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# Association between externalizing disorders and age of onset in patients with bipolar disorder type I and II

## Are the externalizing disorders symptoms predictors of an earlier onset?

Lino Palacios-Cruz,[1] Adriana Arias-Caballero,[1] Francisco Cortés Sotres,[2] Francisco de la Peña-Olvera,[3] Miriam Feria Aranda,[1] Marcela Cárdenas Godinez,[1] Rogelio Apiquian-Guitart,[4] Alfonso Cabrera-Lagunes,[5] Carlos Berlanga,[6] Ana Fresán,[6] Gerhard Heinze-Martin[7]

**Original article**

**SUMMARY**

**Background**

Earlier-onset mania (MIMT), compared with adolescent-onset mania (MIA), has a clinical presentation different from adult-onset classic mania (MIEA). Patients with MIA have a course more similar to MIEA. Externalizing disorders (ADHD, ODD and TC) have been associated with an earlier age of onset of BD and as a marker of poor prognosis. Our goal is to determine the frequency of symptoms related to disruptive behavior disorders in patients with an earlier and early onset BD and in adults retrospectively evaluated.

**Method**

The total sample (N=64) of adolescent and adult patients was obtained from different clinics of the National Institute of Psychiatry (INPRF). The diagnosis was confirmed by the research team. Patients were requested to sign the informed assent and consent. We applied the K SADS PL Mexico, MINI and MINI KID. We used the EEPE-AA for externalizing disorders.

**Results**

There were significant differences in EEPE AA scores compared by groups EIED in the Inattention subscale for GIMT. The presence of ADHD, ODD, TC and suicide risk in the time of evaluation was significantly associated with an earlier onset.

**Discussion and conclusions**

Our data support the clinical usefulness and importance of separating the BD by age of onset. The detection of externalizing disorders could result in an early onset of the disorder. Likewise, it has implications for prognosis and psychopharmacological treatment, since the childhood BD-onset remains in adulthood with similar and difficult characteristics. This suggests that we must have a longitudinal view of this disorder.

**Key Words:** Externalizing disorders, bipolar disorder, age of onset.

**RESUMEN**

**Antecedentes**

La manía de inicio muy temprano (MIMT), comparada con la manía de inicio en la adolescencia (MIA), tiene una presentación clínica distinta a la manía clásica de inicio en la adultez (MIEA). Los pacientes con MIA tienen un curso más parecido a la MIEA. Los trastornos externalizados (TDAH, TND y TC) se han asociado con una edad de inicio más temprano del TBP y como un marcador de mal pronóstico. Nuestro objetivo es determinar la frecuencia de los síntomas relacionados con los trastornos de la conducta disruptiva en pacientes con TBP de inicio muy temprano, temprano y en el adulto evaluados de manera retrospectiva.

**Método**

La muestra total (N=64) de pacientes adolescentes y adultos se obtuvo de distintas clínicas del Instituto Nacional de Psiquiatría (INPRF). El diagnóstico fue confirmado por el equipo de investigación y se solicitó la firma del asentimiento y consentimiento informado. Se aplicaron el K SADS PL México, MINI y MINI KID. Se utilizó la EEPE-AA para los trastornos externalizados.

**Resultados**

Se encontraron diferencias significativas en las puntuaciones del EEPE AA comparadas por los grupos de EIED, en la Subescala de Inaten-

[1] Programa Detección Oportuna y Estudio del TDAH a lo largo de la vida, PROMETEO/Subdirección de Investigaciones Clínicas, Instituto Nacional de Psiquiatría Ramón de la Fuente Muñiz.
[2] Departamento de Apoyo Académico a los alumnos de posgrado, Instituto Nacional de Psiquiatría Ramón de la Fuente Muñiz.
[3] Departamento de Fomento a la Investigación, Instituto Nacional de Psiquiatría Ramón de la Fuente Muñiz.
[4] ARETE Proyectos y Administración S.C., México.
[5] Facultad de Medicina. Universidad Veracruzana, Xalapa, Ver. México.
[6] Subdirección de Investigaciones Clinicas, Instituto Nacional de Psiquiatría Ramón de la Fuente Muñiz.
[7] Departamento de Psiquiatría y Salud Mental, Universidad Nacional Autónoma de México.

Correspondence: Dr. Lino Palacios. Programa Detección Oportuna y Estudio del TDAH a lo largo de la vida, PROMETEO/Subdirección de Investigaciones Clínicas, Instituto Nacional de Psiquatría Ramón de la Fuente Muñiz. Calz. México-Xochimilco 101, San Lorenzo Huipulco, Tlalpan, 14370 México, DF. E-mail: palacioslino@gmail.com

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ción para el GIMT. La presencia de TDAH, TND, TC y riesgo suicida en el momento de la evaluación se relacionó significativamente con un inicio más temprano.

