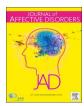
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Research paper

# Depressive symptoms and the role of affective temperament in adults with attention-deficit/hyperactivity disorder (ADHD): A comparison with bipolar disorder



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#### ABSTRACT

*Objectives*: To investigate the characteristics of depressive symptoms and the influence of affective temperament in adults with attention-deficit/hyperactivity disorder (ADHD), in comparison with bipolar disorder (BD) patients and healthy controls (HCs).

Method: Sixty patients with ADHD, 50 patients with BD, and 30 HCs were assessed with instruments for measuring depressive symptoms (Beck Depression Inventory-II), and affective temperaments (Temperament Scale of Memphis, Pisa and San Diego, self-administered version; TEMPS-A). In addition, participants were evaluated with scales for measuring ADHD symptoms, impulsiveness, anxiety, executive dysfunction, and quality of life. Results: ADHD patients showed levels of depressive symptoms similar to BD patients and higher than HCs. Only neurovegetative symptoms of depression differentiated ADHD and BD groups (BD > ADHD). Depressive symptoms in ADHD patients correlated positively with core ADHD, impulsivity, anxiety, and dysexecutive symptoms and negatively with quality of life. Thirty-eight percent of patients with ADHD scored above the cutoff for at least one affective temperament. Cyclothymic was the more common affective temperament (25%). ADHD patients with affective temperamental traits were more depressed and impulsive than patients without those traits and showed a symptomatic profile analogous to BD patients.

Limitations: The small size of resultant samples when ADHD group was stratified by the presence of affective temperament. In addition, results may not generalize to less severe ADHD patients from the community.

Conclusions: Concomitant depressive symptoms constitute a common occurrence in adults with ADHD that carries significant psychopathological and functional consequences. The concept of affective temperaments may be an interesting link for explaining depressive symptomatology and emotional impulsivity in a subgroup of patients with ADHD, beyond the classic idea of comorbidity.

#### 1. Introduction

In recent years, affective disturbances have gained recognition in the literature on attention-deficit/hyperactivity disorder (ADHD) in adulthood. The importance of the affective dimension can be traced both in the magnitude and diversity of its manifestations. Emotional lability has been reliably documented as a feature commonly present in adults with ADHD (Skirrow and Asherson, 2013; Skirrow et al., 2014; Vidal et al., 2014). Likewise, the occurrence of depressive episodes is frequent in ADHD patients during adulthood, with rates of comorbid major depression between 10% and 50% (Biederman et al., 1993; Fischer et al., 2002; Kessler et al., 2006; Sobanski et al., 2007; Biederman et al., 2008; McIntosh et al., 2009). A history of ADHD in childhood and adolescence is associated with elevated risk of

depression through early adulthood (Biederman et al., 2006; Biederman et al., 2008; Chronis-Tuscano et al., 2010; Meinzer et al., 2013; Meinzer et al., 2016). In addition, bipolar disorder (BD) is a common comorbid condition of ADHD, and the differential diagnosis between the two disorders is sometimes difficult because of symptom overlapping (Milberger et al., 1995; Kent and Craddock, 2003; Wilens et al., 2003; Nierenberg et al., 2005; Kessler et al., 2006; Wingo and Ghaemi, 2007; Torralva et al., 2011; Skirrow et al., 2012; Kitsune et al., 2016). In a dimensional perspective, mild or subthreshold depressive symptoms usually accompany the clinical presentation of ADHD patients, who show states of frustration, disinterest, low motivation, and other manifestations of negative affect (McIntosh et al., 2009; Torrente et al., 2011, 2014). Depressive symptoms are associated with increased ADHD symptomatology (Torrente et al., 2014); functional impairment and

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poorer quality of life (Sobanski et al., 2007; Yang et al., 2013); a poorer outcome of both ADHD and depression (Biederman et al., 2008); and suicidal ideation (van Eck et al., 2015).

Different factors have been postulated for explaining depressive symptoms in ADHD, including the existence of shared genetic influences (Faraone and Biederman, 1997; Cross-Disorder Group of the Psychiatric Genomics Consortium, 2013); the occurrence of negative environmental events and interpersonal problems (Daviss, 2008; Humphreys et al., 2013); demoralization and the development of maladaptive cognitive-behavioral patterns (Meinzer et al., 2016; Mitchell et al., 2013; Knouse et al., 2013; Torrente et al., 2014; Strohmeier et al., 2016); impaired reward responsivity (Meinzer et al., 2012); and deficits in emotion processing and regulation (Ibáñez et al., 2011; Seymour et al., 2012; Seymour et al., 2014).

A different but complementary approach to explain affective disturbances in ADHD comes from the study of affective temperaments. Akiskal and Akiskal (2005) defined the concept of affective temperament as an adaptive mixture of stable personality traits associated with mood reactivity that, in extreme cases, can lead to affective disease or enhance the expression of affective states across mood and non-mood disorders (Solmi et al., 2016). Affective temperaments constitute the personality extreme of bipolar spectrum, ranging from subsyndromics affective disorders to the more severe types of BDs. Akiskal et al. (2005) describe five types of affective temperaments: depressive, cyclothymic, hyperthymic, irritable and anxious. Interestingly, each type of temperament has been shown to be associated with specific mood-symptoms and psychopathological dimensions both in clinical (Iasevoli et al., 2013) and non-clinical populations (Walsh et al., 2012), and in consequence the presence of temperamental traits may help to predict the manifestation of specific psychopathology in different conditions. In particular, because many of the affective temperamental traits described by Akiskal et al. (2005) are consistent with mood phenomena previously described in people with ADHD (see Section 2.2 for a description of each temperament), they might be considered as potential personality-linked predisposing factors for the expression of affective symptoms in individuals with ADHD. Despite this, few studies have explored the presence of affective temperamental traits in adults with ADHD. Landaas et al. (2012) reported a very high prevalence of cyclothymic temperament (73% vs. 13% in the control sample) in a large sample of adults with ADHD. Participants with cyclothymic temperament showed more severe symptoms of ADHD, lower levels of education and occupation, more comorbid psychiatric disorders, and increased rate of psychiatric disorders in first-degree relatives. In a smaller study, Ekinci et al. (2013) found that 25% percent of the ADHD sample scored positively for at least one affective temperament. In marked contrast with the report of Landaas et al. (2012), only 7.5% of patients with ADHD presented a cyclothymic temperament. Finally, Eich et al. (2014) found that patients with ADHD showed similar scores on cyclothymic temperament and higher scores in anxious and irritable temperaments than BD patients.

Beyond disparities in methodology and results, positive findings in these previous studies warrant a more profound exploration of the role of affective temperaments in adults with ADHD. Furthermore, many questions arise about the true prevalence of these traits, their impact on affective symptoms and related psychopathology, and similarities and differences with other disorders, mainly BD. Regarding the purpose of the present study, previous research has not addressed the influence of temperament on the expression of different domains and specific symptoms of depression. However, this is an important issue because depressive syndromes frequently display with a marked symptomatic heterogeneity, and consequently an analysis at subsyndromal and symptom-specific levels may provide useful information about causal factors of affective symptoms, differential diagnosis, and even treatment options (Keller et al., 2007; Fried et al., 2014, 2015).

Accordingly, the first aim of this study was to assess the specific characteristics of depressive symptoms in adults with ADHD compared with control participants and patients with BD, and to explore the relationship of these symptoms with other components of the disorder and their functional impact. As aforementioned, depressive symptoms were analyzed considering their global severity but also dimensions and specific symptoms. Our hypothesis was that adults with ADHD would show elevated depressive symptoms in comparison with healthy controls (HCs) but milder than BD patients. In addition, we expected that the BD group would show higher scores for the somatic-affective domain of depression, neurovegetative symptoms, irritability, and suicidal thoughts.

The second objective of this study was to evaluate the presence of affective temperamental traits in the sample of adults with ADHD to examine their impact on depressive symptomatology and other clinical dimensions. For this purpose, participants were assessed with the Temperament Scale of Memphis, Pisa and San Diego, self-administered version (TEMPS-A; Akiskal et al., 2005). We hypothesized that affective temperamental traits in patients with ADHD will be correlated with increased levels of global depressive symptomatology but also with symptoms of the somatic-affective domain of depression, neurovegetative symptoms, irritability, and suicidal ideation.

