indeed based on questionable assumptions and weak methodological demonstrations.

More recently, consistent with the current evolutionary perspective, it has been argued that, even if a personologic/ temperamental profile characterized by hyperthymic and novelty-seeking traits can be assumed to be more frequently, but not necessarily, found in voluntary migrants, this profile can be associated with some kind of pathology. In an evolutionary perspective, a basic hyperthymic temperament profile may predispose to opportunities for adaptive success in times of crisis in which to break new ground and provide new chances, but it could also be associated with specific psychopathologic risk of mania if the cultural leap is too traumatic.³

A study conducted in the province of Buenos Aires in the midst of the worst economic crisis in the history of Argentina, between 2001 and 2002, highlighted a high risk of major depressive disorders (MDDs) in Sardinian immigrants compared to Sardinian residents.⁴ Immigrant Sardinian adult women were found to be at higher risk for depression compared to women of the same age who had not migrated. This finding differed from those of an investigation conducted among Sardinian immigrants to

E-mail: mgcarta@tiscali.it

Submitted May 19 2016, accepted Jul 19 2016, Epub Mar 09 2017.

Paris in the 1990s; in the latter study, carried out during a period of relative economic growth, Sardinian immigrants were more at risk of depression compared to residents, but especially in young males (aged 18-24).⁵

A tentative explanation of these differences led to a working hypothesis³: elective migration selects hyperactive individuals more prone to looking for something new, but at the same time subject to goal-striving stress,⁶ which is associated with the effort in reaching goals. This type of stress is thought to be typical of people in Western communities in times of economic expansion, where the possibility of improving one's conditions is counterbalanced by shared cultural objectives, conveyed and imposed by the media, that are apparently easy to reach but in reality difficult for the most disadvantaged classes. In these contexts, the lifestyle changes imposed by new societies may play a relevant role, especially in young people.

These changes may affect sleep-wake rhythms (because of occupation and leisure),⁷ use of stimulants,⁸ a shift away from the Mediterranean diet,⁹ and introduction of strong liquors in place of wine and beer¹⁰ (light beer is a traditional drink in Sardinia), all factors that may foster emergence of hypo/manic episodes in predisposed and vulnerable youths. Young men coming from traditional communities are thought to be particularly vulnerable to this type of stress because they are exposed to high levels of competition.

Later studies that did not verify these hypotheses were affected by two main limitations: they were not designed to measure association with hyperactivity or hypomania; and they did not assess vulnerability on a genetic basis.⁴

The present study was conducted on a sample of Sardinian immigrants to Argentina and residents of Sardinia to measure the lifetime prevalence of positivity to the Mood Disorder Questionnaire (MDQ), a screening questionnaire for bipolar disorders (BDs), in these two populations. Our hypothesis is that MDQ positivity would be more frequent in the immigrant population. A secondary aim was to ascertain whether such positivity affects quality of life (QoL) similarly in Sardinian immigrants and Sardinian residents.

Methods

Design and setting

This observational, cross-sectional community survey was conducted on a sample of the general population of Sardinian residents in Buenos Aires, Argentina. Data previously acquired during a survey carried out in a representative sample of seven Italian regions (including Sardinia), using a similar methodology for BD screening and QoL measurement, were used for comparison.¹¹

Sample

Research was conducted in the city of Buenos Aires and involved adults over the age of 18. Associations of Sardinian immigrants in Buenos Aires provided lists of immigrant families. One out of every five registered families was randomly selected for inclusion. Interviews were conducted by phone after verification that Sardinian immigrants were living in the household. In addition, we ascertained whether the respondents were first- or second-generation immigrants and, for the latter, if one or both parents were Sardinian; only in the latter case were subjects included in the study. Once preliminary consent had been obtained, participants were asked to provide demographic data (sex, age, residence, educational attainment, marital status, parental status, occupation, place of origin, and length of migratory path) and a subsequent meeting was arranged for administration of questionnaires. The survey took place at the headquarters of the Universidad del Museo Social Argentino, at the association of Sardinian immigrants to Buenos Aires (Sardi Uniti d'America), or at the respondent's home, depending on their location and on the ease of reaching one of the two institutional locations.