**Discusión y conclusión**

Nuestros datos apoyan la importancia y utilidad clínica de separar el TBP por edad de inicio y la detección de trastornos externalizados podría hablarnos de un inicio temprano del trastorno. Asimismo, tiene implicaciones en el pronóstico y tratamiento psicofarmacológico, ya que el TBP de inicio en la infancia permanece en la adultez con características similares, así como de difícil manejo. Es necesario tener una visión longitudinal de este padecimiento.

**Palabras clave:** Trastornos externalizados, trastorno bipolar, edad de inicio.

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## BACKGROUND

Bipolar disorder (BD) is an illness that affects between 1 and 2% of the general adult Mexican population.[1,2] Most of clinicians and researchers agree that the BD diagnosis is phenomenologically heterogeneous and probably represent several different subtypes.[3]

The study of the BD from the age of onset is a useful approach to explain the heterogeneity of the clinical presentation among patients.[4,5] Currently it is accepted that the earlier-onset mania (MIMT, by 13 years of age), compared to the adolescent-onset mania (MIA, between 13 and 18 years of age), has a clinical presentation different than classic mania which frequently starts during adulthood (MIEA),[6] that is, with more psychotic symptoms including first range symptoms.[7] Due to the foregoing it is common that patients with MIMT are wrongly diagnosed as schizophrenic[7,8] or as carriers of a schizoaffective disorder.[9] Patients with adolescent-onset mania have a course more similar to adult-onset classic mania,[10,11] and even that patients with an earlier onset presented a higher probability to receive long-term treatment, more psychotic symptoms and higher chronicity, compared to adult-onset patients, the 15-year prognosis in both groups was similar.[6] Recently the existence of a BD subtype has been suggested from the perspective of development that may be identified since the age of onset.[10,12-18]

Some of these authors have mentioned that the early onset (by 13 years of age) BD and the adolescent-onset BD are associated with a more serious course, with the presence of anxiety disorders, a greater comorbidity with externalizing disorders, substance use, rapid cycling and higher suicidal behavior rates compared to the adult-onset BD, which suggests that an early or earlier onset age predicts a more complex and seriousness course of the BD.[10,17]

Regarding the comorbidity with externalizing disorders, that is the attention deficit-hyperactivity disorder (ADHD), the oppositional defiant disorder (ODD) and the behavioral disorder (TC), it has been detected that 57 - 97% of children with mania meet criteria for ADHD.[19-21] Faraone *et al.* found that adolescents with childhood-onset mania had the same comorbid ADHD indexes than maniac children (90%) and that both groups had higher comorbid ADHD indexes than adolescents with adolescent-onset mania (60%).[22] In the case of TC, the same authors discovered that 69% of bipolar children and adolescents suffered from this comorbidity. The presence of externalizing disorders, mainly ADHD, has been pointed out as a marker of poor prognosis since it indicates an earlier age of onset, confirmed both in epidemiological[23] and clinical studies.[16] Kessler[23] proved that among patients with ADHD there is 7.4 more likely (CI at 95% 4.6 to 12) to present a BD in comparison with those who did not suffer from ADHD. On the other hand, 21.2% of adults with BD presented ADHD compared to only 3.5% of persons without BD.

Considering such evidence, the main objective of this study was to determine the frequency of symptoms related to disruptive behavior disorders in patients with earlier and early onset BD and in adults retrospectively evaluated. We assessed the hypothesis that subjects with earlier-onset BD will have a higher externalizing symptomatology compared to persons in whom BD started from 13 years of age.

## MATERIALS AND METHODS

### Sampling

All patients included accepted to participate voluntarily by signing the informed consent, after the research purpose was explained. In addition, for minor patients, the informed consent of the parents or legal guardians was requested.

Patients who met the DSM-IV diagnostic criteria for type I or type II bipolar disorder diagnosis were included, who —as per the treating physician's discretion— were clinically stable and fit to answer the interview. Patients who suffered from any concomitant medical disease that could mistake the bipolar disorder diagnosis or if the latter was presented secondarily regarding substance use were excluded. All patients who did not attend two appointments were removed from the study, as well as who did not complete the scheduled clinical assessments.

The final sampling was made up by 73 patients with bipolar I and II disorders from the Outpatient Services (Servicio de Consulta Externa) (n=25), the Affective Disorder Clinic (Clínica de Trastornos Afectivos) (n=38) and the Adolescent Clinic (Clínica de Adolescencia) (n=20) of the National Institute of Psychiatry Ramón de la Fuente Muñiz (Instituto Nacional de Psiquiatría Ramón de la Fuente Muñiz).

The initial diagnosis was obtained through the DSM-IV criteria and was corroborated by the Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS-PL) interview, version for Mexico.

