University of Groningen

Relationship between affective temperament and major depressive disorder in older adults

Mauer, Sivan; Santos de Siqueira, Alaise Silva; Borges, Marcus Kiiti; Biella, Marina Maria; Voshaar, Richard C. Oude; Aprahamian, Ivan

Published in:
Journal of Affective Disorders

DOI:
[10.1016/j.jad.2020.09.038](https://doi.org/10.1016/j.jad.2020.09.038)
[10.1016/j.jad.2020.09.038](https://doi.org/10.1016/j.jad.2020.09.038)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2020

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Mauer, S., Santos de Siqueira, A. S., Borges, M. K., Biella, M. M., Voshaar, R. C. O., & Aprahamian, I. (2020). Relationship between affective temperament and major depressive disorder in older adults: A case-control study. *Journal of Affective Disorders*, 277, 949-953. <https://doi.org/10.1016/j.jad.2020.09.038>, <https://doi.org/10.1016/j.jad.2020.09.038>

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

Research paper

Relationship between affective temperament and major depressive disorder in older adults: A case-control study

Sivan Mauer^{a,b,*}, Alaise Silva Santos de Siqueira^a, Marcus Kiiti Borges^a, Marina Maria Biella^a, Richard C. Oude Voshaar^c, Ivan Aprahamian^{a,d}

^a Department and Institute of Psychiatry, Faculty of Medicine, University of São Paulo, São Paulo, Brazil

^b Department of Psychiatry, Tufts Medical Center, Tufts University School of Medicine, Boston, MA, USA

^c Department of Psychiatry, University Medical Center Groningen, University of Groningen, Groningen, Netherlands

^d Geriatrics Division, Department of Internal Medicine, Faculty of Medicine of Jundiaí, Jundiaí, Brazil

ARTICLE INFO

Keywords:

Older adults
Affective temperaments
Cyclothymia
Hyperthymia
Dysthymia
Major depression

ABSTRACT

Background: : In clinical practice it is often challenging to determine whether mood disturbances should be considered a state or trait characteristics. This study is important to understand the influence of temperaments in the diagnosis of depression. The objective of the present study was to compare the frequency of three types of affective temperament (dysthymia, hyperthymia and cyclothymia) among older adults with major depression compared to non-psychiatric control patients.

Methods: : A case-control study comparing 50 patients with major depression aged 65 years or above with a comparison group of 100 non-psychiatric controls. Affective temperaments were assessed using the TEMPS-A questionnaire. The 17-item Hamilton Depression Rating Scale and the Young mania Rating Scale were used for the assessment of symptoms of depression and mania, respectively.

Results: : In the sample 80% had an affective temperament, most commonly hyperthymia (67.3%). In depressive patients 48% had criteria for hyperthymic temperament against 77% of the controls (OR = 0.3, 95%CI 0.1–0.7). 38.8% of these patients presented cyclothymic temperament, whereas among controls, 12% fulfilled criteria (OR = 2.9, 95%CI 1.1–7.2).

Limitations: : The sample was relatively small, and their educational level was very low.

Conclusion: : A cyclothymic temperament may predict major depression unlike hyperthymia. Whether the effectiveness of mood stabilizers in unipolar disorder is moderated by a cyclothymic temperament and should be explored in future randomized controlled trials.

1. Introduction

The affective spectrum is described as a continuum between cyclothymia, bipolar disorder type I and type II, as well as subthreshold and major depressive disorder (Evans et al., 2008; Lewinsohn et al., 2003). Affective temperaments can be conceptualized as part of the spectrum of affective disorders. The modern concept of temperament is part of Kraepelin's view on manic-depressive illness. He hypothesized that recurrences of affective disorders arose from lasting dispositions of depression, cyclothymia and mania (Akiskal, 2001). The definitions of the three main types of affective temperaments can be conceptualized as follows: hyperthymia, dysthymia and cyclothymia. Hyperthymia involves mild manic symptoms as part of the personality. These subjects

have a higher energy level, less need for sleep, higher sexual drive, are very sociable and susceptible to alcohol and other drug abuse (Akiskal et al., 2005, 2000). Dysthymia represents mild depressive symptoms as part of the personality. Among its features, the patient has a low energy level, need for more hours of sleep than the average, decreased of sexual drive, greater inclination to have concerns related to personal failures (Akiskal, 2001; Kwapil et al., 2013). Cyclothymia is a constant alternation between mild manic symptoms and depressive states daily, or for days, which end up not meeting the temporal criteria for complete affective syndromes. These people show characteristics such as lability, anger and irritability, in addition to presenting attentional difficulties (Akiskal, 2001).