A detailed description of the control sample has been published elsewhere.^{11,12} In bried, controls were randomly drawn from municipal records of the adult population in seven different areas of Italy, including several localities with wide variations in socioeconomic conditions. The regions of Sicily, Sardinia, and Puglia in the South, Tuscany and Abruzzo in central Italy, and Friuli-Venezia Giulia in the North were included. In each region, both an urban and a rural subarea were selected. Randomization was performed after stratification by sex and into four different age groups (18-24, 25-44, 45-64, or > 64). The size of the Sardinian sample was n=465.

Tools

Demographic information was collected using a tool adopted for a previous survey conducted in 2001.⁴ To screen for hypomania, we used the MDQ¹³ in its Italian¹⁴ and Argentine Spanish¹⁵ versions. The MDQ is a useful tool for BD screening and identification of lifetime manic/ hypomanic and "sub-threshold" hyperactivity episodes, according to the new interpretation of this instrument.¹⁶ According to the Italian¹⁴ and Argentine Spanish validations,¹⁵ a score of at least seven symptoms would identify lifetime presence of bipolarity.

We also administered the Short-Form Health Survey-12 (SF-12) QoL questionnaire¹⁷ in its Italian¹⁸ and Argentinian¹⁹ versions. This tool consists of 12 items extracted from a longer version, the SF-36.²⁰ The short version has been used in several international studies and has proved to be appropriate not only for clinical samples, but also for investigations of epidemiology studies in the community. It measures individual perception about wellbeing relative to various dimensions in the month before the interview. Higher scores indicate better perception of QoL related to eight different aspects of health: physical activity, role limitations due to physical health, emotional state, physical pain, perception of general health, vitality, social activities, and mental health. The scoring allows formulation of two health indices: physical and psychological state. The Advanced Neuropsychiatric Tools and Assessment Schedule (ANTAS-SCID),¹¹ a semi-structured clinical interview partially derived from the Structured Clinical

Table 1 Study samples			
	Sardinians in Argentina (n=306)	AIFA study Sardinian sample (n=309)	AIFA study Italian overall sample (n=3,398)
Gender (male) Age ≤ 40 years Graduate-level education First generation	47.7 14.4 38.6 48 (15.9)	$\begin{array}{l} 47.8 \; (\chi^2=0.01, \; 1df, \; p=0.999) \\ 37.9 \; (\chi^2=46.90, \; 1df, \; p \; < \; 0.001) \\ 24.6 \; (\chi^2=13.89, \; 1df, \; p \; < \; 0.001) \end{array}$	$\begin{array}{l} 42.3 \; (\chi^2=0.23,\; 1df,\; p=0.634) \\ 43.4 \; (\chi^2=98.32,\; 1df,\; p<0.001) \\ 26.2 \; (\chi^2=21.68,\; 1df,\; p<0.001) \end{array}$

Data presented as % unless noted otherwise.

AIFA = Associazione Italiana del Farmaco (AIFA); df = degree of freedom.

Interview I for DSM-IV (SCID-I),²¹ was used to test for psychiatric disorders. This interview was administered by a trained clinician to 40 randomly selected individuals (positive and negative at MDQ) for quality control of screening accuracy. Overall, 10 individuals had MDQ scores \geq 7 and 30 had scores < 7. The diagnosis of BD was assumed as the gold standard.

Interviewers were psychiatric rehabilitation technicians or physicians, and were trained by a native speaker of Italian with a good knowledge of Spanish. ANTAS-SCID interviews were only administered by trained psychiatrists.

Statistical analysis

The statistical analysis involved comparisons between positivity to the MDQ (dependent variable) and three independent variables – sex, age, and SF-12 score – through multivariate logistic regression analysis, as well as a comparison between the immigrant and resident subsamples using a direct standardization method.

Direct standardization-based analysis was conducted by comparing the immigrant sample against each of the other two samples in four cells divided by gender and age as a category (\ge or < 40 years); direct standardization for age and sex was performed according to the previous four cells.