A third aim was to compare depressive symptoms and other clinical characteristics in adults with ADHD with affective temperamental traits (ADHD-TEMPS+), adults with ADHD without affective temperamental traits (ADHD-TEMPS-), individuals with BD, and HCs. We expected that the ADHD group with affective temperamental traits would show higher levels of depressive symptoms than the ADHD group without affective temperamental traits but equivalent to the BD group. We also expected that the pattern of specific depressive symptoms and subdomains in ADHD with affective temperamental traits would be similar to that of the BD group.

#### 2. Methods

#### 2.1. Subjects

The present study is composed of three samples of 60 patients with ADHD, 50 BD patients, and 30 HCs. Clinical samples were consecutively selected from intake interviews to the specialized Clinics of ADHD and Mood Disorders at the Institute of Cognitive Neurology (INECO) within September 2007 and December 2012 as a part of a larger line of study of emotional and mood disturbances in adults with ADHD. All selected patients met the following inclusion criteria: age between 18 and 65 years, and DSM-IV (APA, 1994) diagnosis of BD or ADHD established through the MINI-Plus Structured Interview (Sheehan et al., 1998). Bipolar patients were enrolled in a current depressive phase, full or in partial remission, or else in euthymic state with minimal depressive symptoms. On the contrary, we excluded comorbid cases between ADHD and BD, patients who met criteria for a current hypomanic or mixed episode (because the object of the study were clinical and subclinical depressive symptoms), and any other potentially confounding comorbid psychiatric or neurological condition, including but not limited to schizophrenia, traumatic brain injury, intellectual disability, or

Assessment of ADHD patients also followed the protocol for adults suggested by Murphy and Gordon (2006) and described in previous publications of our group (Torralva et al., 2011; Torrente et al., 2011, 2014), including extended clinical interviews with patients and informants, self-report ratings of ADHD, and a comprehensive neuropsychological assessment. All participants were assessed before initiating treatment with specific drugs for ADHD. The final sample included 50 patients with ADHD combined type and 10 with ADHD predominantly inattentive type.

In the case of BD patients, in addition to the diagnostic interview by a trained psychiatrist, routine evaluation included the assessment through psychometric instruments, interviews with informants when available, and routine medical studies. The BD sample consisted of 36 patients with BD-II diagnosis, 6 patients with BD-I, and 8 with BD-not otherwise specified. Assessment was made during intake and before initiating pharmacological treatment, but since it was carried out in a clinical setting some patients were already medicated with mood stabilizers.

Finally, HCs (n=30) were recruited from a larger pool of volunteers who were screened to reject current or previous psychiatric disorders. All participants gave their informed consent prior to the inclusion in the study. The study was approved by the ethics committee at the Institute of Cognitive Neurology.

#### 2.2. Measures

- 1. Temperament Scale of Memphis, Pisa and San Diego, self-administered version (TEMPS-A; Akiskal et al., 2005). The TEMPS-A is a questionnaire designed to evaluate the fundamental affective temperaments-dysthymic, cyclothymic, hyperthymic, and irritable, plus the anxious temperament. The scale consists of 110 items that are scored as true or false. The different subscales provide a profile of mood, cognitive, psychomotor, and circadian rhythms that may predispose to major affective disorders. Depressive temperament, often referred as dysthymic, may be characterized as pessimistic, self-blaming, sensible to criticism, self-denying, and dependable. People who have a cyclothymic temperament often experience endogenous mood changes that result in short cycles of depression or hypomania; they are labile with rapid shifts in mood, variable in sleep, energy, self-esteem, and socialization. An irritable temperament person may be depicted as critical, bad-tempered, complaining, and anger and violence prone. Individuals with hyperthymic traits are optimistic, extroverted, hyperactive, confident, intrusive, and risk-takers, among other characteristics. Finally, anxious temperament is associated with worrying, interpersonal sensitivity, and phobic and avoidant features (Hantouche and Akiskal, 2005). The TEMPS-A has been adapted to Argentina's population and validated satisfactorily (Vázquez et al., 2007). Chronbach alphas were .7 (depressive) and .8 (anxious, cyclothymic, irritable and hyperthymic). The cutoff scores established for the Argentinean version correspond to two standard deviations above the mean for each subscale (Vázquez et al., 2007: dysthymic > 14; cyclothymic > 15; hyperthymic > 19; irritable > 12; anxious > 18).
- 2. ADHD Rating Scale for Adults (Barkley and Murphy, 1998). The ADHD Rating Scale for Adults is a self-report questionnaire that contains the 18 items based on the DSM-IV diagnostic criteria for ADHD. Respondents rate the intensity of ADHD symptoms on a 4-point Likert scale, ranging from 0 (never or rarely) to 3 (very often). The scale provides three scores: total scale (ADHD-RS-T), inattention (ADHD-RS-I), and hyperactivity-impulsivity (ADHD-RS-HI). In previous studies within the same population (Torrente et al., 2011, 2014), the ADHD-RS showed adequate psychometric properties. Also, in the present study the ADHD-RS showed high internal consistency for the total scale (α = .91).
- 3. Adult ADHD Quality of Life Scale (AAQoL; Brod et al., 2006). The AAQoL is a specific instrument designed to assess quality of life during the previous 2 weeks in adults with ADHD. This scale was exclusively completed by subjects with ADHD and only the total score was included in the analysis. As revealed in a previous study in the local population (Torrente et al., 2014), the AAQoL has shown good internal consistency and adequate convergent validity with measures of ADHD, depression, and anxiety symptoms. In the present study, the AAQoL showed good internal consistency (α = .84).
- 4. Beck Depression Inventory-II (Beck et al., 1996). The Beck Depression Inventory-II (BDI-II) is a widely used 21-item self-report instrument developed to measure severity of depression symptoms. The BDI-II has been successfully adapted to the local population of the present study (Brenlla and Rodríguez, 2006), showing adequate psychometric properties ( $\alpha = .88$  for clinical sample and .86 for

normative sample, r = .86 for test-retest reliability, adequate concurrent validity with other measures of depression, and good discriminatory power between clinical and non-clinical population). Factor analysis of this instrument in the original study (Beck et al., 1996) revealed two factors in the sample of psychiatric outpatients, most of them with mood disorders. The first factor includes such symptoms as fatigue, loss of energy, loss of interest, loss of pleasure, changes in appetite, changes in sleep patterns, loss of interest in sex, crying, irritability, restlessness, and indecision. The authors consider this factor as representative of a "somatic-affective" dimension of depression. The second factor includes symptoms of failure, impairment, feelings of guilt, dissatisfaction with oneself, self-criticism, feelings of punishment, pessimism, suicidal thoughts, and sadness. This factor reflects a "cognitive" dimension of depression. These dimensions were replicated in the local population (Brenlla and Rodríguez, 2006). BDI-II also includes specific items to assess changes in appetite, sleep disturbances, and loss of sexual desire. These three items are indicators of neurovegetative changes associated with rhythmic biological processes of depression (Cassano et al., 2009).

- 5. State-Trait Anxiety Inventory—Trait Subscale (STAI-T; Spielberger et al., 1970). The STAI is a widely used measure of transient and more enduring symptoms of anxiety. The first 20 items assess state anxiety (STAI-S), or how the participant feels right now; the second 20 items assess trait anxiety (STAI-T), or how the participant generally feels. Only the STAI-T was used in this study. Previously adapted to the local population (Leibovich de Figueroa, 1991), the STAI-T has shown a high internal consistency ( $\alpha$  = .90) and test–retest reliability (r = .93).
- 6. The Barratt Impulsiveness Scale (BIS-11). The BIS-11 is a 30-item self-report instrument designed to assess impulsivity traits (Patton et al., 1995). The BIS-11 has demonstrated good internal consistency ( $\alpha = .84$ ) and acceptable indicators of construct and discriminative validity in a validation study at the local population (López et al., 2012).
- 7. The Frontal Systems Behaviors Scale (FrSBe; Grace and Malloy, 2001). The FrSBe is a 46-item psychometric instrument for measuring behaviors associated with disturbances or damage of the frontal brain systems. For this study, the self-report version of the executive dysfunction subscale (FrSBe-DE) was used. A Spanish version of the FrSBe has shown its suitability for its use with adults with ADHD in the local population (Torrente et al., 2008). In the present study, the FrSBe-DE showed an adequate internal consistency ( $\alpha = .80$ ).