The different types of temperament are constitutionally based

* Corresponding author at: Department and Institute of Psychiatry, Faculty of Medicine/University of São Paulo – Rua Dr. Ovídio Pires de Campos, 785/1° andar/sala 1C 015 – 05403-903 São Paulo SP – Brazil.

E-mail address: sivanmauer@yahoo.com.br (S. Mauer).

<https://doi.org/10.1016/j.jad.2020.09.038>

Received 26 May 2020; Received in revised form 27 July 2020; Accepted 7 September 2020

Available online 11 September 2020

0165-0327/ © 2020 Elsevier B.V. All rights reserved.

affective-behavioral dispositions with a strong genetic origin. Healthy relatives of patients with bipolar disorder for example have a higher degree of temperamental dysregulation compared to healthy controls (Evans et al., 2008). Family studies have identified a higher prevalence of cyclothymic temperament among with a positive affective family history, in particular for first-degree relatives of patients with bipolar I disorder (Chiaroni et al., 2005). The three types of temperament described above can be measured with a self-report questionnaire, i.e. the Memphis, Pisa, Paris and San Diego scale, called TEMPS-A. The prevalence of affective temperaments depends on the cut off level applied. Using a cut-off of 50%, i.e. half of the items of a subscale needs to be confirmed, most subjects with mood disorders would present the definitions for affective temperaments (Vohringer et al., 2012). Increasing the TEMPS-A cut-off to 75% reveals that among patients with mood disorders 40% of the sample met the criteria for cyclothymia, 15% for hyperthymia, and 10% for dysthymia, with some patients presenting with two types of temperaments. Around 50% of these patients, however, did not show any kind of temperament.

To our knowledge, this study would be the first exploration of affective temperaments among older persons with a diagnosis of major depressive disorder. We aimed to compare the frequency of the three main types of affective temperament between depressed older patients and a non-psychiatric comparison group.

2. Methods

2.1. Design and subjects

A cross-sectional case-control study comparing patients with unipolar major depressive disorder, and non-psychiatric controls. Cases were recruited at a university-based Psychogeriatrics Outpatient Clinic in São Paulo, Brasil, where they received outpatient regular care. The non-psychiatric comparison group was composed of 100 patients recruited at a university-based Rheumatology Outpatient Clinic.

Inclusion criteria were 1) an age of 65 years or over, 2) signed informed consent, and finally 3) an established diagnosis of unipolar major depressive disorder based on chart review for cases and a life-time absence of this diagnosis for controls. The life-time absence of any mood disorder in controls was based on a retrospective medical chart evaluation.

Exclusion criteria were 1) surgery in the last 3 months; 2) cognitive impairment defined as an established diagnosis of dementia or Mini Mental State Examination (MMSE) sum score below 18 points (Aprahamian et al., 2011; Folstein et al., 1975), 3) a recent (past 6-month) history of a stroke, 4) current treatment for cancer, and finally 5) functional or sensory impairment which would interfere with reliably data collection.

This study followed the standards established by the National Council of Health and was approved by the ethical committee of the Faculty of Medicine of University of São Paulo. All patients agreed to participate by signing an informed consent form.

2.2. Rating scales

Primary outcome parameter - Affective temperaments were assessed with the Brazilian version of the TEMPS-A self-report questionnaire (Temperament Scale of Memphis, Pisa, Paris and San Diego Autoquestionnaire) (Woodruff et al., 2011). The Brazilian version has six subscales, i.e. a dysthymic, cyclothymic, hyperthymic, irritable, worrying and anxious temperament, measured with 45 items. Each item represents a statement for which the patient has to be rated (true or false) whether this applies to him or her. Only the first three subscales were used in the present study. Each of these subscales consists of 8 items; the result of each subscale multiplied by 12.5 yields a total score that ranged between 0 and 100. A temperament was considered present when at least 75% of one sub scale was confirmed (Vohringer et al.,

2012). Although patients can score positive for more than one type, overlap is generally minimal when using the 75% cut-off.