Statistical significance on 2 \times 2 tables was calculated with the chi-square (χ^2) test. Measures are expressed as odds ratios (ORs) with 95% confidence intervals (95% CIs), and were calculated using the Miettinen method.²²

The multivariate logistic regression analysis was conducted on the sample of immigrants alone as well as on a database obtained from the sum of participants of the Buenos Aires study and those of the Italian study. The SF-12 score was dichotomized by subdividing the sample on the basis of score distribution (\leq or > 36), taking into account the characteristics of the previously published Italian community sample.^{11,23} The same subdivision was used for the Argentine distribution.

In a quality control survey on the accuracy of screening tests, the sensitivity and specificity of MDQ at the same cutoff used in this research was recalculated, using the diagnosis of BD as the gold standard, in a group of 10 MDQ-positive and 30 MDQ-negative individuals.

Ethical aspects

The subjects were provided full information about the nature and purpose of the study, and were informed of the possibility of terminating the interview at any time. Participants were asked to sign an informed consent form, and those enrolled were given information about data protection and privacy laws. Specifically, the interviewers explained that the collected data would be used to compile an anonymous database and that confidentiality would be maintained in accordance with Argentinian and Italian laws on data protection.

This study was conducted in accordance with the ethical principles contained in the Declaration of Helsinki. The Ethics Committee of Azienda Ospedaliero-Universitaria di Cagliari and the board of the Universidad del Museo Social Argentino approved the final study protocol.

Results

The sample in this survey consisted of 306 individuals of Sardinian origin who were first- or second-generation migrants to Argentina and resided in the city of Buenos Aires.

Of the 367 individuals selected from the lists provided by Sardinian clubs in Buenos Aires, 61 (16.6%) did not participate because they could not be traced, were not available, or refused to participate.

Table 1 shows the characteristics of the sample of Sardinian immigrants to Argentina and of the two comparison samples. Sardinian immigrants did not differ in gender distribution; they were significantly older and had a significantly higher rate of graduates. Only 48 immigrants (15.7%) were first-generation, all of whom were over age 40.

Table 2 shows the lifetime prevalence of MDQ positivity (score \geq 7) among Sardinian immigrants and in the two samples from the Associazione Italiana del Farmaco (AIFA) study on prevalence of mood disorders (Sardinians in Sardinia and other Italians). The sample of immigrants to Argentina showed a significantly higher frequency of MDQ positivity than residents in Sardinia or other Italians, and the differences increased after standardization.

Comparisons between the two samples of Sardinians (immigrants and residents) showed no significant differences considering the four age and gender cells, but immigrant women showed a higher frequency of MDQ positivity, regardless of age, on comparison against the total Italian sample.

After pooling the age and gender cells, only the comparison between immigrant women showed a higher frequency of MDQ positivity if compared with the total Italian sample, but not on comparison with the Sardinian resident sample. In both age strata, MDQ positivity was more common in immigrants than in the total Italian sample; only in the older age stratum was the frequency
 Table 2
 Lifetime prevalence of MDQ positivity in Sardinian immigrants vs. residents of Sardinia and of six different regions of

 Italy (AIFA study database)