#### 2.3. Statistical analysis

Comparisons between groups were made using one-way ANOVA followed by Tukey's HSD or Tamhane T2 *post hoc* comparisons when appropriate. Correlations between measures were carried out by using the Pearson correlation coefficient. Finally, when analyzing categorical variables, the Pearson chi-square test was used.

#### 3. Results

#### 3.1. Demographic and clinical findings

Table 1 shows the demographic and clinical characteristics of the three samples under study. No significant between-groups differences were found in gender ( $\text{Chi}^2 = 4.95$ , p = .08) or age (F(2,137) = 52; p = .59).

Regarding clinical variables, significant between-groups differences were found for inattention (ADHD-RS-I; F(2,137)=34.53; p<.001), hyperactivity/impulsivity (ADHD-RS-HI; F(2,137)=15.98; p<.001), impulsivity (BIS-11; F(2,137)=29.45; p<.001). and anxiety (STAI-R; F(2,137)=17.71; p<.001). Post-hoc analysis showed that the ADHD

Table 1
Comparison of general clinical measures, depressive symptoms, and affective temperaments between ADHD, BD, and HCs groups.

|                    | ADHD<br>(n = 60) |       | BD (n = 50) |       | HCs<br>(n = 30) |       | ANOVA |        | Post-Hoc tests |            |           |  |
|--------------------|------------------|-------|-------------|-------|-----------------|-------|-------|--------|----------------|------------|-----------|--|
|                    | Mean             | SD    | Mean        | SD    | Mean            | SD    | F     | p      | ADHD vs HCs    | ADHD vs BD | BD vs HCs |  |
| Sex (m/f)          | 41               | 1/19  | 26/24       |       | 14/16           |       | _     | _      | _              | _          | _         |  |
| Age                | 34.68            | 11.12 | 37.02       | 10.87 | 35.69           | 14.89 | .52   | ns     | ns             | ns         | ns        |  |
| General measures   |                  |       |             |       |                 |       |       |        |                |            |           |  |
| ADHD-RS-I          | 14.53            | 6.32  | 10.36       | 5.73  | 4.1             | 3.5   | 34.53 | < .001 | < .001         | .001       | < .001    |  |
| ADHD-RS-HI         | 11.97            | 5.99  | 9.54        | 5.38  | 5.13            | 3.94  | 15.98 | < .001 | < .001         | ns         | < .001    |  |
| BIS-11             | 64.57            | 16.26 | 55.18       | 13.63 | 38.27           | 16.09 | 29.45 | < .001 | < .001         | .005       | < .001    |  |
| STAI-R             | 36.10            | 10.65 | 36.84       | 12.02 | 22.27           | 12.57 | 17.71 | < .001 | < .001         | ns         | < .001    |  |
| FrSBE-DE           | 47.51            | 10.52 | _           | _     | -               | -     | _     | -      | _              | _          | _         |  |
| AAQoL              | 42.91            | 17.51 | _           | _     | -               | -     | _     | -      | _              | _          | _         |  |
| Depressive sympton | ns               |       |             |       |                 |       |       |        |                |            |           |  |
| BDI-II Total       | 20.72            | 12.25 | 25.52       | 11.75 | 6.77            | 5.53  | 28.08 | < .001 | < .001         | ns         | < .001    |  |
| BDI-II AS          | 12.98            | 7.43  | 16.06       | 7.29  | 4.28            | 4.11  | 27.94 | < .001 | < .001         | ns         | < .001    |  |
| BDI-II COG         | 8.03             | 6.10  | 9.46        | 5.23  | 2.53            | 2.47  | 17.45 | < .001 | < .001         | ns         | < .001    |  |
| BDI-II NV          | 2.80             | 1.74  | 3.96        | 2.06  | 1.23            | 1.43  | 21.47 | < .001 | < .001         | .003       | < .001    |  |
| BDI Suic           | .42              | .59   | .62         | .67   | .10             | .31   | 7.71  | .001   | .004           | ns         | < .001    |  |
| BDI Irrit          | .85              | 1.00  | .90         | .81   | .76             | .88   | 4.65  | .011   | .01            | ns         | .002      |  |
| Affective temperam | ents             |       |             |       |                 |       |       |        |                |            |           |  |
| TEMPS-D            | 9.53             | 3.91  | 9           | 4.19  | 5.33            | 2.11  | 13.66 | < .001 | < .001         | ns         | < .001    |  |
| TEMPS-C            | 10.12            | 5.53  | 10.38       | 6.05  | 4.03            | 3.7   | 15.59 | < .001 | < .001         | ns         | < .001    |  |
| TEMPS-H            | 9.57             | 4.59  | 8.8         | 5.05  | 9.1             | 3.8   | .38   | ns     | ns             | ns         | ns        |  |
| TEMPS-I            | 7.23             | 4.62  | 7.32        | 4.44  | 3.03            | 3.08  | 11.60 | < .001 | < .001         | ns         | < .001    |  |
| TEMPS-A            | 10.85            | 5.54  | 10.92       | 6     | 5.73            | 3.96  | 10.63 | < .001 | < .001         | ns         | < .001    |  |

Note: ADHD-RS-I = ADHD Rating Scale-Inattention; ADHD-RS-HI = ADHD Rating Scale-Hyperactivity/Impulsivity; BIS-11 = Barratt Impulsivenes Scale-11; STAI-R = State-Trait Anxiety Inventory-Trait Subscale; FrSBe-DE = Frontal Systems Behaviors Scale - Executive dysfunction subscale; AAQoL = Adult ADHD Quality of Life Scale; BDI II = Beck Depression Inventory II; BDI-II AS = somatic-affective domain of BDI-II; BDI-II COG = cognitive domain of BDI-II; BDI-II NV = neurovegetative symptoms of BDI-II; BDI-II Suic = suicidal thoughts item of BDI-II; BDI Irrit = irritability item of BDI-II; TEMPS-D = Depressive Temperament; TEMPS-C = Cyclothymic Temperament; TEMPS-H = Hyperthymic Temperament; TEMPS-I = Irritable Temperament; TEMPS-A = Anxious Temperament.

group showed significantly higher scores than the BD group in the scales of inattention (p=.001) and impulsivity (p=.005). However, no differences between these two groups were found regarding hyperactivity/impulsivity and trait anxiety. Also, as expected, both ADHD and BD groups showed significantly higher scores than HCs in all the general clinical measures (see Table 1).

#### 3.2. Depressive symptoms in ADHD patients versus BD and HC groups

Significant between-groups differences were found for all variables related to depressive symptoms, namely, total depressive symptoms ( $F(2,137)=28.08;\ p<.001$ ), somatic-affective symptoms ( $F(2,137)=27.94;\ p<.001$ ), cognitive symptoms ( $F(2,137)=17.45;\ p<.001$ ), neurovegetative symptoms ( $F(2,137)=21.47;\ p<.001$ ), suicidal thoughts ( $F(2,137)=7.71,\ p=.001$ ), and irritability ( $F(2,137)=4.65,\ p=.011$ ). The post-hoc analysis of these comparisons revealed that both clinical groups (ADHD and BD) showed significantly higher scores on all measures of depressive symptoms compared with non-clinical controls. In contrast, the ADHD and BD groups differed from each other only by neurovegetative symptoms of depression (p=.003), for which the BD group showed significantly higher scores than the ADHD group.

#### 3.3. Correlates of depressive symptoms in ADHD patients

Significant positive correlations were found between depressive symptoms (total BDI-II score) and measures of inattention (ADHD-RS-I;  $r=.39,\ p<.001$ ), hyperactivity/impulsivity (ADHD-RS-HI;  $r=.48,\ p<.001$ ), impulsivity (BIS-11;  $r=.32,\ p<.05$ ), trait anxiety (STAI-R;  $r=.72,\ p<.001$ ), and executive deficits (FrSBe;  $r=.56,\ p<.001$ ). A significant negative correlation between depressive symptoms and quality of life in patients with ADHD (AAQoL;  $r=-.78,\ p<.001$ ) was observed.

