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Research report

# Affective temperaments and antidepressant response in the clinical management of mood disorders

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ABSTRACT

*Background:* The aim of this study was to investigate the presence of a relationship between affective temperament and antidepressant treatment response in mood disorder patients.
*Methods:* The lifetime history of antidepressant response of 90 bipolar disorder patients and 88 major depressive disorder patients were retrospectively evaluated and then assigned to one of four subgroups: complete response (CR), partial response (PR), no response (NR), and antidepressant associated mania response (AAMR). Using TEMPS-Rio de Janeiro – the brief Brazilian version of TEMPS-A – we compared affective temperament subscale scores across these groups.
*Results:* We observed a statistically significant relationship between depressive and anxious affective temperaments and no antidepressant response. In bipolar disorder patients, cyclothymic temperament ($p < 0.01$) and hyperthymic temperament ($p < 0.05$) were associated with antidepressant-associated mania. Hyperthymic temperament was associated with complete antidepressant responses in major depressive disorder patients.
*Limitations:* The evaluation of antidepressant response was retrospective.
*Conclusions:* Our data are consistent with the theory that affective temperament traits are factors that can influence the antidepressant response and the recovery from depressive episodes, but more longitudinal studies are needed to confirm this theory and our findings.


## 1. Introduction

In the general approach to patients with mood disorders the characterization of affective temperament may be an important parameter. It may be useful in the differential diagnosis of mood disorders as studies have consistently shown that cyclothymic temperament is significantly more prominent in bipolar versus unipolar depressive patients (Mendlowicz et al., 2005a) and that cyclothymic traits may represent vulnerability markers found in clinically healthy relatives of bipolar disorder (BD) patients (Mendlowicz et al., 2005b; Aguiar Ferreira et al., 2013). So, when assessing depressive patients, we should consider the hypothesis of bipolar disorder, especially the patient has first degree relatives with BD and high cyclothymic temperament scores. A hyperthymic temperament has also been associated with bipolarity (Goto et al., 2011), but might actually constitute a "protective factor" in subjects without susceptibility to bipolar disorder (Evans et al., 2005; Mendlowicz et al., 2005b).

Henry et al. (1999) assessed both depressive temperament (DT) and hyperthymic temperament (HT) in a dimensional approach (Akiskal and Mallya, 1987). They found statistically significant associations between a higher DT score or a lower HT score and a greater number of mood episodes in bipolar disorder patients. Furthermore, a higher DT score was strongly associated with a higher percentage of major depressive episodes and with a history of suicide attempts, while a higher HT score was associated with a trend to manic rather than depressive episodes (Henry et al., 1999). Additionally, there is evidence suggesting that among patients with Major Depressive Disorder (MDD), mood lability predicts switching to Bipolar II Disorder (Akiskal et al., 1995), and that in recurrent depressive patients cyclothymic temperament is associated with several clinical factors which are predictive of bipolarity (Mechri et al., 2011). Rihmer et al. (2013) found a statistically significant association between depressive and cyclothymic affective temperament and a personal history of suicide

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attempts, and between cyclothymic and anxious temperament and a family history of completed suicide in first and second degree relatives. These data are consistent with the theory that affective temperament traits are familial and may constitute markers which predict vulnerability and may help to identify those at risk of developing a specific type of mood disorder and or a propensity to suicidal behavior.

Another important issue in the clinical management of mood disorders is the ability to predict a response to antidepressant pharmacotherapy. Antidepressants treatments have beneficial and adverse effects; they can be efficacious, ineffective, or even harmful. Henry et al. (2001) found that bipolar disorder patients with a hyperthymic temperament have a greater risk of experiencing antidepressant-associated mania. Kaneda et al. (2011), using the Japanese version of the Cloninger's temperament and character inventory (TCI) (Kijima et al., 1996), suggested that personality characteristics of patients with MDD may influence the antidepressant response time. In this study, the early responders showed less harm avoidance (HA) and more self-directedness than later responders and non-responders groups. In their systematic review and meta-analysis, Kampman and Poutanen (2011) reported that an indisputable association existed between TCI scores (particularly HA) and the antidepressant treatment response experienced by patients with MDD. In studies of MDD patients, a consistent negative change in HA was found during treatment and this change was even more clearly associated with treatment response (Kampman and Poutanen, 2011).

Building on these evidences, we used the Temperament Evaluation of Memphis, Pisa, Paris, and San Diego (TEMPS), an instrument designed for measuring affective temperaments (Akiskal et al., 2005), to investigate the influence of personality factors on antidepressant response. The self-administered questionnaire version (TEMPS-A) is a Yes-or-No type instrument which contains 110 items. It assesses dysthymic (items 1–22), cyclothymic (items 23–42), hyperthymic (items 43–63), irritable (items 64–84) and anxious (items 85–110) temperaments.

