

Research report

Bipolar disorders and affective temperaments: A national family study testing the “endophenotype” and “subaffective” theses using the TEMPS-A Buenos Aires

Gustavo H. Vázquez^{a,*}, Clara Kahn^b, Claudia E. Schiavo^b, Aníbal Goldchluk^c, Luis Herbst^c, Maria Piccione^c, Norberto Saidman^c, Hernán Ruggeri^d, Alfredo Silva^c, Jorge Leal^d, Gerardo García Bonetto^d, Rodolfo Zaratiegui^e, Eduardo Padilla^f, Juan J. Vilapriño^g, María Calvó^h, Gonzalo Guerrero^h, Sergio A. Strejilevichⁱ, Marcelo G. Cetkovich-Bakmasⁱ, Kareen K. Akiskal^j, Hagop S. Akiskal^j

^a Department of Neuroscience, University of Palermo, Buenos Aires, Argentina

^b Department of Mental Health, Teodoro Alvarez Hospital, Buenos Aires, Argentina

^c Out-patient Service, José T. Borda Hospital, Buenos Aires, Argentina

^d Center for Clinical Investigation, San Nicolas Private Clinic, Córdoba, Argentina

^e Psinapsys Psychiatric Private Center, La Plata, Argentina

^f Nestor Sequeiros Psychiatric Hospital, San Salvador de Jujuy, Argentina

^g Prof Vilapriño Psychiatric Institute, Mendoza, Argentina

^h Institute of Psychopathology, San Salvador de Jujuy, Argentina

ⁱ Department of Psychiatry INECO and Institute of Neurosciences Favaloro Foundation, Buenos Aires, Argentina

^j International Mood Center, La Jolla, CA, USA

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Abstract

Background: The purpose of this study is to examine the prevalence of affective temperaments between clinically unaffected relatives of bipolar patients and secondarily to investigate the impact of these “subaffective” forms on their quality of life (QoL).

Methods: The study was performed in seven sites across Argentina. We administered the scales TEMPS-A and Quality of Life Index to a sample of 114 non-ill first degree relatives of bipolar disorder patients (“cases”) and 115 comparison subjects without family history of affective illness (“controls”). We used The Mood Disorder Questionnaire to rule out clinical bipolarity.

Results: Mean scores on all TEMPS-A subscales were significantly higher in cases, except for hyperthymia. The prevalence of affective temperaments, according to Argentinean cut-off points, was also higher, with statistical significance for cyclothymic and anxious temperaments. Regarding QoL, we found no significant differences between both groups, except for interpersonal functioning, which was better in controls. A detailed subanalysis showed significant effects of QoL domains for all temperaments, except for the hyperthymic.

Limitations: We used self-report measures. A larger sample size would have provided us greater statistical power for certain analyses.

* Corresponding author. Department of Neuroscience, University of Palermo, Mario Bravo 1259, C.P. 1425. Buenos Aires, Argentina. Tel./fax: +54 11 4826 0770.

E-mail address: gvazquez@palermo.edu (G.H. Vázquez).

Conclusions: Our findings support the concept of a spectrum of subthreshold affective traits or temperaments – especially for the cyclothymic and anxious – in bipolar pedigrees. We further demonstrated that, except for the hyperthymic, quality of life was affected by these temperaments in “clinically well” relatives. Overall, our data are compatible with the “endophenotype” and “subaffective” theses for affective temperaments.

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1. Introduction

Kraepelin (1921) described four basic affective dispositions – depressive, manic, irritable and cyclothymic – which he believed to be subclinical forms of affective psychosis and stated that they could be found in the family members of manic–depressive patients. These temperaments could be either characteristic for each individual, without developing any affective illness, or constitute a predisposition pattern for an affective episode.