#### 3.4. Affective temperaments in ADHD patients

Significant differences between groups were found in depressive (F (2,137) = 13.66; p < .001), cyclothymic (F(2,137) = 15.59; p < .001), anxious (F(2,137) = 10.63; p < .001), and irritable temperaments scores (F(2,137) = 11.6; p < .001). In contrast, no differences were found regarding hyperthymic temperament. Post-hoc analysis showed that ADHD and BD groups presented higher scores than HC group in the four mentioned temperaments, whereas there were no differences between ADHD and BD groups in any of the five temperaments (see Table 1).

Of the 60 patients with ADHD included in the sample, 23 of them (38.3%) surpassed the cutoff score for at least one of the five affective temperaments evaluated by the scale TEMPS-A. Cyclothymic temperament was the most frequent (n = 15; 25%), followed by irritable temperament (n = 10; 16.7%) and then, in equal proportions, the depressive and anxious temperaments (n = 6; 10% respectively). None of the patients presented scores above the cutoff score for hyperthymic temperament.

#### 3.5. Correlates of affective temperamental traits in ADHD patients

Significant positive correlations were observed between total depressive symptoms and scores of depressive (r=.52, p<.001), cyclothymic (r=.49, p<.001), irritable (r=.55, p<.001) and anxious (r=.48, p<.001) temperaments (see Table 2). In addition, significant positive correlations were found between the same four temperaments and the scores for somatic-affective domain of BDI-II (r=.45, p<.001; r=.46, p<.001; r=.45, p<.001; r=.46, p<.001, respectively) cognitive domain of BDI-II (r=.51, p<.001; r=.44, p<.001; r=.58, p<.001; r=.41, p=.001) and irritability (r=.43, p=.001; r=.27, p=.041; r=.41, p=.001; r=.35, p<.01). Meanwhile, suicidal thoughts were positively correlated with cyclothymic (r=.31, p=.017), irritable (r=.37, p<.01), and anxious (r=.26, p=.047)

**Table 2**Correlations between affective temperamental traits, depressive symptoms, and other clinical measures in patients with ADHD.

|              | TEMPS-D | TEMPS-C | TEMPS-H | TEMPS-I | TEMPS-A |
|--------------|---------|---------|---------|---------|---------|
| BDI-II Total | .52***  | .49***  | 11      | .54***  | .48***  |
| BDI-II AS    | .45***  | .46***  | 20      | .45***  | .46***  |
| BDI-II Cog   | .51***  | .44***  | .02     | .58***  | .41**   |
| BDI-II NV    | .19     | .31*    | 10      | .21     | .23     |
| BDI-II Suic  | .25     | .31*    | .02     | .37**   | .26*    |
| BDI-II Irrit | .43**   | .27*    | 11      | .42**   | .35**   |
| ADHD-RS-I    | .33*    | .20     | 08      | .26     | .25     |
| ADHD-RS-HI   | .23     | .27*    | .30*    | .53***  | .39**   |
| BIS-11       | .20     | .39**   | .27*    | .42**   | .12     |
| STAI-R       | .52***  | .43**   | 16      | .55***  | .51***  |
| AAQoL        | 37**    | 44**    | 02      | 52***   | 40**    |
| FrSBe-DE     | .40**   | .35*    | 07      | .42**   | .33*    |

Note: TEMPS-D = Depressive Temperament; TEMPS-C = Cyclothymic Temperament; TEMPS-H = Hyperthymic Temperament; TEMPS-I = Irritable Temperament; TEMPS-A = Anxious Temperament; BDI II = Beck Depression Inventory II; BDI-II AS = somatic-affective domain of BDI-II; BDI-II Cog = cognitive domain of BDI-II; BDI-II NV = neurovegetative symptoms of BDI-II; BDI-II Suic = suicidal thoughts item of BDI-II; BDI-III irrit = irritability item of BDI-II; ADHD-RS-I = ADHD Rating Scale-Inpatention; ADHD-RS-HI = ADHD Rating Scale-Hyperactivity/Impulsivity BIS-11 = Barratt Impulsivenes Scale-11; STAI-R = State-Trait Anxiety Inventory-Trait Subscale; AAQoL = Adult ADHD Quality of Life Scale; FrSBe-DE = Frontal Systems Behaviors Scale - Executive dysfunction subscale.

temperaments. Finally, scores corresponding to the neurovegetative symptoms of depression showed a significant positive correlation only with cyclothymic temperament scores (r = .31, p < .05).

Regarding other clinical measures, inattention (ADHD-RS-I) was positively correlated with depressive temperament (r=.33, p<.05), and hyperactivity/impulsivity (ADHD-RS-HI) was positively correlated with cyclothymic (r=.27, p<.05), hyperthymic (r=.30, p<.05), irritable (r=.53, p<.001), and anxious (r=.39, p<.01) temperaments

Scores of impulsivity (BIS-11) were positively correlated with cyclothymic ( $r=.39,\,p<.01$ ), hyperthymic ( $r=.27,\,p<.05$ ), and irritable ( $r=.42,\,p<.01$ ) temperaments scores. Trait anxiety scores (STAI-R) were positively correlated with depressive ( $r=52,\,p<.001$ ), cyclothymic ( $r=.43,\,p<.01$ ), irritable ( $r=.55,\,p<.001$ ), and anxious ( $r=.51,\,p<.001$ ) temperaments.

Finally, significant negative correlations were observed between the scores of quality of life (AAQoL) and the scores corresponding to depressive (r=.37, p<.01), cyclothymic (r=.44, p<.01), irritable (r=.52, p<.001), and anxious (r=.40, p<.01) temperaments. Meanwhile, dysexecutive symptoms were positively correlated with depressive (r=.40, p<.01), cyclothymic (r=.35, p<.05), irritable (r=.42, p<.01), and anxious (r=.33, p<.05) temperaments.

## 3.6. Depressive symptoms in ADHD patients with affective temperamental traits versus ADHD patients without affective temperamental traits, BD patients, and HCs

For this analysis, the ADHD group was stratified in two subgroups: those who scored positive (above the cutoff) for the presence of any of the affective temperaments (ADHD-TEMPS+) and those who not (ADHD-TEMPS-). Significant differences were found between ADHD-TEMPS+, ADHD-TEMPS-, BD, and HC, when comparing overall scores of the BDI-II ( $F(3,136)=28.02,\ p<.001$ ), somatic-affective subdomain of BDI-II ( $F(3,136)=25.15,\ p<.001$ ), cognitive subdomain of BDI-II ( $F(3,136)=20.89,\ p<.001$ ), neurovegetative symptoms ( $F(3,136)=15.5,\ p<.001$ ), irritability ( $F(3,136)=7.09,\ p<.001$ ) and suicidal thoughts ( $F(3,136)=7.53,\ p<.001$ ) (see Table 3). Post-hoc analysis of these comparisons showed that ADHD-TEMPS+ and BD

groups showed significantly higher means for all measures of depressive symptoms compared with the HC group (see Table 3). The ADHD-TEMPS— group showed significant differences from the HC group in total depressive symptoms (p < .001), the somatic-affective dimension of the BDI-II (p < .001), cognitive subdomain of BDI-II (p = .043), and neurovegetative symptoms of depression (p = .026) and no differences in symptoms of irritability and suicidal thoughts. The ADHD-TEMPS+ group presented significantly higher means than the ADHD-TEMPS-group in total depressive symptoms (p = .001), somatic-affective dimension of BDI-II (p = .007), and cognitive dimension of BDI-II (p = .002). No significant differences for other measures of mood between these two groups were found.

The ADHD-TEMPS+ group did not differ significantly in any of the depressive measures compared with the BD group. However, significant differences between ADHD-TEMPS- and BD groups were found for total depressive symptoms (p=.001), the somatic-affective dimension of the BDI-II (p=.001), cognitive dimension of BDI-II (p=.004), neurovegetative symptoms of depression (p=.001), and suicidal thoughts (p<.027). Finally, no differences between ADHD-TEMPS- and BD were found regarding irritability.