Descriptive parameters - We assessed global cognitive functioning with the Mini Mental State Examination (Aprahamian et al., 2011; Folstein et al., 1975), depressive symptom severity with the 17-item Hamilton Depression Rating Scale, anxiety with the Hamilton Rating Scale for Anxiety, and finally manic symptoms with the Young mania Rating Scale for the assessment of mania, respectively (Hamilton, 1960, 1959; Vilela et al., 2005).

We collected the following data in the interview of participants: age, sex, level of education, marital status, ethnicity, and religion. Data on psychiatric antecedents such as previous psychiatric hospitalization, electroconvulsive therapy, suicide attempts, self-harm and childhood abuse were also collected, including the family psychiatric history and clinical comorbidities.

2.3. Statistical analysis

Logistic regression modeling was applied to study the association between the depressive disorder (dependent variable) and the three temperaments (independent variables). The multivariable model was adjusted for age, sex, educational level, MMSE, and depressive symptoms severity. Statistical analysis was performed using the software “R” version 3.5.1 (R Development Core Team, 2013).

3. Results

3.1. Study sample

Of the 162 eligible patients, 12 were excluded (8 because a treatment for cancer, 4 for having dementia), leaving a final sample of 50 cases with unipolar depressive disorder and 100 non-psychiatric controls.

Table 1 presents the demographic, psychiatric and medical characteristics for the whole sample as well as stratified in cases and controls. Regarding their psychiatric history, cases had significantly higher frequency of hospitalizations, suicide attempts, history of sexual abuse and other types of childhood abuse compared to controls. Cases also displayed a higher level of anxiety symptoms, whereas depressive symptom severity did not differ significantly between groups. Cases also had significantly more diabetes, hypertension, obesity and chronic pain as clinical comorbidities compared to controls.

3.2. Association between temperament and major depression

The prevalence of the three types of temperaments for unipolar depression and controls are presented in Table 2. Controls had more often hyperthymic temperament (77%) and less often dysthymic temperament (5%) than patients with depressive disorder - hyperthymic temperament (48%) and dysthymic temperament (14%) (see Table 2). The strongest association of unipolar depression in the multivariable model is with cyclothymic temperament and the weakest is with hyperthymic temperament.

4. Discussion

To our knowledge, this is the first study on affective temperaments in geriatric outpatients suffering from unipolar depression. While the overall prevalence of affective temperaments did not differ between patients with depressive disorder and non-psychiatric controls, patients with depression had significantly more often a dysthymic and cyclothymic temperament and less often a hyperthymic temperament. Eventhough we applied the higher cut-off value of 75%, only 24% of depressed patients and 18% of non-psychiatric controls did not qualify for any affective temperament.

Few studies have been carried out in other age groups (Maina et al.,

Table 1
Characteristics of the study populations by group status.