In line with this tradition, and Kretschmer’s model (1936), the senior authors of this article (Akiskal et al., 1979; Akiskal and Mallya, 1987; Akiskal and Akiskal, 1992) developed operational criteria to identify these temperaments which are relevant for affective illness postulated as a *continuum* of several disorders, ranging from subthreshold affective traits at one end to severe schizoaffective bipolar type disorder at the other end (Akiskal and Pinto, 1999). A special instrument for assessing the four traditional (and the anxious) temperaments was developed in the Temperament Evaluation of Memphis, Pisa, Paris and San Diego, first as an interview format (Placidi et al., 1998; Akiskal et al., 1998), and ultimately in an auto-questionnaire version (TEMPS-A; Akiskal and Akiskal, 2005a).

The purpose of this study is first and foremost to examine the prevalence of affective temperaments between first degree relatives of bipolar patients without affective disorders using the local version of the TEMPS-A [TEMPS-A Buenos Aires (Vázquez and Akiskal, 2005; Vázquez et al., 2007)]. Secondly we wished to investigate the functional impact of these “subaffective” forms on the quality of life in these “clinically well” relatives.

2. Methods

2.1. Subjects

We studied 114 first degree relatives (parents, children and siblings) of patients under treatment for a

DSM-IV diagnosis of bipolar disorder (“cases”). The comparison group was a sample of 115 people without present or past psychiatric illness and without any history of affective illness in their first degree relatives (“controls”).

Subjects under 18 years old and cases with clinical diagnosis for bipolar disorder were excluded. In line with the ethical guidelines for research subjects in Argentina and the participating hospitals, they gave written informed consent to participate in the study after the procedures had been fully explained. All interviews were conducted between September 26th 2005 and June 10th 2006 by a local expert on clinical affective field in each site from five cities across Argentine Republic (Table 1): Hospital Neuropsiquiátrico Provincial (Córdoba), Hospital Teodoro Álvarez (Capital Federal), Hospital Nestor Sequeiros (San Salvador de Jujuy), Instituto de Psicopatología (San Salvador de Jujuy), Hospital José T. Borda (Capital Federal), Instituto Vilapriño (Mendoza) y Psinapsys (La Plata).

The “well relatives” (cases) were 78 women and 36 men, mean age 43 ± 17.2 years. 38.6% were sons of a bipolar patient, 34.2% were parents and 23.7% siblings. About two thirds had bipolar I relatives and the other third bipolar II. A complete sociodemographic profile of the total sample is displayed in Table 2. Controls were slightly younger and more educated. We did not find

Table 1
Participants by site and group

Site	Group		Total
	Controls	Cases	
Hospital José T. Borda	16	17	33
Hosp. Neuropsiquiátrico Provincial	15	10	25
Hospital Alvarez	52	52	104
Hospital N. Sequeiros	2	6	8
Inst. de Psicopatología	8	11	19
Instituto Vilapriño	10	9	19
Psinapsys	12	9	21
Total	115	114	229

Table 2
Demographic characteristics of the sample

Variables	Categories	Groups		<i>p</i> associated
		Cases	Controls	
		<i>n</i> =114	<i>n</i> =115	
Age	Mean±SD*	43±17.2	39±13.9	0.05 ^(a)
Sex <i>n</i> (%)	Female	78 (68.4)	71 (61.7)	0.29 ^(b)
	Male	36 (31.6)	44 (38.3)	
Marital status** <i>n</i> (%)	Single	42 (36.9)	51 (45.5)	0.45 ^(c)
	Married	56 (49.1)	49 (43.7)	
	Divorced	4 (3.5)	4 (3.6)	
	Split	4 (3.5)	5 (4.5)	
Level of education*** <i>n</i> (%)	<High school	22 (19.8)	8 (7.1)	0.004 ^(b)
	High school	49 (44.2)	44 (38.9)	
	but <university			
	University complete	40 (36.0)	61 (54.0)	
Relative's bipolar type <i>n</i> (%)	I	75 (65.8)	0	–
	II	39 (34.2)	0	

^(a)*t*-Student test, ^(b)Chi-square Test, ^(c)Fisher's Exact Test.

* SD: Standard deviation.

** : 3 missing data in the control group.

*** : 3 missing data in cases and 2 in controls.

any statistically significant difference between sex and marital status.