### 3.7. Other clinical measures in ADHD-TEMPS+ group versus ADHD-TEMPS-, BD, and HC groups

Significant differences between ADHD-TEMPS+, ADHD-TEMPS-, BD, and HC groups were found in impulsivity scores (BIS-11; F(3,136) = 24.32, p < .001). The post-hoc analysis of these comparisons revealed that the ADHD-TEMPS+ group showed significantly higher levels of impulsivity compared with the ADHD-TEMPS- (p = .01), BD (p < .001), and HC groups (p < .001). Meanwhile, the ADHD-TEMPS-group presented significantly higher levels of impulsivity than the HC group (p < .001), but showed no significant differences with the BD group. In addition, the BD group showed significantly higher levels of impulsivity in comparison with the HC group (p < .001).

Regarding anxiety, significant differences between groups were obtained (F = 18.82, p < .001). Post-hoc analysis revealed that the ADHD-TEMPS+ group showed significantly higher levels of anxiety compared with the ADHD-TEMPS- (p < .001) and HC groups (p < .001) but not compared with the BD group. The BD group showed higher levels of anxiety than the HC group (p < .001) but no differences with both ADHD groups. The ADHD-TEMPS- group manifested higher levels of anxiety than the HC group (p = .004).

Finally, significant differences between ADHD-TEMPS+ and ADHD-TEMPS- groups were found when comparing dysexecutive symptoms (F (1,49) = 15.30, p < .001), and quality of life scores (F(1,47) = 14.38, p < .001).

#### 4. Discussion

This study investigated the characteristics of depressive symptoms and the role of affective temperamental traits in adults with ADHD, BD patients, and HCs. The main findings revealed, first, that the ADHD group as a whole showed levels of depression comparable to BD patients, and only neurovegetative symptoms of depression distinguished the two conditions. Second, more than a third of ADHD patients presented affective temperamental traits that were associated with more severe depressive symptoms, anxiety, and impulsivity. Third, this subgroup of patients expressed a similar pattern of depressive symptoms than bipolar patients and may be considered an affective variant of ADHD.

In more detail, the first aim of this study was to assess the specific characteristics of depressive symptoms and their clinical and functional impact in adults with ADHD compared with patients with BD and HC participants. As expected, the results indicated that patients with ADHD had significantly higher levels than non-clinical controls in all variables related to depressive symptoms. On the contrary, these scores did not

<sup>\*</sup> p < .05.

<sup>\*\*</sup> p < .01.

<sup>\*\*\*</sup> p < .001.

**Table 3**Comparison of depressive symptoms, impulsivity, and anxiety between ADHD TEMPS+, ADHD TEMPS-, BD, and HC groups.

|              | ADHD TEMPS + $(n = 23)$ |       | ADHD TEMPS— $(n = 37)$ |       | BD (n = 50) |       | HCs<br>(n = 30) |       | ANOVA |        | Post-Hoc tests         |                 |                |                 |                  |           |
|--------------|-------------------------|-------|------------------------|-------|-------------|-------|-----------------|-------|-------|--------|------------------------|-----------------|----------------|-----------------|------------------|-----------|
|              | Mean                    | SD    | Mean                   | SD    | Mean        | SD    | Mean            | SD    | F     | p      | TEMPS+<br>vs<br>TEMPS- | TEMPS+<br>vs BD | TEMPS + vs HCs | TEMPS–<br>vs BD | TEMPS–<br>vs HCs | BD vs HCs |
| BDI-II Total | 28.26                   | 12.11 | 16.03                  | 9.86  | 25.52       | 11.75 | 6.77            | 5.53  | 28.02 | < .001 | .001                   | ns              | < .001         | .001            | < .001           | < .001    |
| BDI-II AS    | 17.00                   | 7.52  | 10.49                  | 6.25  | 16.06       | 7.29  | 4.28            | 4.11  | 25.15 | < .001 | .007                   | ns              | < .001         | .001            | < .001           | < .001    |
| BDI-COG      | 11.78                   | 6.33  | 5.70                   | 4.68  | 9.46        | 5.23  | 2.53            | 2.47  | 20.89 | < .001 | .002                   | ns              | < .001         | .004            | .005             | < .001    |
| BDI-II NV    | 3.30                    | 1.84  | 2.49                   | 1.63  | 3.96        | 2.06  | 1.23            | 1.43  | 15.50 | < .001 | ns                     | ns              | < .001         | .001            | .026             | < .001    |
| BDI-II Suic  | .65                     | .71   | .27                    | .45   | .62         | .67   | .10             | .31   | 7.53  | < .001 | ns                     | ns              | .01            | .027            | ns               | < .001    |
| BDI Irrit    | 1.32                    | 1.25  | .57                    | .69   | .90         | .81   | .33             | .61   | 7.09  | < .001 | ns                     | ns              | .012           | ns              | ns               | .019      |
| BIS-11       | 72.30                   | 15.30 | 59.76                  | 15.10 | 55.18       | 13.63 | 38.27           | 16.09 | 24.32 | < .001 | .01                    | < .001          | < .001         | ns              | < .001           | < .001    |
| STAI-R       | 43.48                   | 9.50  | 31.51                  | 8.62  | 36.84       | 12.02 | 22.27           | 12.57 | 18.82 | < .001 | < .001                 | ns              | < .001         | ns              | .004             | < .001    |

Note: BDI II = Beck Depression Inventory II; BDI-II AS = somatic-affective domain of BDI-II; BDI-II COG = cognitive domain of BDI-II; BDI-II NV = neurovegetative symptoms of BDI-II; BDI-II Suic = suicidal thoughts item of BDI-II; BDI Irrit = irritability item of BDI-II; BIS-11 = Barratt Impulsiveness Scale-11; STAI-R = State-Trait Anxiety Inventory-Trait Subscale.

show significant differences with the BD group regarding total intensity of depressive symptoms, symptomatic subdomains of the BDI-II, irritability, and suicidal thoughts. The latter result departs from the previsions of our hypotheses and highlights the relevance of depressive symptoms in ADHD. However, significant differences between ADHD and BD groups were observed on neurovegetative symptoms of depression (symptoms of sleep, appetite, and sexual desire). This result is important because, as an expression of dysregulated biological mechanisms in mood disorders, neurovegetative symptoms of depression may be a useful marker in differential diagnosis between ADHD and primary affective disorders. Otherwise, these findings underscore the relevance of the assessment of specific symptoms of depression, instead of global ratings of severity (Fried, 2015).

In addition, as expected, the presence of depressive symptoms in patients with ADHD correlated with greater intensity of core ADHD symptoms, that is, inattention and hyperactivity/impulsivity. This last point was also corroborated in impulsivity scores measured through the BIS-11 scale. One possible explanation for these effects lies in the executive deficits associated with depression. Several studies in major depression have shown deficits in neuropsychological tests associated with executive tasks, as well as evidence of dysregulated neural activity in prefrontal areas (Rogers et al., 2004; Clark et al., 2009). Our results confirmed the positive association between depression scores and executive deficits. Hence depressive symptoms may amplify primary executive deficit, which, in turn, could increase inattention and impulsivity due to decreased inhibitory control.

In addition, depressive symptoms in the present study correlated positively with the presence of anxiety symptoms measured with the STAI-R scale. This finding is consistent with the broad general literature showing the usual co-presence of depression and anxiety syndromes (Brown et al., 1998, 2001; Brown and Barlow, 2009) and previous studies in ADHD in which depression and anxiety usually coexist (Fischer et al., 2007; Yang et al., 2013; Torrente et al., 2014). Finally, higher levels of depressive symptoms were associated with lower levels of quality of life, confirming the idea that depressive symptoms contribute to the burden of disease.

The second objective of this study was to evaluate the prevalence and clinical influence of affective temperamental traits in adults with ADHD. The results revealed that patients with ADHD presented higher scores than the HC group for all temperamental traits, except for hyperthymic temperament, but no differences with the BD group in any of them. This pattern of results is mostly in agreement with previous studies about affective temperaments in adults with ADHD (Landaas et al., 2012; Ekinci et al., 2013; Eich et al., 2014). In addition, a considerable percentage of patients with ADHD (38%) scored above the cutoff score for at least one temperament. The most common variant was found to be cyclothymic temperament (25%), followed in

frequency by irritable temperament (16.7%). Interestingly, these two temperaments are associated with traits of instability that can be linked with the emotional lability described in adults with ADHD (Skirrow et al., 2013). In comparison with preceding studies about affective temperaments in ADHD, the rates of this study were higher than the global 25% reported by Ekinci et al. (2013), but much lower than the 75% obtained by Landaas et al. (2012) for cyclothymic temperament. Although the differences with the former may be attributed to differences in the samples under study, the latter may be accounted for by a lower cutoff used in the study by Landaas et al. (2012).