	Depression (n = 50)	Controls (n = 100)	Total (n = 150)
<i>Socio-demographics:</i>			
• Age (mean ± SD)	74.2 ± 6.4	72.3 ± 5.3	72.9 ± 5.7
• Sex - Female (%)	86.0	88.0	87.3
• Education level (mean ± SD)	5.5 ± 3.8	4.5 ± 3.3	4.9 ± 3.5
• Marital Status- widower (%)	46.0	41.0	42.6
• Retired - yes (%)	82.0	90.0	87.3
• Religion – Catholic (%)	70.0	75.0	74.6
• Ethnicity – White (%)	94.0	92.0	92.6
<i>Presence of a psychiatric history (% yes)</i>			
• Psychiatric hospitalization (%)	8.0	0	2.6
• Electroconvulsive therapy (%)	2.0	0	0.6
• Psychotherapy (%)	32.0	9.0	16.6
• Suicide attempt (%)	10.0	1.0	4.0
• Child abuse (%)	6.0	2.0	3.3
• Self-Harm (%)	0	0	0
• Sexual Abuse (%)	4.0	3.0	3.3
<i>Psychopathology (current):</i>			
• Mini mental State Examination (mean ± SD)	26.3 ± 3.1	26.7 ± 3.1	26.6 ± 3.1
• Hamilton Depression Rating Scale (mean ± SD)	4.5 ± 5.3	2.0 ± 1.7	2.9 ± 3.6
• Hamilton Rating Scale for Anxiety (mean ± SD)	9.4 ± 7.6	4.7 ± 3.8	6.3 ± 5.8
• Young Mania Rating Scale (mean ± SD)	2.3 ± 3.8	3.2 ± 2.8	2.9 ± 3.1
<i>Somatic disease burden:</i>			
• Diabetes (%)	24.0	17.0	19.3
• Hypertension (%)	72.0	60.0	64.0
• Stroke (%)	6.0	6.0	6.0
• Myocardial infarction (%)	2.0	4.0	3.3
• Coronary insufficiency (%)	4.0	2.0	2.6
• Congestive heart failure (%)	2.0	2.0	2.0
• Chronic kidney failure (%)	2.0	0	0.6
• Chronic obstructive pulmonary disease (%)	2.0	1.0	1.3
• Obesity (%)	4.0	2.0	2.6
• Chronic pain (%)	4.0	3.0	3.3
• Hypothyroidism (%)	22.0	23.0	22.6
• Arthritis / Arthrosis (%)	38.0	65.0	56.0
• Osteoporosis (%)	14.0	32.0	26.0
• None	4.0	0	2.6

Abbreviations: SD = Standard deviation.

2010; Perugi et al., 2018). The vast majority of these studies relate affective temperaments to various types of bipolar disorders and less with unipolar depressive disorder. In contrast to most studies in younger age samples (Vohringer et al., 2012; Maina et al., 2010; Goto et al., 2011), the majority of patients in our study had a hyperthymic temperament (67.3%). An interesting hypothesis that might explain this difference is a possible relationship between this type of temperament and longevity. Few studies relate these two variables. One of them studied personality using the Guilford-Zimmerman Temperament Survey in patients with an average of 50 years. Authors concluded that patients with similar characteristics to hyperthymic patients were more long-lived. Characteristics as extraversion decreased mortality by 13% and low neuroticism decreased by 15% (Terracciano Antonio et al., 2008). Another study showed that hyperthymic patients had better functionality after mania treatment compared to cyclothymic patients who had residual depressive symptoms (Perugi et al., 2018).

Direct comparison of actual prevalence rates of affective temperament is difficult due to difference in study population, cut-off values,

and assessment of temperament. Among 104 Italian depressed outpatients, the prevalence of cyclothymic, dysthymic and hyperthymic temperament were only 12.3%, 7.5% and 2.8%, respectively when assessed with semistructured interview version of the TEMPS (Maina et al., 2010). Using the TEMPS-autoquestionnaire as we did, all 46 patients with mixed types of mood disorders had some type of temperament. Among patients with major depression, 72% had dysthymic temperament, 31% hyperthymic and 75% dysthymic (Goto et al., 2011). Interestingly, we found a very low frequency of dysthymic temperament (14%) and the strongest association was with cyclothymic temperament. A study with three years of follow up interviewed 112 subjects at risk for bipolar disorders and 145 controls. Cyclothymic temperament predicted the onset of major depressive disorder (OR 2.13, 95%CI 1.27–3.60), which is in line with our study (OR 2.9, 95%CI 1.1–7.2). Moreover, hyperthymic temperament was associated with a lower odds on becoming depressed (OR = 0.72, 95% C.I. 0.58–0.88) also in line with our results (Degeorge et al., 2014). Just one study with mean age more than 60 years was found. This study compared patients

Table 2
Prevalence of affective temperament types stratified by group status.