2.2. Measures

To rule out clinical bipolarity in our samples, we used the Mood Disorder Questionnaire (MDQ). This is a one-page auto administered instrument that constitutes a quick and convenient way to assess the presence of bipolar disorders.

The MDQ is a self-report inventory that screens for bipolar I and II disorders with 13 yes/no items derived from both DSM-IV criteria and clinical experience (Hirschfeld et al., 2000). A positive screen requires that seven or more items be endorsed, that at least several of the items co-occurred, and that the symptoms caused at least moderate psychosocial impairment. The Mood Disorder Questionnaire was validated in a U.S. national general population (Hirschfeld et al., 2003). In this study we used a local version of the MDQ that was adapted for Argentina by one of the authors (R.Z.) by means of the double translation method.

The auto-questionnaire version of the Temperament Evaluation of Memphis, Pisa, Paris and San Diego (TEMPS-A) is a self-report instrument developed by the senior authors (K.K.A. and H.S.A.) of this article (Akiskal and Akiskal, 2005a,b). It consists of 110 items

Table 3
Descriptive data for cases and healthy controls on each temperament subscale

Subscale	Group	Scores		Affective temperaments ^a <i>N</i> (%)
		Mean	SD	
Dysthymia	Cases	8.92**	0.376	11 (12.54)
	Controls	6.44	0.306	5 (5.75)
Cyclothymia	Cases	6.26*	0.448	8 (9.12) [§]
	Controls	4.69	0.378	0 (0)
Hyperthymia	Cases	8.97	0.408	0 (0)
	Controls	9.13	0.409	1 (1.15)
Irritability	Cases	4.91*	0.357	4 (4.56)
	Controls	3.66	0.284	2 (2.3)
Anxiousness	Cases	9.25**	0.547	9 (10.26) [‡]
	Controls	6.19	0.416	1 (1.15)

p*<0.01; *p*<0.001 for total scores (*t* test).

[§]*p*<0.003; [‡]*p*<0.01 (Fisher's Test).

^a According to cut-off points for Argentine population (+2 SD above the mean, Vázquez et al., 2007).

that measure affective temperamental traits, present in the subject's whole life, represented in five dimensional scales: depressive, cyclothymic, hyperthymic, irritable and anxious. The original questionnaire was translated into the Spanish language spoken in Argentina by a

Table 4
Frequencies and proportion of true responses for items corresponding to the Dysthymic Subscale, among cases and controls

Item number Dysthymic Subscale	Cases <i>n</i> (%)	Controls <i>n</i> (%)	Test's statistics	Associated <i>p</i> *
1	20 (17.5)	5 (4.3)	10.25	0.001
2	14 (12.3)	13 (11.3)	0.052	0.82
3	50 (43.9)	25 (21.7)	12.72	<0.0001
4	30 (26.3)	18 (15.7)	3.93	0.047
5	23 (20.2)	13 (11.3)	3.4	0.065 **
6	13 (11.4)	9 (7.8)	0.844	0.36
7	34 (29.8)	22 (19.1)	3.54	0.06 **
8	45 (39.5)	22 (19.1)	11.45	0.001
9	56 (49.1)	49 (42.6)	0.98	0.32
10	70 (61.4)	49 (42.6)	8.1	0.004
11	64 (56.1)	37 (32.3)	13.34	<0.0001
12	32 (28.1)	20 (17.4)	3.72	0.054 **
13	71 (62.3)	46 (40.0)	11.37	0.001
14	93 (81.6)	99 (86.1)	0.86	0.35
15	66 (57.9)	54 (47.0)	2.75	0.097 **
16	97 (85.1)	90 (78.3)	1.78	0.18
17	49 (43.0)	29 (25.2)	8.05	0.005
18	75 (65.8)	76 (66.1)	0.002	0.96
19	42 (36.8)	25 (21.7)	6.31	0.012
20	32 (28.1)	13 (11.3)	10.19	0.001
21	41 (36.0)	27 (23.5)	4.28	0.04

Data in bold indicate level of significance α 5%.