Regarding their clinical impact, the scores of affective temperamental traits correlated positively with the intensity of total symptoms, subdomains, and specific symptoms of depression, in accordance with the hypothesis that affective temperaments may enhance the expression of mood disturbances across disorders (Solmi et al., 2016). Likewise, the scores of affective temperamental traits were positively correlated with scores of ADHD core symptoms, impulsivity, and anxiety and negatively correlated with scores of quality of life. These observations support the idea that affective temperamental traits are globally associated with more severe clinical manifestations in adults with ADHD, as reported by Landaas et al. (2012).

A third aim was to compare depressive symptoms and other clinical characteristics in adults with ADHD with affective temperamental traits, ADHD without affective temperamental traits, individuals with BD, and HCs. As hypothesized, the ADHD-TEMPS+ group presented higher scores than the ADHD-TEMPS- group for total depressive and somatic-affective symptoms, but there were no differences with the BD group in any of the depression-related measures. In contrast, the BD group showed higher scores than the ADHD-TEMPS- group for total depressive symptoms, somatic-affective dimension, neurovegetative symptoms, and suicidal thoughts. The comparison between ADHD-TEMPS- and BD groups revealed the clear differences that we originally expected to find between BD patients and the whole group of ADHD regarding depression severity and symptomatic profile. Despite this, it is necessary to remark that the ADHD-TEMPS- group continued to show higher levels of depression than did the HCs. Consequently, the comparison between ADHD-TEMPS- and ADHD-TEMPS+ groups depicted two distinguishable clinical presentations concerning depressive symptoms in ADHD patients: on one hand, a more typical ADHD group with milder depressive symptoms, and on the other hand, an affectivelike variant of ADHD with a heavy load of depressive symptoms and with the symptom profile of an affective disorder. This characterization is in concordance with Landaas et al. (2012), but the proportion of patients in each group differs between studies, being in our case that the typical ADHD with mild depressive symptoms was more frequent. Notably, the ADHD-TEMPS+ group also showed higher levels of impulsivity than did the ADHD-TEMPS- and BD groups. Hence, as already

suggested by correlational analysis, the presence of temperamental traits not only amplifies affective symptoms but also enhances some of the specific features of ADHD itself. In other words, ADHD patients with affective temperament seem to constitute a mixed clinical presentation with characteristics both of ADHD and of a primary affective disorder.

#### 4.1. Limitations

The first limitation of this study is the reduced size of the samples under study. Specially, stratifying the ADHD sample to compare subgroups with and without affective temperamental traits may have led to a loss of statistical power to detect small differences between groups. However, it is reassuring that the differences found in such comparisons were statistically robust.

As a second limitation, because the sample was obtained in a single clinic specialized in the treatment of adults with ADHD, it is possible that patients portrayed in this investigation represent an extreme in the continuum of severity of the disorder. Thus we cannot to rule out that individuals from a community sample display less severe depressive symptoms. For this reason, it should be emphasized that the interpretation and application of these results should be restricted to clinical contexts analogous to the present study.

Lastly, because of its cross-sectional design, the capacity to establish causal relationships from the obtained data is limited. Although the relationship between affective temperamental traits and depressive symptoms is reflected significantly both in correlational analyzes and in between-groups comparisons, the demonstration of a causal link between them and its direction would require a further predictive or experimental study. Also, considering that both ADHD and affective temperaments have their roots in childhood, a longitudinal study may help to elucidate the developmental relationship between them and their reciprocal influences along life.

#### 5. Conclusions

Overall, the findings of this study add evidence about the importance of affective symptoms in adults with ADHD, and in particular of depressive manifestations, along with mood lability and irritability. The data presented here show that depressive symptoms may be present in adults with ADHD with different severity ranges and with a heterogeneous symptomatic profile. Furthermore, depressive symptoms are associated with more severe nuclear symptomatology of ADHD and worse quality of life. Therefore, the first clinical implication of this work is the need to carefully assess depressive symptoms in adults with ADHD, both in their intensity and symptom profile, for the purposes of differential diagnosis and adequate treatment. For diagnosis, the presence of pronounced neurovegetative alterations should alert one as a probable marker of a BD. Regarding treatment, this study reinforces the need for including specific interventions for depressive symptoms in the usual treatment of adults with ADHD, such as those proposed in cognitive-behavioral approaches (Safren, 2006; Knouse and Safren, 2010).

Our study also supports the conception of affective temperaments as dimensional traits that may predispose for the expression of depressive and other affective manifestations in individuals with ADHD. Patients with these traits may be viewed as a complex clinical variant with more severe affective troubles, enhanced core symptoms, and a more negative prognosis. Consequently, through the evaluation of temperamental traits in clinical settings, it would be possible to identify the ADHD patients who are at a higher risk for developing affective complications and who may require a more intensive and specific treatment.

#### Conflict of interest

The authors declare no conflict of interest regarding the material presented.