Temperament types	Prevalence Depression (n = 50)	Controls (n = 100)	Odds ratio compared to controls OR [95% CI] Univariable model	OR [95% CI] Multivariable model*
• Dysthymia	14.0%	5.0%	3.1 [0.9 – 10.1]	1.2 [0.3 – 5.0]
• Hyperthymia	48.0%	77.0%	0.3 [0.1 – 0.6]	0.3 [0.1 – 0.7]
• Cyclothymia	38.8%	12.0%	4.5 [2.1 – 96.6]	2.9 [1.1 – 7.2]
• None	24.0%	18.0%		

Abbreviations: CI = Confidence Interval OR = Odds ratio.

* Adjusted for age, sex, educational level, MMSE, and depressive symptoms severity.

with Parkinson disease with and without depression and related with temperament (using the Turkish version of TEMPS-A). Hyperthymic was higher among non-depressive patients and cyclothymic was higher among depressive, what is similar of what we found in our results (Dogan et al., 2019). One meta-analysis pooled data from 6 studies and a total of 1344 subjects comparing major depressive disorder and controls. Cyclothymic TEMPS scores were significantly higher in depressed patients. Conversely hyperthymic TEMPS scores were lower in the major depressive disorder group when compared to healthy controls. These findings are comparable to those of our study (Solmi et al., 2016).

4.1. Clinical importance

Cyclothymic and hyperthymic temperaments are considered to be part of the bipolar spectrum (Ghaemi and Dalley, 2014). In our sample, 62% of subjects with major depression would be part of a bipolar spectrum. Bipolar disorder is often missed in clinical practice, especially milder forms. Diagnostic re-evaluation of 65 older outpatients who suffered from recurrent major depressive disorder showed that 22 patients were screen-positive for bipolar disorder and 11 (16.9%) actually met DSM-criteria for bipolar disorder. A hyperthymic temperament was significantly associated with being screen-positive for bipolar disorder (Lee et al., 2014). In addition to diagnostic importance, affective temperament may also be associated with treatment response. A retrospective evaluation of treatment response, showed that a dysthymic temperament was association with non-response on antidepressants among patients with major depression and that cyclothymic as well as hyperthymic temperament was associated with antidepressant-induced mania in bipolar patients (de Aguiar Ferreira et al., 2014). These findings could raise the question if patients with unipolar depression and cyclothymic temperament would respond better to mood stabilizers? Or clinically these patients need more caution when prescribing antidepressants.

4.2. Limitations

This study has some limitations. Firstly, diagnosis of depression was made clinically without the use of any structured interview even based on experienced psychogeriatricians. While this may limit the diagnostic reliability, it enhances the external validity as structured interview are hardly used in clinical practice and a more extensive assessment might have introduced selection bias due to non-attrition. Because of this we can have around of 30% of bipolar illness, i.e., type I or type II, undiagnosed after clinical evaluation (Angst et al., 2011). Secondly, the generalization of this study is compromised, since more than 90% of the sample was made up Caucasians and 87.3% were women. Thirdly, the level of education is rather low, with an average of about 5 years of study what can explain the outlier number of hyperthymia among controls (77%). Nonetheless, this is quite common in older age samples, especially in middle-income countries like Brazil. Finally, this is a cross-sectional case-control study limiting conclusion about causality. One important limitation in our study is the lack of information about substance abuse as alcohol, tobacco, heroin and psychotropic drugs. This could be a confounding bias in the diagnosis of depression due to substance use (Pacini et al., 2009; Rovai et al., 2017). Nonetheless, temperament is considered a trait characteristic that can be assumed to be present even before the age of onset of first depressive episode. Furthermore, the actual level of depressive symptoms was low, which limits confounding by a depressed state.

5. Conclusions

In conclusion, older patients diagnosed with depression much more often has a cyclothymic temperament. This should alert clinicians as it might point to a missed diagnosis of bipolar disorder and/or

antidepressant induced mania. This latter reasoning, however, should be tested in future studies in depressed older patients. In addition, it is important to carry out follow-up studies to understand the role of temperaments in episodes of relapse of mood illnesses.

Funding source

This research did not receive any specific grant.