Over the past ten years, the TEMPS-A has been translated into more than 25 languages, including a brief Brazilian version (TEMPS-Rio de Janeiro, we which abbreviate TEMPS-RJ), a validated compact scale with a total of 45 items. TEMPS-RJ consists of eight items assigned to each of the five original subscales and five items to the "worrying" subscale, which corresponds to a "general distress factor" (Woodruff et al., 2011).

In the present study, using the TEMPS-RJ in a Brazilian sample, we evaluated the temperament profiles of bipolar and unipolar depressive patients against the antidepressant response in these groups. We hypothesized that affective temperament is a moderator of antidepressant response in mood disorder patients.

## 2. Methods

The patients for the study were recruited from the Mental Health Treatment Unit of the Medical Sciences Faculty of Minas Gerais (FCMMG), the Mood Disorders Treatment Units of UFMG (Universidade Federal, Minas Gerais) and Raul Soares Institute/FHEMIG. Diagnosis was made by a trained psychiatrist using a structured interview, MINI-PLUS, following DSM-IV criteria (Amorim, 2000). A complete review of medical records and an interview with the patient and at least one close relative was made to determine the lifetime history of the first antidepressant treatment. Severity of mood symptoms during the interview was assessed using the 17 item version of the Hamilton Depression Rating Scale (HDRS-17) (Hamilton, 1960) and the Young Mania Rating Scale (YMRS) (Young et al., 1978). To be eligible subjects had to score less than eight on the HDRS and YMRS, and had to have had at least one depressive episode treated with a selective serotonin reuptake inhibitor (SSRI) for eight weeks.

We enrolled 178 subjects: (1) Bipolar I/II Disorder patients [$n=90$; 35.5% men; mean age$=38.4$ ($\pm 12.0$) yr]; (2) major depressive disorder patients [$n=88$; 25% men; mean age$=46.8$ ($\pm 11.9$) yr]. The research protocol and consent forms and procedures were approved by each institution's Ethics Committee, in accordance with the Helsinki Declaration. Written informed consent was obtained from all subjects.

Using the TEMPS-RJ instrument, affective temperament profiles were generated for all subjects. BD and MDD groups were each divided by treatment response into four subgroups. BD patients who had a total remission of depressive symptoms after eight weeks of antidepressant treatment were considered complete responders (CR). Partial responders (PR) had an antidepressant response, but it was incomplete. Non-responders (NR) had no improvement of depressive symptoms, i.e., no antidepressant response. Patients who experienced a manic or hypomanic episode during the eight weeks of treatment were assigned to the antidepressant-associated mania response (AAMR) group. MDD patients were divided following the same criteria. The treatment responses for the 90 BD patients were classified as 13 CR, 26 PR, 19 NR and 32 AAMR. The treatment responses of the 88 MDD patients were classified as 31 CR, 35 PR and 22 NR.

We used t-tests and chi-square to analyze the differences between patients regarding demographic (sex, age) characteristics. Differences in TEMPS-Rio de Janeiro dimensions between antidepressant response groups in each BD and MDD patients were performed by one-way ANOVA. Tukey's HSD post-hoc test was used to investigate how treatment response groups differed from each other. In BD patients analysis, the non-cycling individuals (CR+PR+NR) were aggregated to permit specific comparison with AAMR group. All analyses were performed using SPSS for Windows version 19.0.

## 3. Results

Among BD patients, there were no statistically significant differences between the CR, PR, NR and AAMR subgroups with regard to sex [$\lambda^2(3)=1.17$, $p>0.05$] or to age [$F(3)=0.99$, $p>0.05$]. Similarly, no difference was found for these variables when we considered the comparison between non-cycling subgroups combined (CR+PR+NR) and the AAMR subgroup [sex $\lambda^2$ $(1)=0.45$, $p>0.05$; age $t$ $(88)=0.37$, $p>0.05$].

Table 1 presents the BD patients' mean temperament subscales scores as measured by the TEMPS-RJ for each of the antidepressant response subgroups.

One-way ANOVA found statistically significant differences were across the four BD subgroups on TEMPS-RJ subscale scores. Specific post-hoc comparisons using the Tukey HSD are summarized in Table 2.

Depressive ($p<0.001$) and anxious ($p<0.05$) temperament subscale scores were higher for the NR subgroup as compared to the CR subgroup and the differences were statistically significant. Affective temperament scores in the CR subgroup did not differ from patients who developed a manic or hypomanic episode while taking an antidepressant (the AAMR subgroup). Finally, cyclothymic and hyperthymic temperaments were associated with antidepressant-associated mania in the specific comparison between non-cycling patients and AAMR subgroup.

In the analysis of MDD patients no statistically significant differences were found with regard to sex or age when we considered comparisons across the three antidepressant response subgroups [sex $\lambda^2$ $(2)=0.80$, $p>0.05$; age $F(2)=0.18$, $p>0.05$].