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#### References

- Akiskal, K.K., Akiskal, H.S., 2005. The theoretical underpinnings of affective temperaments: implications for evolutionary foundations of bipolar disorder and human nature. J. Affect. Disord. 85, 231–239.
- 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.
- APA, 1994. Diagnostic and Statistical Manual of Mental Disorders, 4th ed. American Psychiatric Association, Washington DC.
- Barkley, R.A., Murphy, K.R., 1998. Attention-Deficit Hyperactivity Disorder: A Clinical Workbook, 2nd ed. Guilford Press, New York.
- Beck, A.T., Steer, R.A., Brown, G.K., 1996. Manual for the Beck Depression Inventory-II. Psychological Corporation, San Antonio, TX.
- Biederman, J., Faraone, S.V., Spencer, T., Wilens, T., Norman, D., Lapey, K.A., Mick, E., Lehman, B.K., Doyle, A., 1993. Patterns of psychiatric comorbidity, cognition, and psychosocial functioning in adults with attention-deficit hyperactivity disorder. Am. J. Psychiatry 150, 1792–1798.
- Biederman, J., Monuteaux, M.C., Mick, E., Spencer, T., Wilens, T.E., Silva, J.M., Faraone, S.V., 2006. Young adult outcome of attention deficit hyperactivity disorder: a controlled 10-year follow-up study. Psychol. Med. 36, 167–179.
- Biederman, J., Ball, S.W., Monuteaux, M.C., Mick, E., Spencer, T.J., Mc-Creary, M., Cote, M., Faraone, S.V., 2008. New insights into the co-morbidity between ADHD and major depression in adolescent and young adult females. J. Am. Acad. Child Adolesc. Psychiatry 47, 426–434.
- Brenlla, M.E., Rodríguez, C.M., 2006. Adaptación argentina del Inventario de Depresión de Beck (BDI-II) [Argentine adaptation of the Beck Depression Inventory (BDI-II)]. In: Beck, A., Steer, R., Brown, G. (Eds.), BDI-II. Inventario de Depresión de Beck [BDI-II. Beck Depression Inventory], 2nd ed. Buenos Aires, Paidós.
- Brod, M., Johnston, J., Able, S., Swindle, R., 2006. Validation of the adult attention-deficit/hyperactivity disorder quality-of-life Scale (AAQoL): a disease-specific quality-of-life measure. Qual. Life Res. 15, 117–129.
- Brown, T.A., Chorpita, B.F., Barlow, D.H., 1998. Structural relationships among dimensions of the DSM-IV anxiety and mood disorders and dimensions of negative affect, positive affect, and autonomic arousal. J. Abnorm. Psychol. 107, 179–192.
- Brown, T.A., Campbell, L.A., Lehman, C.L., Grisham, J.R., Mancill, R.B., 2001. Current and lifetime comorbidity of the DSM-IV anxiety and mood disorders in a large clinical sample. J. Abnorm. Psychol. 110, 585–599.
- Brown, T.A., Barlow, D.H., 2009. A proposal for a dimensional classification system based on the shared features of the DSM-IV anxiety and mood disorders: implications for assessment and treatment. Psychol. Assess. 21, 256–271.
- Cassano, G.B., Benvenuti, A., Miniati, M., Calugi, S., Mula, M., Maggi, L., Rucci, P., Fagiolini, A., Perris, F., Frank, E., 2009. The factor structure of lifetime depressive spectrum in patients with unipolar depression. J. Affect. Disord. 115, 87–99.
- Clark, L., Chamberlain, S.R., Sahakian, B.J., 2009. Neurocognitive mechanisms in depression: implications for treatment. Annu. Rev. Neurosci. 32, 57–74.
- Chronis-Tuscano, A., Molina, B.S.G., Pelham, W.E., Applegate, B., Dahlke, A., Overmyer, M., Lahey, B.B., 2010. Very early predictors of adolescent depression and suicide attempts in children with attention-deficit/hyperactivity disorder. Arch. Gen. Psychiatry 67, 1044–1051.
- Cross-Disorder Group of the Psychiatric Genomics Consortium, 2013. Genetic relationship between five psychiatric disorders estimated from genome-wide SNPs. Nat. Genet. 45, 984–994.
- Daviss, W.B., 2008. A review of co-morbid depression in pediatric ADHD: etiology, phenomenology, and treatment. J. Child Adolesc. Psychopharmacol. 18, 565–571.
- Eich, D., Gamma, A., Malti, T., Vogt Wehrli, M., Liebrenz, M., Seifritz, E., Modestin, J., 2014. Temperamental differences between bipolar disorder, borderline personality disorder, and attention deficit/hyperactivity disorder: some implications for their diagnostic validity. J. Affect. Disord. 169, 101–104.
- Ekinci, S., Ozdel, K., Oncu, B., Colak, B., Kandemir, H., Canat, S., 2013. Temperamental characteristics in adults with attention-deficit hyperactivity disorder: a comparison with bipolar disorder and healthy control groups. Psychiatry Investig. 10, 137–142.
- Faraone, S.V., Biederman, J., 1997. Do attention deficit hyperactivity disorder and major depression share familial risk factors? J. Nerv. Ment. Dis. 185, 533–541.
- Fischer, A.G., Bau, C.H., Grevet, E.H., Salgado, C.A., Victor, M.M., Kalil, K.L., Belmonte-de-Abreu, P., 2007. The role of comorbid major depressive disorder in the clinical presentation of adult ADHD. J. Psychiatr. Res. 41, 991–996.
- Fischer, M., Barkley, R.A., Smallish, L., Fletcher, K., 2002. Young adult follow-up of hyperactive children: self-reported psychiatric disorders, comorbidity, and the role of childhood conduct problems and teen CD. J. Abnorm. Child Psychol. 30, 436–475.

- Fried, E.I., Nesse, R.M., Zivin, K., Guille, C., Sen, S., 2014. Depression is more than the sum score of its parts: individual DSM symptoms have different risk factors. Psychol. Med. 44, 2067–2076.
- Fried, E.I., Nesse, R.M., 2015. Depression sum-scores don't add up: why analyzing specific depression symptoms is essential. BMC Med. 13, 1.
- Grace, J., Malloy, P., 2001. FrSBe, Frontal Systems Behavior Scale: Professional Manual. Psychological Assessment Resources, Lutz, FL.
- Hantouche, E.G., Akiskal, H.S., 2005. Toward a validation of atripartite concept of a putative anxious temperament: psychometric data from a French national primary care medicine study. J. Affect. Disord. 85, 37–43.
- Humphreys, K.L., Katz, S.J., Lee, S.S., Hammen, C.L., Brennan, P.A., Najman, J.M., 2013. The association of ADHD and depression: mediation by peer problems and parent-child difficulties in two complementary samples. J. Abnorm. Psychol. 122, 854–867.
- Iasevoli, F., Valchera, A., Di Giovambattista, E., Marconi, M., Rapagnani, M.P., De Berardis, D., Buonaguro, E.F., 2013. Affective temperaments are associated with specific clusters of symptoms and psychopathology: a cross-sectional study on bipolar disorder inpatients in acute manic, mixed, or depressive relapse. J. Affect. Disord. 151, 540-550.
- Ibáñez, A., Petroni, A., Urquina, H., Torrente, F., Torralva, T., Hurtado, E., Guex, R., Blenkmann, A., Beltrachini, L., Muravchik, C., Baez, S., Cetkovich, M., Sigman, M., Lischinsky, A., Manes, F., 2011. Cortical deficits of emotional face processing in adults with ADHD: its relation to social cognition and executive function. Soc. Neurosci. 6, 464–481.
- Keller, M.C., Neale, M.C., Kendler, K.S., 2007. Association of different adverse life events with distinct patterns of depressive symptoms. Am. J. Psychiatry 164, 1521–1529.
- Kent, L., Craddock, N., 2003. Is there a relationship between attention deficit hyperactivity disorder and bipolar disorder? J. Affect. Disord. 73, 211–221.
- Kessler, R.C., Adler, L., Barkley, R., Biederman, J., Conners, C.K., Demler, O., Faraone, S.V., Greenhill, L.L., Howes, M.J., Secnik, K., Spencer, T., Ustun, T.B., Walters, E.E., Zaslavsky, A.M., 2006. The prevalence and correlates of adult ADHD in the United States: results from the National Comorbidity Survey Replication. Am. J. Psychiatry 163, 716–723.
- Kitsune, G.L., Kuntsi, J., Costello, H., Frangou, S., Hosang, G.M., McLoughlin, G., Asherson, P., 2016. Delineating ADHD and bipolar disorder: a comparison of clinical profiles in adult women. J. Affect. Disord. 192, 125–133.
- Knouse, L.E., Zvorsky, I., Safren, S.A., 2013. Depression in adults with attention-deficit/ hyperactivity disorder (ADHD): the mediating role of cognitive-behavioral factors. Cogn. Ther. Res. 37, 1220–1232. http://dx.doi.org/10.1007/s10608-013-9569-5.
- Knouse, L.E., Safren, S.A., 2010. Current status of cognitive behavioral therapy for adult attention-deficit hyperactivity disorder. Psychiatr. Clin. North Am. 33, 497–509.
- Landaas, E.T., Halmoy, A., Oedegaard, K.J., Fasmer, O.B., Haavik, J., 2012. The impact of cyclothymic temperament in adult ADHD. J. Affect. Disord. 142, 241–247.
- Leibovich de Figueroa, N.B., 1991. Ansiedad: algunas concepciones teóricas y su evaluación [Anxiety: theoretical conceptions and assessment]. In: Casullo, M.M., Leibovich de Figueroa, N.B., Aszkenazi, M. (Eds.), Teoría Y Técnicas de Evaluación Psicológica [Theory and techniques of psychological assessment]. Buenos Aires, Psicoteca, pp. 123–155.
- Lopez, P.L., Cetkovich-Bakmas, M., Lischinsky, A., Alvarez Prado, D., Torrente, F., 2012.Psychometric properties of the Barratt Impulsiveness Scale in a sample of the city of Buenos Aires. Vertex 23, 85–91.
- McIntosh, D., Kutcher, S., Binder, C., Levitt, A., Fallu, A., Rosenbluth, M., 2009. Adult ADHD and comorbid depression: a consensus-derived diagnostic algorithm for ADHD. Neuropsychiatr. Dis. Treat. 5, 137–150.
- Meinzer, M.C., Pettit, J.W., Waxmonsky, J.G., Gnagy, E., Molina, B.S., Pelham, W.E., 2016. Does childhood attention-deficit/hyperactivity disorder (ADHD) predict levels of depressive symptoms during emerging adulthood? J. Abnorm. Child Psychol. 44, 787-797
- Meinzer, M.C., Pettit, J.W., Leventhal, A.M., Hill, R.M., 2012. Explaining the covariance between attention-deficit hyperactivity disorder symptoms and depressive symptoms: the role of hedonic responsivity. J. Clin. Psychol. 68, 1111–1121.
- Meinzer, M.C., Lewinsohn, P.M., Pettit, J.W., Seeley, J.R., Gau, J.M., Chronis-Tuscano, A., Waxmonsky, J.G., 2013. Attention deficit-hyperactivity disorder in adolescence predicts onset of major depressive disorder through early adulthood. Depression Anxiety 30, 546–553.
- Milberger, S., Biederman, J., Faraone, S.V., Murphy, J., Tsuang, M.T., 1995. Attention deficit hyperactivity disorder and comorbid disorders: issues of overlapping symptoms. Am. J. Psychiatry 152, 1793–1799.
- Mitchell, J.T., Benson, J.W., Knouse, L.E., Kimbrel, N.A., Anastopoulos, A.D., 2013. Are negative automatic thoughts associated with ADHD in adulthood? Cogn. Ther. Res. 37, 851–859.
- Murphy, K.R., Gordon, M., 2006. Assessment of adults with ADHD. In: Barkley, R.A. (Ed.), Attention-Deficit Hyperactivity Disorder: A Handbook for Diagnosis and Treatment. Guilford Press, New York, pp. 425–452.
- Nierenberg, A.A., Miyahara, S., Spencer, T., Wisniewski, S.R., Otto, M.W., Simon, N., Pollack, M.H., Ostacher, M.J., Yan, L., Siegel, R., Sachs, G.S., 2005. Clinical and diagnostic implications of lifetime attention-deficit/hyperactivity disorder comorbidity in adults with bipolar disorder: data from the first 1000 STEP-BD participants. Biol. Psychiatry 57, 1467–1473.