CRediT authorship contribution statement

Sivan Mauer: Conceptualization, Methodology, Formal analysis, Writing - original draft, Writing - review & editing. **Alaise Silva Santos de Siqueira:** Data curation, Writing - original draft. **Marcus Kiiti Borges:** Data curation, Writing - original draft. **Marina Maria Biella:** Data curation, Writing - original draft. **Richard C. Oude Voshaar:** Supervision, Writing - original draft, Writing - review & editing. **Ivan Aprahamian:** Conceptualization, Methodology, Writing - review & editing, Supervision.

Declaration of Competing Interest

None.

Acknowledgment

Prof. Aprahamian received a national public grant level 2 from the National Council for Scientific and Technological Development (Ministry of Science, Technology, Innovation and Communications, Brazil).

References

- Akiskal, H.S., 2001. Dysthymia and cyclothymia in psychiatric practice a century after Kraepelin. *J. Affect. Disord.* 62, 17–31.
- Akiskal, H.S., Akiskal, K.K., Haykal, R.F., Manning, J.S., Connor, P.D., 2005. TEMPS-A: progress towards validation of a self-rated clinical version of the Temperament Evaluation of the Memphis, Pisa, Paris, and San Diego Autoquestionnaire. *J. Affect. Disord.* 85, 3–16.
- Akiskal, H.S., Bourgeois, M.L., Angst, J., Post, R., Moller, H.J., Hirschfeld, R., 2000. Re-evaluating the prevalence of and diagnostic composition within the broad clinical spectrum of bipolar disorders. *J. Affect. Disord.* 59, 5–30.
- Angst, J., Azorin, J.-M., Bowden, C.L., Perugi, G., Vieta, E., Gamma, A., Young, A.H., 2011. Prevalence and characteristics of undiagnosed bipolar disorders in patients with a major depressive episode: the BRIDGE study. *Arch. Gen. Psychiatry* 68, 791–798.
- Aprahamian, I., Martinelli, J.E., Cecato, J., Yassuda, M.S., 2011. Screening for alzheimer's disease among illiterate elderly: accuracy analysis for multiple instruments. *J. Alzheimer's Dis.* 26, 221–229.
- Chiaroni, P., Hantouche, E.-G., Gouvenet, J., Azorin, J.-M., Akiskal, H.S., 2005. The cyclothymic temperament in healthy controls and familiarly at risk individuals for mood disorder: endophenotype for genetic studies? *J. Affect. Disord.* 85, 135–145.
- de Aguiar Ferreira, A., Vasconcelos, A.G., Neves, F.S., Correa, H., 2014. Affective temperaments and antidepressant response in the clinical management of mood disorders. *J. Affect. Disord.* 155, 138–141.
- Degeorge, D.P., Walsh, M.A., Barrantes-Vidal, N., Kwapi, T.R., 2014. A three-year longitudinal study of affective temperaments and risk for psychopathology. *J. Affect. Disord.* 164, 94–100.
- Dogan, B., Akyl, A., Memis, C.O., Sair, A., Akyildiz, U., Sevincok, L., 2019. The relationship between temperament and depression in Parkinson's disease patients under dopaminergic treatment. *Psychogeriatrics* 19, 73–77.
- Evans, L.M., Akiskal, H.S., Greenwood, T.A., Nievergelt, C.M., Keck, P.E., Mcelroy, S.L., Sadovnick, A.D., Remick, R.A., Schork, N.J., Kelsoe, J.R., 2008. Suggestive linkage of a chromosomal locus on 18p11 to cyclothymic temperament in bipolar disorder families. *Am. J. Med. Genet. Part B Neuropsychiatr. Genet.* 147, 326–332.
- Folstein, M.F., Folstein, S.E., McHugh, P.R., 1975. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J. Psychiatr. Res.* 12, 189–198.
- Ghaemi, S.N., Dalley, S., 2014. The bipolar spectrum: conceptions and misconceptions. *Aust. N. Z. J. Psychiatry* 48, 314–324.
- Goto, S., Terao, T., Hoaki, N., Wang, Y., 2011. Cyclothymic and hyperthymic temperaments may predict bipolarity in major depressive disorder: a supportive evidence for bipolar III/2 and IV. *J. Affect. Disord.* 129, 34–38. <https://doi.org/10.1016/j.jad.2010.07.016>.
- Hamilton, M., 1960. A rating scale for depression. *J. Neurol. Neurosurg. Psychiatry* 23,