Age, gender	Sardinian immigrants	Sardinians in Sardinia	Italians	Comparison vs. Sardinians	Comparison vs. Italians
\leqslant 40, male	1 (8.3)	1 (2.2)	25 (3.7)	χ^2 with Yates correction = 1.04, p = 0.316; OR = 4.00	χ^2 with Yates correction = 0.004, p = 0.952; OR = 2,33
\leqslant 40, female	4 (12.5)	3 (4.2)	28 (3.4)	95%CI 0.10-162.24 χ^2 with Yates correction = 1.30, p = 0.254; OR = 3.28 95%CI 0.57-20.09	γ^{2} with Yates correction = 4.656, p = 0.031; OR = 4.00 γ^{2} (1 1 1 1 3 1
> 40, male	8 (6.0)	2 (1.9)	24 (3.1)	$\chi^2 = 2.33, p = 0.126; OR = 3.10$ 95%Cl 0.61-22.38	$\chi^2 = 2.73, p = 0.098; OR = 1.97$ 95%CI 0.79-4.75
> 40, female	9 (7.2)	3 (3.3)	26 (2.3)	χ^2 = 1.32, p = 0.256; OR = 2.15 95%CI 0.51-0.34	$\chi^2 = 9.67, p = 0.002; OR = 3.24$ 95%CI 1.37-7.44
Male	9 (6.1)	49 (3.4)	3 (2.0)	χ ² = 2.08, p = 0.09; OR = 1.86 95%Cl 0.83-0.404	χ ² = 3.28, p = 0.007; OR = 3.17 95%Cl 0.87-15.01
Female	13 (8.0)	8 (4.9)	54 (2.7)	χ ² = 1.27, p = 0.267; OR = 1.68 95%Cl 0.52-4.58	χ ² = 14.35, p < 0.001; OR = 3.17 95%Cl 1.60-6.14
≤ 40	5 (11.4)	4 (3.5)	53 (3.5)	χ ² = 1.32, p = 0.255; OR = 2.15 95%Cl 0.51-0.34	χ ² = 3.90, p = 0.048; OR = 3.61 95%Cl 1.0-15.1
> 40	17 (6.5)	50 (2.6)	5 (2.6)	χ ² = 18.65, p = 0.001; OR = 2.59 95%Cl 1.71-4.70	χ ² = 7.49, p = 0.008; OR = 3.45 95%Cl 1.14-9.63
Total	22 (7.2)	9 (2.9)	103 (3.0)	χ ² = 5.97, 1 df; p = 0.015; OR = 2.47 95%Cl 1.49-4.06	$\label{eq:constraint} \begin{split} \chi^2 = 14.79, \ 1 \ DF; \ p < 0.001; \ OR = 2.32 \\ 95\% CI \ 1.39\text{-}5.38 \end{split}$
Total after direct standardization by sex and age	25.9 (8.5)	-	103 (3.0)	-	$\label{eq:constraint} \begin{split} \chi^2 = 25.53, 1\text{DF}; p < 0.001; \text{OR} = 2.95 \\ 95\%\text{Cl} 1.83\text{-}4.70 \end{split}$
Total after direct standardization by sex and age	26.3 (8.6)	9 (2.9)	-	$\label{eq:constraint} \begin{split} \chi^2 = 26.65, \mbox{ 1 df; } p < 0.001; \mbox{ OR = 3.0} \\ 95\% \mbox{Cl 1.87-4.77} \end{split}$	-

Data presented as n (%).

95%CI = 95% confidence interval; df = degree of freedom; MDQ = Mood Disorder Questionnaire; OR = odds ratio.

Table 3 Linear regression: factors related to MDQ	positivity in Sardinian immigrants to Argentina
--	---

	•	•	-	<u> </u>	
MDQ positivity	Coef	SD	Z	p-value > z	95%CI
Gender (male) Age SF-12 ≥ 36 Constant	-0.2445912 -0.0671245 -1.940893 2.308484	0.5097969 0.0110636 0.5301076 0.8383879	-0.48 -6.07 -3.66 2.75	0.631 0.000 0.000 0.006	-1.243775 to 0.7545923 -0.0888088 to -0.0454402 -2.979885 to -0.9019014 0.665274 to 3.95169
e en eta n	2.000.01	0.00000.0		0.000	

95%CI = 95% confidence interval; Coef = coefficient; MDQ = Mood Disorder Questionnaire; SD = standard deviation; SF-12 = Short-Form Health Survey-12.

Pseudo R2 = 0.1892.

higher in immigrants than in the sample of Sardinians resident in Sardinia.

Although none of the 48 first-generation Sardinians (all aged > 40 years, 21 [45.8%] male) were MDQpositive, the difference with respect to the remaining 258 immigrants (positivity rate 8.5%) was statistically significant (χ^2 = 4.41, 1 degree of freedom, p = 0.036).

Table 3 shows the results of logistic regression in the immigrant sample. The dependent variable was MDQ positivity, while the independent variables were age, gender, and SF-12 score. Gender was not associated with a specific risk of MDQ positivity, whereas both age and SF-12 scores showed a significant inverse relationship (p < 0.0001).