* Chi-square *p* associated value.

** Significance test at a level $\alpha=0.10$.

Table 5
Frequencies and percentages of true responses for all items in the Cyclothymic Subscale, among cases and controls

Item number Cyclothymic Subscale	Cases <i>n</i> (%)	Controls <i>n</i> (%)	Test's statistics	Associated <i>p</i> *
22	43 (37.7)	31 (20.7)	3.03	0.082 **
23	53 (46.5)	39 (33.9)	3.77	0.052 **
24	33 (28.9)	21 (18.3)	3.63	0.057 **
25	26 (22.8)	18 (15.7)	1.89	0.17
26	35 (30.7)	22 (19.1)	4.1	0.043
27	38 (33.3)	22 (19.1)	5.97	0.015
28	36 (31.6)	31 (27.0)	0.59	0.44
29	29 (25.4)	19 (16.5)	2.75	0.097 **
30	29 (25.4)	17 (14.8)	4.05	0.044
31	44 (38.6)	32 (27.8)	2.99	0.084 **
32	18 (15.8)	10 (8.7)	2.68	0.101
33	23 (20.2)	14 (12.2)	2.71	0.10 **
34	43 (37.7)	27 (23.5)	5.47	0.019
35	35 (30.7)	20 (17.4)	5.56	0.018
36	68 (59.6)	63 (54.8)	0.55	0.46
37	20 (17.5)	24 (20.9)	0.41	0.52
38	45 (39.5)	34 (29.6)	2.49	0.115
39	32 (28.1)	25 (21.7)	1.23	0.27
40	42 (36.8)	38 (33.0)	0.36	0.55
41	9 (7.9)	9 (7.8)	0.001	0.98
42	13 (11.4)	13 (11.3)	0.001	0.98

Data in bold indicate level of significance α 5%.

* *p* value of χ^2 .

** Test significant at level $\alpha=0.10$.

professional official public translator. The questionnaire was then back-translated into English by the first author (G.H.V.) and revised by the senior authors (K.K.A. and H.S.A.) of this article. After appropriate corrections for nuance the final version (TEMPS-A Buenos Aires) was published (Vazquez and Akiskal, 2005) and then validated on a clinically-well sample of our country (Vazquez et al., 2007).

The Quality of Life Index (QLI) (Ferrans and Powers, 1985), in its various language versions, is a concise instrument for comprehensive, culture-informed, and self-rated assessment of health-rated quality of life. It is composed of ten dimensions collated from the international literature, including aspects ranging from physical well-being to spiritual fulfillment, as well as global perception of quality of life. We have used the Quality of Life Index in its Spanish version (QLI-Sp) that has been adapted and validated in Argentina by J.M. Bulacio et al. (2004).

2.3. Statistical analysis

The Chi-square Test and Fisher's Exact Test were used to examine association between groups (case-

control), basal characteristics of population, proportion of true items at TEMPS-A subscales and presence of dominant temperaments. Associations between QLI Test items and the presence of dominant affective temperaments were analysed using the Fisher's Exact Test. Odds ratios and its confidence intervals were calculated in order to measure association between variables. The *t* test and Levene Test were used to compare means and variances of scores between groups. Differences between answers of QLI Test for each group were examined using the Wilcoxon Test.

3. Results

3.1. Comparison between temperaments

We have compared both groups (cases, $N=114$ vs controls, $N=115$) and we have found significant differences on all TEMPS-A subscales, except for the hyperthymic temperament.