- 56–62.
- Hamilton, M., 1959. The assessment of anxiety states by rating. *Br. J. Med. Psychol.* 32, 50–55.
- Kwapil, T.R., Degeorge, D., Walsh, M.A., Burgin, C.J., Silvia, P.J., Barrantes-Vidal, N., 2013. Affective temperaments: unique constructs or dimensions of normal personality by another name? *J. Affect. Disord.* 151, 882–890.
- Lee, C.-I., Jung, Y.-E., Kim, M.-D., Hong, S.-C., Bahk, W.-M., Yoon, B.-H., 2014. The prevalence of bipolar spectrum disorder in elderly patients with recurrent depression. *Neuropsychiatr. Dis. Treat.* 10, 791–795.
- Lewinsohn, P.M., Klein, D.N., Durbin, E.C., Seeley, J.R., Rohde, P., 2003. Family study of subthreshold depressive symptoms: risk factor for MDD? *J. Affect. Disord.* 77, 149–157.
- Maina, G., Salvi, V., Rosso, G., Bogetto, F., 2010. Cyclothymic temperament and major depressive disorder: a study on Italian patients. *J. Affect. Disord.* 121, 199–203.
- Pacini, M., Maremmani, I., Vitali, M., Santini, P., Romeo, M., Ceccanti, M., 2009. Affective temperaments in alcoholic patients. *Alcohol* 43, 397–398.
- Perugi, G., Cesari, D., Vannucchi, G., Maccariello, G., Barbati, M., De Bartolomeis, A., Fagioli, A., Maina, G., 2018. The impact of affective temperaments on clinical and functional outcome of Bipolar I patients that initiated or changed pharmacological treatment for mania. *Psychiatry Res.* 261, 473–480.
- R Development Core Team, 2013. *R: A language and Environment For Statistical computing*. R Foundation For Statistical Computing, Vienna, Austria. R Found. Stat. Comput., Vienna, Austria URL: <http://www.R-project.org/>.
- Rovai, L., Maremmani, A.G.I., Bacciardi, S., Gazzarrini, D., Pallucchini, A., Spera, V., Perugi, G., Maremmani, I., 2017. Opposed effects of hyperthymic and cyclothymic temperament in substance use disorder (heroin- or alcohol-dependent patients). *J. Affect. Disord.* 218, 339–345.
- Solmi, M., Zaninotto, L., Toffanin, T., Veronese, N., Lin, K., Stubbs, B., Fornaro, M., Correll, C.U., 2016. A comparative meta-analysis of TEMPS scores across mood disorder patients, their first-degree relatives, healthy controls, and other psychiatric disorders. *J. Affect. Disord.* 196, 32–46.
- Terracciano Antonio, E., Löckenhoff Corinna, B., Zonderman Alan, T., Ferrucci Luigi, T., Costa Paul, T., 2008. Personality Predictors of Longevity: activity, Emotional Stability, and Conscientiousness. *Psychosom. Med.* 70, 621–627.
- Vilela, J.A.A., Crippa, J.A.S., Del-Ben, C.M., Loureiro, S.R., 2005. Reliability and validity of a Portuguese version of the Young Mania Rating Scale. *Brazilian J. Med. Biol. Res.* 38, 1429–1439.
- Vohringer, P.A., Whitham, E.A., Thommi, S.B., Holtzman, N.S., Khrad, H., Ghaemi, S.N., 2012. Affective temperaments in clinical practice: a validation study in mood disorders. *J. Affect. Disord.* 136, 577–580.
- Woodruff, E., Genaro, L.T., Landeira-Fernandez, J., Cheniaux, E., Laks, J., Jean-Louis, G., Nardi, A.E., Versiani, M.C., Akiskal, H.S., Mendlowicz, M.V., 2011. Validation of the Brazilian brief version of the temperament auto-questionnaire TEMPS-A: the brief TEMPS-Rio de Janeiro. *J. Affect. Disord.* 134, 65–76.