Table 4 shows the results of logistic regression analysis of the database obtained from the sum of Buenos Aires study participants and Italian study participants, using the same dependent and independent variables as in the analysis carried out on the immigrant sample. Regarding

Rev Bras Psiquiatr. 2017;39(2)

comparisons within the immigrant sample alone, gender did not appear to be associated with a specific risk of MDQ positivity, whereas both age and SF-12 scores showed a significant inverse relationship with risk of MDQ positivity (p < 0.0001).

Table 5 shows the results of the quality control survey carried out to evaluate the accuracy of the MDQ (cutoff \ge or < 7). We found a sensitivity of 66.6%, a specificity of 78.3%, a positive predictive value of 20%, and a negative predictive value of 96.6%.

Discussion

To our knowledge, this was the first study to show a higher lifetime prevalence of manic/hypomanic episodes in a general-population sample of individuals who emigrated to a foreign country (Argentina) compared to a sample of individuals from the same population who still reside in their country of origin. Screening positivity for

Table 4 Logistic regression analysis of a database obtained by pooling the Buenos Aires and Italian study samples, using the same dependent (MDQ positivity) and independent variables, plus residency in Argentina, compared with analysis carried out in the immigrant sample alone (Table 3)

MDQ positivity	Coef	SD	Z	p-value $> z$	95%CI
Gender (male)	-0.2834746	0.2017998	-1.40	0.160	-0.6789949 to 0.1120458
Age	-0.029837	0.0053552	-5.57	0.000	-0.040333 to -0.019341
SF-12 ≥ 36	-1.351082	0.2149486	-6.29	0.000	-1.772373 to -0.9297904
Argentina	0.9896406	0.2633408	3.76	0.000	0.4735021 to 1.505779
Constant	-0.8220475	0.3258493	0.012	0.012	-1.4607 to -0.1833946

95%CI = 95% confidence interval; Coef = coefficient; MDQ = Mood Disorder Questionnaire; SD = standard deviation; SF-12 = Short-Form Health Survey-12.

Pseudo R2 = 0.0662.

Table 5 Accuracy of the Mood Disorder Questionnaire

 screening for bipolar disorder in the specific study sample

Sensitivity	66.6%
Specificity	78.3%
Positive predictive value	20.0%
Negative predictive value	96.6%

Cutoff: 7. Gold standard: Advanced Neuropsychiatric Tools and Assessment Schedule (ANTAS-SCID) diagnosis of bipolar disorder I, bipolar disorder II, or cyclothymic disorder.

ever having experienced a manic episode was more common in women living in Argentina compared to women living in Italy but not in Sardinia. Positive screening for mania was associated with lower satisfaction with QoL in a way that did not differ between Sardinians in Argentina and those in their country of origin.

If we accept the hypothesis that the characteristics of hyperthymia/bipolarity are more dependent on basic genetic heritage than those of non-bipolar depression,^{24,25} our study appears to confirm – for the first time through a standardized, reproducible methodology – the hypothesis that migration, or at least this specific migration, may involve individuals with a higher risk of manic episodes (thus, with baseline hyperthymic characteristics). However, in apparent contradiction to this theory, and certainly in contrast with the "selective migration" hypothesis that migrants are unstable and vulnerable to mental illness, first-generation Sardinians did not appear to share this risk of greater MDQ positivity.

The concept that migration flows may select hyperthymic individuals had in fact been advanced by popular science literature more than proven by scientific research. In the United States in particular, the book The Hypomanic Edge: The Link Between (A Little) Craziness and (A Lot of) Success in America,26 which advanced such a hypothesis, enjoyed considerable success in the media. This seemingly "naïve theory" agreed with the point of view of Akiskal, who pointed out the possible "evolutionary positive" role of the soft bipolar spectrum, considering a number of factors including novelty seeking, geographical instability, and risk-taking behavior as typical of this spectrum.²⁷ This hypothesis has been evoked to comment on the lower BD rates found in the U.S. compared to Europe, both in patients referred to general practice²⁸ and in community surveys.²⁹ However, differences in healthcare systems in the first case and dishomogeneity in survey adherence rates in the second may have affected the results regardless of the real rates of BD in the two populations. We have found that the selective migration of hyperthymic people may explain the decrease in depression highlighted in an epidemiological study repeated several times over 30 years in a mining district of Sardinia, in which there had been progressive depopulation due to mine closures.³⁰ This is in agreement with the fact that sensation-seeking and affective temperaments were found to be common in subjects with DSM-IV-defined MDD and current depression.³¹