3.1.1. Dysthymic Temperament Scale

In Table 3 distributions of temperaments for cases and controls on each subscale is displayed. For dysthymia,

Table 6
Frequencies and percentages of true responses for all items in the Hyperthymic Subscale, among cases and controls

Item number Hyperthymic Subscale	Cases <i>n</i> (%)	Controls <i>n</i> (%)	Test's statistics	Associated <i>p</i> *
43	71 (62.3)	87 (75.7)	4.79	0.029
44	26 (22.8)	25 (21.7)	0.04	0.85
45	32 (28.1)	45 (39.1)	3.14	0.076 **
46	79 (69.3)	84 (73.0)	0.39	0.53
47	71 (62.3)	73 (63.5)	0.04	0.85
48	54 (47.4)	49 (42.6)	0.52	0.47
49	64 (56.1)	69 (60.0)	0.35	0.55
50	56 (49.1)	45 (39.1)	2.32	0.13
51	48 (42.1)	47 (40.9)	0.04	0.85
52	53 (46.5)	61 (53.0)	0.98	0.32
53	56 (49.1)	58 (50.4)	0.04	0.84
54	52 (45.6)	55 (47.8)	0.11	0.74
55	37 (32.5)	43 (37.4)	0.61	0.43
56	23 (20.2)	19 (16.5)	0.51	0.48
57	40 (35.1)	34 (29.6)	0.80	0.37
58	50 (43.9)	50 (43.5)	0.003	0.95
59	40 (35.1)	34 (29.6)	0.80	0.37
60	46 (40.4)	43 (37.4)	0.21	0.65
61	52 (45.6)	55 (47.8)	0.11	0.74
62	33 (28.9)	37 (32.2)	0.28	0.60
63	40 (35.1)	47 (40.9)	0.81	0.37

Data in bold indicate level of significance α 5%.

* *p* value of χ^2 .

** Test significant at level $\alpha=0.10$.

Table 7

Frequencies and percentages of true responses for all items in Irritability Subscale, according cases and controls

Irritability Subscale item number	Cases <i>n</i> (%)	Controls <i>n</i> (%)	Test's statistics	Associated <i>p</i> *
64	25 (21.9)	15 (13.0)	3.14	0.08 **
65	18 (15.8)	8 (7.0)	4.44	0.035
66	41 (35.9)	25 (21.7)	5.65	0.02
67	56 (49.1)	48 (41.7)	1.16	0.26
68	61 (53.5)	64 (55.7)	0.11	0.75
69	58 (50.9)	42 (36.5)	4.80	0.03
70	25 (21.9)	15 (13.0)	3.14	0.08 **
71	24 (21.1)	9 (7.8)	8.12	0.004
72	27 (23.7)	20 (17.4)	1.39	0.24
73	21 (18.4)	17 (14.8)	0.55	0.46
74	58 (50.9)	54 (47.0)	0.35	0.55
75	10 (8.8)	9 (7.8)	0.07	0.80
76	13 (11.4)	11 (9.6)	0.21	0.65
77	21 (18.4)	15 (13.0)	1.25	0.26
78	22 (19.3)	15 (13.0)	1.65	0.20
79	11 (9.6)	4 (3.5)	3.56	0.06 **
80	4 (3.5)	3 (2.6)	^a	0.72
81	24 (21.1)	19 (16.5)	0.77	0.38
82	22 (19.3)	20 (17.4)	0.14	0.71
83	6 (5.3)	2 (1.7)	^a	0.17
84	11 (9.6)	6 (5.2)	1.64	0.20

Data in bold indicate level of significance α 5%.

* *p* value of χ^2 .

** Test significant at level $\alpha=0.10$.

^a Fisher's Exact Test.

mean score for cases was 8.92 and lower to 6.44 for controls ($t=5.11$, $p<0.001$). Scores variance are different in both groups ($F=8.37$, $p=0.004$). A comparison of the proportion of true responses on each item for the dysthymia subscale between cases and controls was performed (Table 4).

3.1.2. Cyclothymic Temperament Scale

Cases present a distribution and scores higher and more variable than controls (Table 3). Significant differences were found for cyclothymia's mean score between cases and controls ($t=2.69$, $p=0.008$), without differences between variables for both groups ($F=3.37$, $p=0.068$). 50% of cases have scores equal or higher than 6, meanwhile 50% of controls have scores below 3. Table 5 shows frequencies and percentages of true responses for cyclothymia items, by cases and controls.