- Patton, J., Stanford, M., Barratt, E., 1995. Factor structure of the Barratt Impulsiveness Scale. J. Clin. Psychol. 51, 768–774.
- Rogers, M.A., Kasai, K., Koji, M., Fukuda, R., Iwanami, A., Nakagome, K., Kato, N., 2004. Executive and prefrontal dysfunction in unipolar depression: a review of neuropsychological and imaging evidence. Neurosci. Res. 50, 1–11.
- Safren, S.A., 2006. Cognitive-behavioral approaches to ADHD treatment in adulthood. J. Clin. Psychiatry 67 (Suppl. 8), 46–50.
- Seymour, K.E., Chronis-Tuscano, A., Halldorsdottir, T., Stupica, B., Owens, K., Sacks, T., 2012. Emotion regulation mediates the relationship between ADHD and depressive symptoms in youth. J. Abnorm. Child Psychol. 40, 595–606.
- Seymour, K.E., Chronis-Tuscano, A., Iwamoto, D.K., Kurdziel, G., MacPherson, L., 2014. Emotion regulation mediates the association between ADHD and depressive symptoms in a community sample of youth. J. Abnorm. Child Psychol. 42, 611–621.
- Sheehan, D.V., Lecrubier, Y., Sheehan, K.H., Amorim, P., Janavs, J., Weiller, E., Hergueta, T., Baker, R., Dunbar, G.C., 1998. The mini-International neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J. Clin. Psychiatry 59 (Suppl. 2), 22–33-57.
- Skirrow, C., Asherson, P., 2013. Emotional lability, comorbidity and impairment in adults with attention-deficit hyperactivity disorder. J. Affect. Disord. 147, 80–86.
- Skirrow, C., Ebner-Priemer, U., Reinhard, I., Malliaris, Y., Kuntsi, J., Asherson, P., 2014. Everyday emotional experience of adults with attention deficit hyperactivity disorder: evidence for reactive and endogenous emotional lability. Psychol. Med. 44, 3571–3583.
- Skirrow, C., Hosang, G.M., Farmer, A.E., Asherson, P., 2012. An update on the debated association between ADHD and bipolar disorder across the lifespan. J. Affect. Disord. 141, 143–159.
- Sobanski, E., Bruggemann, D., Alm, B., Kern, S., Deschner, M., Schubert, T., Philipsen, A., Rietschel, M., 2007. Psychiatric comorbidity and functional impairment in a clinically referred sample of adults with attention-deficit/hyperactivity disorder (ADHD). Eur. Arch. Psychiatry Clin. Neurosci. 257, 371–377.
- Solmi, M., Zaninotto, L., Toffanin, T., Veronese, N., Lin, K., Stubbs, B., 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.
- Spielberger, C., Gorsuch, R., Lushene, R., 1970. STAI: Manual for the State-trait Anxiety Inventory, Palo Alto, CA. Consulting Psychologists Press, Palo Alto, CA.
- Strohmeier, C.W., Rosenfield, B., DiTomasso, R.A., Ramsay, J.R., 2016. Assessment of the relationship between self-reported cognitive distortions and adult ADHD, anxiety, depression, and hopelessness. Psychiatry Res. 238, 153–158.
- Torralva, T., Gleichgerrcht, E., Torrente, F., Roca, M., Strejilevich, S.A., Cetkovich, M., Lischinsky, A., Manes, F., 2011. Neuropsychological functioning in adult bipolar disorder and ADHD patients: a comparative study. Psychiatry Res. 186, 261–266.
- Torrente, F., Lischinsky, A., Torralva, T., López, P., Manes, F., 2008. Evaluación de síntomas frontales en pacientes con trastorno por déficit de atención (TDA) con y sin hiperactividad mediante el cuestionario FrSBe (frontal systems behaviour scale). [assessment of frontal symptoms in adults with attention deficit disorder through the FrSBe questionnaire]. Rev. Neurol. Argent. [Argent. J. Neurol.] 21–52.
- Torrente, F., Lischinsky, A., Torralva, T., López, P., Roca, M., Manes, F., 2011. Not always hyperactive? Elevated apathy scores in adolescents and adults with ADHD. J. Atten. Disord. 15, 545–556.
- Torrente, F., Lopez, P., Alvarez Prado, D., Kichic, R., Cetkovich-Bakmas, M., Lischinsky, A., Manes, F., 2014. Dysfunctional cognitions and their emotional, behavioral, and functional correlates in adults with attention deficit hyperactivity disorder (ADHD): is the cognitive-behavioral model valid? J. Atten. Disord. 18, 412–424.
- Van Eck, K., Ballard, E., Hart, S., Newcomer, A., Musci, R., Flory, K., 2015. ADHD and suicidal ideation: the roles of emotion regulation and depressive symptoms among college students. J. Atten. Disord. 19, 703–714.
- Vázquez, G.H., Nasetta, S., Mercado, B., Romero, E., Tifner, S., Ramón, M., del, L., Garelli, V., Bonifacio, A., Akiskal, K.K., Akiskal, H.S., 2007. Validation of the TEMPS-A Buenos Aires: Spanish psychometric validation of affective temperaments in a population study of Argentina. J. Affect. Disord. 100, 23–29.
- Vidal, R., Valero, S., Nogueira, M., Palomar, G., Corrales, M., Richarte, V., Bosch, R., Gomez-Barros, N., Corominas, M., Casas, M., Ramos-Quiroga, J.A., 2014. Emotional lability: the discriminative value in the diagnosis of attention deficit/hyperactivity disorder in adults. Compr. Psychiatry 55, 1712–1719.
- Walsh, M.A., Royal, A.M., Barrantes-Vidal, N., Kwapil, T.R., 2012. The association of affective temperaments with impairment and psychopathology in a young adult sample. J. Affect. Disord. 141, 373–381.
- Wilens, T.E., Biederman, J., Wozniak, J., Gunawardene, S., Wong, J., Monuteaux, M., 2003. Can adults with attention-deficit/hyperactivity disorder be distinguished from those with comorbid bipolar disorder? Findings from a sample of clinically referred adults. Biol. Psychiatry 54, 1–8.
- Wingo, A.P., Ghaemi, S.N., 2007. A systematic review of rates and diagnostic validity of comorbid adult attention-deficit/hyperactivity disorder and bipolar disorder. J. Clin. Psychiatry 68, 1776–1784.
- Yang, H.N., Tai, Y.M., Yang, L.K., Gau, S.S.F., 2013. Prediction of childhood ADHD symptoms to quality of life in young adults: adult ADHD and anxiety/depression as mediators. Res. Dev. Disabil. 34, 3168–3181.