However, in the analyses that followed our previous studies, an attempt to apply this theory to Sardinian emigration in Argentina led us to state that it could apply to male Sardinian immigrants only. Unlike for men, who chose to migrate, for women in the 1950s and 1960s, migration was more often imposed by the duty to follow their fiances or husbands wherever the latter had decided to go more than a consequence of a new desire and impulse to explore.⁴

Recently, investigators have argued that MDQ positivity does not identify individuals with a diagnosis of BD, but rather people affected by a comprehensive set of disorders called the bipolar spectrum; in this context, people with a diagnosis of BD supposedly represent the tip of the iceberg.¹⁶ Taking this consideration into account, the low positive predictive value we found in our quality control study, as well as in previous studies, is no wonder, as the gold standard employed is simplistic compared to the wide spectrum of illness that is identified by MDQ positivity.

It should be noted that in the Argentine sample, as well as in the sample of the Italian study, MDQ positivity was associated with lower QoL scores.

If MDQ positivity does not reveal the presence of a BD *tout court*, it is in any case indicative of a state of malaise or even disease, as confirmed by the low level of QoL (as in the present study) and by other indicators often associated with MDQ positivity, such as consumption of drugs and health care resources, consumption of alcohol and other substances, risk of a high frequency of depressive episodes, and risk of suicidality comorbid with other psychiatric conditions.¹⁶

However, the fact that the frequency of MDQ positivity appears high in second-generation migrants but low in first-generation ones does not necessarily mean that the latter had no genetic risk profile for bipolar spectrum disorder. One explanation is that the same genotype may not have manifested as a pathological condition in a changing world in which exploration and competition could be strongly adaptive.

If we hypothesize that mood disorders are increasing in the current world and that, according to the theories of HB Murphy,³² the forms of these disorders we know have appeared as mass phenomena at least since the 17th century, we must also postulate that at least some common genotypic features must have an adaptive advantage in determined and specific frameworks; otherwise, mood disorders would have disappeared. Our results are in agreement with the hypothesis that hyperactive/novelty-seeking features may represent an adaptive substrate in certain conditions of social change.

Many Sardinians who now have reached a solid social standing in Paris (starting from the 1990s) and in Argentina (starting from the 1960s) had to face a difficult challenge in a world completely different from their traditional one. A certain attitude towards challenges and hyperactivity may have facilitated their choice to make the social change or decide to emigrate. However, it bears stressing that social interactions, such as in the case of Sardinian couples, may have caused the selection of women resigned to pessimism and a sense of duty.

At the same time, new opportunities may also represent a risk: those who accept the challenge agree to live in a more stressful world in which the gene expression of heredity may be different in their children.

One could also imagine that, in a world that is stable and in which opportunities are fewer than in the exploratory period, adaptive attitudes to social mediation – rather than competition and exploration – can become gradually stronger.

This study has a limitation often typical of research into communities of migrants: it investigates a population whose characteristics are unknown. The Sardinians identified by migrants' clubs may not be representative of the universe of migrants, especially considering the fact that many names of Sardinian origin have been changed in the registers of Argentinian municipalities and, thus, clubs which have conducted research on Sardinian surnames may not have a complete picture of migrant population. For example, we do not know whether the high frequency of graduates in the sample of Sardinian migrants is a real feature of the universe of Sardinian migrants or is rather determined by a selection bias.

Another limitation is that we do not have sufficient reference information about normative data for the means used in the Argentine population.

In this specific study, we did not conduct any analysis of socioeconomic conditions during the survey. Thus, we have consequentially considered a measurement of lifetime prevalence of the condition (MDQ positivity). In future papers, using measures of point prevalence of mood disorders, we will consider comparisons between economic conditions at the time of the present survey and those of a previous study conducted in 2001-2002.