3.1.3. Hyperthymic Temperament Scale

Hyperthymic scale score's distribution was similar in both controls and cases, with the same median and almost the same variance (Table 3). There were no significant differences between mean scores ($t=0.27$, $p=0.79$), nor on variance ($F=0.33$, $p=0.57$). Distribu-

Table 8

Frequencies and percentages of true responses for all items in the Anxiety Subscale, according cases and controls

Anxiety Subscale item number	Cases <i>n</i> (%)	Controls <i>n</i> (%)	Test's statistics	Associated <i>p</i> *
85	41 (35.9)	27 (23.5)	4.28	0.04
86	74 (64.9)	55 (47.8)	6.79	0.01
87	59 (51.8)	37 (32.2)	9.02	0.003
88	40 (35.1)	18 (15.7)	11.43	0.001
89	58 (50.9)	30 (26.1)	14.87	<0.001
90	25 (21.9)	20 (17.4)	7.45	0.39
91	25 (21.9)	18 (15.7)	1.48	0.22
92	56 (49.1)	43 (37.4)	3.21	0.073
93	24 (21.1)	11 (9.6)	5.84	0.02
94	52 (45.6)	31 (27.0)	8.62	0.003
95	35 (30.7)	36 (31.3)	0.01	0.92
96	15 (13.2)	6 (5.2)	4.33	0.04
97	32 (28.1)	24 (20.9)	1.61	0.21
98	58 (50.9)	42 (36.5)	4.80	0.03
99	42 (36.8)	36 (31.3)	0.78	0.38
100	36 (31.6)	17 (14.8)	9.08	0.003
101	41 (35.7)	23 (20.0)	7.25	0.01
102	42 (36.8)	20 (17.4)	10.97	0.001
103	61 (53.5)	57 (49.6)	0.36	0.55
104	12 (10.5)	4 (3.5)	4.38	0.036
105	36 (31.6)	43 (37.4)	0.86	0.36
106	39 (34.2)	14 (12.2)	15.03	<0.001
107	46 (40.4)	35 (30.4)	2.46	0.12
108	41 (36.0)	22 (19.1)	8.14	0.004
109	14 (12.3)	6 (5.2)	3.58	0.06 **
110	53 (46.5)	37 (32.2)	4.92	0.03

Data in bold indicate level of significance α 5%.

* *p* value of χ^2 .

** Test significant at level $\alpha=0.10$.

tion of frequencies and percentages of true responses among cases and controls are displayed in Table 6.

3.1.4. Irritable Temperament Scale

Control's irritability scores are clearly lower than those of cases, in spite of medians being close. Mean scores for cases and controls (Table 3) are different ($t=2.74$, $p=0.007$). There were no differences comparing each group score's variability ($F=3.77$, $p=0.054$). Differences between proportions of positive responses for cases and controls are displayed in Table 7.

Table 9

Presence of dominant temperament(s) by group

Group	Cases	Controls	Total
Without a dominant temperament	90	108	198
At least one dominant temperament*	24	7	31
Total	114	115	229

* >2 SD from mean scores of TEMPS-A Buenos Aires.

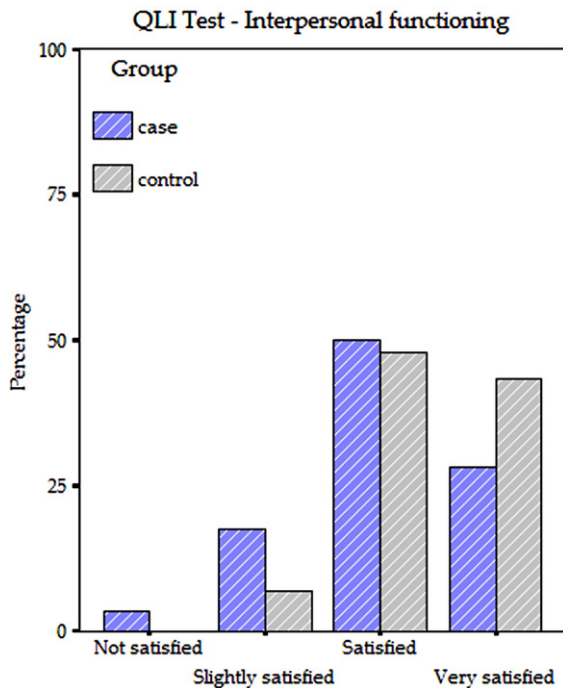


Fig. 1. Interpersonal functioning (QLI-Sp 5) by group.