In conclusion, we believe this was the first study to show a higher lifetime prevalence of manic/hypomanic episodes in a general population of offspring of individuals who migrated to a foreign country. Our results are in agreement with the hypothesis that hyperactive/novelty-seeking features may represent an adaptive substrate in certain conditions of social change.

Acknowledgements

Three authors (AP, MA, SD'O) received funding from the Globus Placement project, Universitè degli studi di Cagliari, to conduct research in Argentina.

Disclosure

The authors report no conflicts of interest.

References

- Foville A. Des Divers modes de l'assistance publique applicables aux aliénés. Paris: Martinet; 1865. [cited 2016 Feb]. gallica.bnf.fr/ark/ 12148/bpt6k5619439r/f2.image.
- 2 Ødegaard Ø. Emigration and Insanity. A study of mental disease among the Norwegian born population of Minnesota. Acta Psychiatr Neurol Scand. 1932;Suppl 4:1-206.
- 3 Carta MG. Social change and increasing of bipolar disorders: an evolutionary model. Clin Pract Epidemiol Ment Health. 2013;9:103-9.
- 4 Carta MG, Reda MA, Consul ME, Brasesco V, Cetkovich-Bakmans M, Hardoy MC. Depressive episodes in Sardinian emigrants to Argentina: why are females at risk? Soc Psychiatry Psychiatr Epidemiol. 2006; 41:452-6.
- 5 Carta MG, Kovess V, Hardoy MC, Morosini P, Murgia S, Carpiniello B. Psychiatric disorders in Sardinian immigrants in Paris: a comparison with Parisians and Sardinians resident in Sardinia. Soc Psychiatry Psychiatr Epidemiol. 2002;37:112-7.
- 6 Kleiner RJ, Parker S. Social-psychological aspects of migration and mental disorder in a negro population. Am Behav Sci. 1969;13: 104-25.
- 7 Abreu T, Bragança M. The bipolarity of light and dark: a review on bipolar disorder and circadian cycles. J Affect Disord. 2015;185: 219-29.
- 8 Chen J, Fang Y, Kemp DE, Calabrese JR, Gao K. Switching to hypomania and mania: differential neurochemical, neuropsychological, and pharmacologic triggers and their mechanisms. Curr Psychiatry Rep. 2010;12:512-21.
- 9 Beyer JL, Payne ME. Nutrition and bipolar depression. Psychiatr Clin North Am. 2016;39:75-86.
- 10 Ratheesh A, Cotton SM, Betts JK, Chanen A, Nelson B, Davey CG, et al. Prospective progression from high-prevalence disorders to bipolar disorder: exploring characteristics of pre-illness stages. J Affect Disord. 2015;183:45-8.
- 11 Carta MG, Aguglia E, Bocchetta A, Balestrieri M, Caraci F, Casacchia M, et al. The use of antidepressant drugs and the lifetime prevalence of major depressive disorders in Italy. Clin Pract Epidemiol Ment Health. 2010;6:94-100.
- 12 Carta MG, Moro MF, Lorefice L, Picardi A, Trincas G, Fenu G, et al. Multiple sclerosis and bipolar disorders: the burden of comorbidity and its consequences on quality of life. J Affect Disord. 2014; 167:192-7.
- 13 Hirschfeld RM, Williams JB, Spitzer RL, Calabrese JR, Flynn L, Keck PE Jr, et al. Development and validation of a screening instrument for bipolar spectrum disorder: the mood disorder questionnaire. Am J Psychiatry. 2000;157:1873-5.
- 14 Hardoy MC, Cadeddu M, Murru A, Dell'Osso B, Carpiniello B, Morosini PL, et al. Validation of the Italian version of the "Mood Disorder Questionnaire" for the screening of bipolar disorders. Clin Pract Epidemiol Ment Health. 2005;1:8.
- 15 Zaratiegui RM, Vázquez GH, Lorenzo LS, Marinelli M, Aguayo S, Strejilevich SA, et al. Sensitivity and specificity of the mood disorder questionnaire and the bipolar spectrum diagnostic scale in Argentinean patients with mood disorders. J Affect Disord. 2011;132:445-9.
- 16 Carta MG, Angst J. The screening of bipolar disorders: a public health issue. J Affect Disord. 2016;205:139-43.
- 17 Ware J Jr, Kosinski M, Keller SD. A 12-item short-form health survey: construction of scales and preliminary tests of reliability and validity. Med Care. 1996;34:220-33.