3.1.5. Anxiety Temperament Scale

In this scale, cases displayed higher and more variability scores. Mean scores (Table 3) are higher for cases, in a significance level ($t=4.46, p<0.001$). 50% of cases have a score equal or above 8, and a general variance in a range from 0 to 23. Controls have scores from 0 to 19, and 50% have a score equal or above 5. Score's variance among cases is higher than controls ($F=10-17, p=0.002$). True responses proportion differences are shown in Table 8.

3.2. Prevalence of affective temperaments according to cut-off points

In order to identify affective temperaments, a cut-off of two standard deviations (+2 SD) higher than mean scores of Argentine version of TEMPS-A (Vázquez and Akiskal, 2005; Vázquez et al., 2007) was used (Table 9). First degree relatives of bipolar patients showed higher prevalence of cyclothymic and anxious as main temperaments (Fisher's Test, $p=0.003$ and 0.01 , respectively). The resulting relative's odds ratio for being cyclothymic was 18.44 ($CI_{95}=1.05-323$) and for having anxious temperament was 9.78 ($CI_{95}=1.22-78.51$).

On the other hand, we did not find evidence of an association between cases and dysthymia ($\chi^2=2.48, p=0.116$), hyperthymia (Fisher's Test, $p=1$) or irritability (Fisher's Test, $p=0.45$) as main temperaments.

Table 9 shows that 24 cases (21.1%) and 7 controls (6.1%) have at least one predominant temperament, with a significant difference between both groups ($\chi^2=10.95, p<0.001$).

3.3. Quality of life and affective temperaments

We did not find any significant differences between the quality of life between both groups in the present study, except for item number 5 (interpersonal functioning). Controls displayed statistically significant higher scores than cases ($W=14290.5, p=0.0005$) in their interpersonal functioning (Fig. 1).

We have also studied the quality of life, measured by the Quality for Life Index-Spanish version (QL-Sp), of those subjects with at least one dominant affective temperament (Vázquez et al., 2007) compared with the

Table 10

Associated probabilities of each item of the QLI-Sp with the presence of dominant affective temperaments

Item of QLI-Sp	Temperament				
	Dysthymic	Cyclothymic	Hyperthymic	Irritable	Anxious
1: Physical well-being	<0.0001	0.013	NS	NS*	0.003
2: Psychological/emotional well-being	<0.0001	<0.0001	NS	NS*	0.027
3: Personal care and independent functioning	<0.0001	0.008	NS	0.022	0.010
4: Occupational functioning	NS*	0.037	NS	0.041	NS
5: Interpersonal functioning	0.045	NS	NS	NS	NS*
6: Social/emotional support	NS	NS	NS	NS	NS*
7: Governmental and services support	NS	NS	NS	NS	NS
8: Personal fulfillment	<0.0001	0.007	NS	0.023	0.043
9: Spiritual fulfillment	0.025	NS*	NS	NS	NS
10: Global perception of quality of life	<0.0001	0.038	NS	0.013	0.041

NS: No significance at level of $\alpha=0.05$.

* Significant at level of $\alpha=0.10$.

individuals that did not present any dominant temperament. Table 10 displays the associated probabilities of each item of the QLI-Sp with the presence of dominant affective temperaments using the Fisher's Test.

The proportion of answers for the categories grouped of the QLI-Sp has a statistically significant difference between the subjects with and without dysthymic temperament in items 1, 2, 3, 5, 8, 9 and 10. For the cyclothymic temperament, the differences were founded in items 1, 2, 3, 4, 8 and 10; for the irritable temperament the differences were present in items 3, 4, 8 and 10, and for the anxiety temperament the differences were detected in items 1, 2, 3, 8 and 10. The hyperthymic temperament did not present significant differences in the proportions of answers of none of the QLI-Sp test's items, so it is the only affective temperament that would not influence the quality of life of the subjects that have these particular traits. On the other hand, the affective temperaments that would have more impact on the subjects' quality of life are dysthymic, cyclothymic, anxiety and irritable, respectively.

4. Discussion

The present study confirms that clinically healthy relatives of bipolar probands exhibit higher levels of temperamental traits than normal controls. These results are in line with previous studies (Chiaroni et al., 2005; Evans et al., 2005; Mendlowicz et al., 2005) and demonstrate that affective temperaments can serve as an endophenotype for bipolar disorder as judged by the fact that "clinically well" relatives show these traits at a statistically significantly higher than appropriately chosen controls.

Cyclothymic and anxious temperament scores differentiated between healthy relatives of bipolar probands and normal controls, thereby suggesting that some healthy relatives of bipolar patients have a subclinical instability in, for example mood, activity, biological rhythms, and sleep. This cluster of cyclothymic subaffective traits could serve as a potential vulnerability marker, and gives support for the concept of the bipolar spectrum at the level of temperamental dysregulation (Akiskal and Mallya, 1987; Akiskal, 1995; Akiskal and Pinto, 1999).

We also found that healthy relatives of bipolar patients exhibited significantly higher scores on the anxious temperament subscale than controls. This could be interpreted as reflecting the presence of a vulnerability for developing an anxiety disorder, a very common comorbidity in patients with bipolar disorders (Perugi et al., 1999; Akiskal et al., 2006).

On the other hand, we have found that dysthymic, hyperthymic and irritable temperament scores did not differentiate between those of healthy relatives of bipolar patients and normal controls. These results are similar to previous publications (Mendlowicz et al., 2005; Chiaroni et al., 2005), but show discrepancy with other studies which postulate that not only cyclothymic temperament but also hyperthymic or dysthymic temperament is significantly more prevalent between relative-group of bipolar patients than healthy controls (Kesebir et al., 2005; Evans et al., 2005).

In this paper we go beyond these considerations to test the hypothesis that the "well relatives" of bipolar probands not only exhibit such traits, but could also show some impairment as a result of their temperamental baseline. Our results support the idea that predominant temperaments (e.g., with higher scores on TEMPS-A) have a significant impact on their quality of life (QoL).

A large body of data that focus on the functional outcome and disability in bipolar disorder was recently published (Jaeger and Vieta, 2007). Functioning and QoL are increasingly being taken into account in assessing the impact of bipolar disorder on the individual, so we wanted to investigate the impact of affective temperaments in our population. We found a significant difference on interpersonal functioning measured by the QLI-Sp in "healthy" relatives of bipolar probands compared with a control population across our country. We also found that those individuals with dominant temperaments (Vázquez et al., 2007) were affected on several aspects of their quality of life. Those subjects with high temperamental scores on all subscales (except hyperthymic) displayed different impact on various aspects of their QoL, with some particular differences among them. The dysthymic, cyclothymic, anxious and irritable (in that order) were the affective temperaments that have the greatest impact on several items of the QLI-Sp. On the other hand, the absence of impairment on the global functioning of individuals with hyperthymic temperament could be considered to be potentially beneficial to face some environmental challenges, conferring specific advantages over other temperaments on social group (Akiskal and Akiskal, 2005b).

The impact of affective temperaments on occupational adjustment has been demonstrated in Japan (Sakai et al., 2005) among company employees; paralleling our findings here, the hyperthymic faced job stress more robustly than the other affective temperaments. However, the Japanese study was not a genetic investigation. To the best of our knowledge, our Argentinean study is

the first to demonstrate the true functional impact of affective temperaments on several items of the quality of life of *healthy subjects among the relatives of bipolar probands*, and we can therefore conclude that our data support a true “subaffective” position for several affective temperaments.

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Conflict of interest

No conflict declared.

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