- 18 Carta MG, Aguglia E, Caraci F, Dell'Osso L, Di Sciascio G, Drago F, et al. Quality of life and urban/rural living: preliminary results of a community survey in Italy. Clin Pract Epidemiol Ment Health. 2012;8:169-74.
- 19 Guex JJ, Avril L, Enrici E, Enriquez E, Lis C, Taïeb C. Quality of life improvement in Latin American patients suffering from chronic venous disorder using a combination of Ruscus aculeatus and hesperidin methyl-chalcone and ascorbic acid (quality study). Int Angiol. 2010;29:525-32.
- 20 McHorney CA, Ware JE Jr. Construction and validation of an alternate form general mental health scale for the Medical Outcomes Study Short-Form 36-Item Health Survey. Med Care. 1995;33: 15-28.
- 21 First M, Spitzer R, Gibbon M, Williams J. Structured Clinical Interview for DSM-IV Axis I Disorders, Research Version, Non-Patient Edition (SCID-I/NP). New York: Biometrics Research, New York State Psychiatric Institute; 1997.
- 22 Miettinen OS, Nurminen M. Comparative analysis of two rates. Stat Med. 1985;4:213-26.
- 23 Carta MG, Aguglia E, Balestrieri M, Calabrese JR, Caraci F, Dell'Osso L, et al. The lifetime prevalence of bipolar disorders and the use of antidepressant drugs in bipolar depression in Italy. J Affect Disord. 2012;136:775-80.
- 24 Schulz PE, Arora G. Depression. Continuum (Minneap Minn). 2015; 21(3 Behavioral Neurology and Neuropsychiatry):756-71.
- 25 Genetics of Personality Consortiumde Moor MH, van den Berg SM, Verweij KJ, Krueger RF, Luciano M, et al. Meta-analysis of genome-wide

association studies for neuroticism, and the polygenic association with major depressive disorder. JAMA Psychiatry. 2015;72:642-50.

- 26 Gardner DJ. The hypomanic edge: the link between (a little) craziness and (a lot of) success in America. New York: Simon & Schuster; 2005.
- 27 Lara DR, Bisol LW, Ottoni GL, de Carvalho HW, Banerjee D, Golshan S, et al. Validation of the "rule of three," the "red sign" and temperament as behavioral markers of bipolar spectrum disorders in a large sample. J Affect Disord. 2015;183:195-204.
- 28 Stubbs B, Vancampfort D, Solmi M, Veronese N, Fornaro M. How common is bipolar disorder in general primary care attendees? A systematic review and meta-analysis investigating prevalence determined according to structured clinical assessments. Aust N Z J Psychiatry. 2016;50:631-9.
- 29 Merikangas KR, Akiskal HS, Angst J, Greenberg PE, Hirschfeld RM, Petukhova M, et al. Lifetime and 12-month prevalence of bipolar spectrum disorder in the National Comorbidity Survey replication. Arch Gen Psychiatry. 2007;64:543-52.
- 30 Carta MG, Mura G, Lecca ME, Moro MF, Bhat KM, Angermeyer MC, et al. Decreases in depression over 20years in a mining area of Sardinia: due to selective migration? J Affect Disord. 2012;141:255-60.
- 31 Fornaro M, Ventriglio A, De Pasquale C, Pistorio ML, De Berardis D, Cattaneo CI, et al. Sensation seeking in major depressive patients: relationship to sub-threshold bipolarity and cyclothymic temperament. J Affect Disord. 2013;148:375-83.
- 32 Murphy HB. The advent of guilt feelings as a common depressive symptom: a historical comparison on two continents. Psychiatry. 1978;41:229-42.