## INSTRUMENTS AND PROCEDURES

In order to confirm the presence of an externalizing disorder such as the attention deficit-hyperactivity disorder (ADHD), the behavioral disorder (TC), the oppositional defiant disorder (ODD), the patients were assessed through the Kiddie-SADS-PL; for adult patients, questions were made properly and retrospectively. K-SADS-PL is a semistructured diagnostic interview designed to assess current and past psychopathology episodes in children and adolescents (6-18 years of age) according to the DSM-III-R and DSM-IV criteria, which has been previously validated within Mexican population.[24]

For the rest of the psychiatric comorbidity the Mini International Neuropsychiatric Interview (MINI) was conducted in its original adult version and in the MINI Kid children and adolescent version.[25] Once the diagnoses and inclusion-exclusion criteria were confirmed, we applied the Assessment Auto-Applicable Scale of Externalizing Problems for Adolescents and Young Adults (EEPE-AA, appendix 2), an instrument made up by five subscales: a) inattention, b) oppositional-defiant, c) hyperactive-impulsive, d) dissocial-predatory and e) dissocial-non-predatory. The EEPE-AA has shown an appropriate validity and reliability in Mexican psychiatric population.[26]

Demographic (i.e., age, marital status, education, occupation) and clinical (i.e., hospital stay, onset age) characteristics of patients were obtained through a direct interview with the patient and his/her family. This information was gathered in a form previously designed for the study.

From the information obtained, the sampling was divided into three groups in accordance with the onset age of the affective symptoms (either the onset of depressive or manic/hippomanic symptoms): 1. Earlier-onset bipolar disorder (TBPIMT, in Spanish): When the onset of the bipolar disorder, either depressive or manic/hippomanic symptoms, presented by 13 years of age. 2. Early-onset bipolar disorder (TBPIT, in Spanish): When the onset of the bipolar disorder, either depressive or manic/hippomanic symptoms, presented by 18 years of age. 3. Adult-onset bipolar disorder (TBIA, in Spanish): When the onset of the bipolar disorder, either depressive or manic/hippomanic symptoms, presented from 19 years of age.

### Statistical Analysis

For the sociodemographic variables we used measures of central tendency and dispersion. Likewise, for the categorical variables, we used the Pearson's chi-square ($\chi^2$) test or Fisher's exact test in the case there were less than five measurements per variable; and regarding dimensional variables Student's t-test for independent samples. Furthermore, simple ANOVAS were used to compare the three groups determined under the onset age of the affective symptoms. Finally, we built an interactive model of the study variables through the AMOS *software*, obtained through an analysis based on the structural equation model.

## RESULTS

From the initial sampling of 73 patients tested, eight were discarded because they did not complete the relevant initial evaluations and another one because his bipolar affective disorder was related to substance use. Thus, the final sampling of our study was made up by 64 patients.

In the earlier-onset group (GIMT), the average age of the beginning of the first depressive episode was 9.8 years of age (SD=1.9 years), compared to the average age in the early-onset group (GIT) of 16.5 years of age (SD=3.6 years) and to the adult-onset group (GIA) of 23.4 years of age (SD=7.7 years). In accordance with this classification, slightly more than 70% of patients with BD I and BD II presented their first depressive episode by 18 years of age. A higher percentage of adolescents resulted in the (GIMT) in contrast to the percentage of adults who reported their first depressive episode by thirteen years of age. The starting age of the dysfunction resulted younger in the GIMT in contrast to the GIT and the GIA. No other significant differences were found in the remaining demographic variables or in the comorbidity with externalizing disorders, in accordance with the beginning of the first depressive episode (Table 1).

The starting age of the dysfunction (Table 2) was significantly younger than in the GIMT (13.4 years of age, SD=3.3 years) compared to the GIT (18.4 years of age, SD=4.9 years) and to the GIA (23.1 years of age, DE=6.6 years; $F[2,59]=17.351, p<0.001$). Although no significant differences were reported in the scores of the EEPE-AA subscales, a trend in the GIMT was observed presenting a greater severity in the assessed dimensions.

*First manic/hippomanic episode*: No differences were found concerning the sociodemographic variables of the group (Table 3). The presence of the attention deficit-hyperactivity disorder (ADHD), the oppositional defiant disorder (ODD), the behavioral disorder (TC) and the suicide risk in the time of evaluation was associated with an earlier BD onset. There were no significant differences for the rest of the Axis I and Axis II disorders.

The average age of the subjects who belonged to the GIMT, at the moment of the interview, was two years older compared to the GIT, which was significantly younger than the GIA (Table 4). The average age of the first hippomanic or manic episode was significantly younger than in the GIMT

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**Table 1.** Comparison of clinical and sociodemographic variable percentages from the onset age of the first depressive episode

| | First depressive episode Starting | | | | | | |
|---|---|---|---|---|---|---|---|
| | Earlier onset | | Early onset | | Adulthood onset | | |
| Variable | n | % | N | % | N | % | Significance |
| Type I BD | 16 | 32.0 | 21 | 42.0 | 13 | 26.0 | $\chi^2(2)=0.955$, p=0.620 |
| Type II BD | 6 | 46.2 | 4 | 30.8 | 3 | 23.1 | |
| 18 years old or younger | 10 | 55.6 | 8 | 44.4 | 0 | 0.0 | $\chi^2(2)=0.617$, p=0.008 |
| 19 years old or older | 12 | 26.7 | 17 | 37.8 | 16 | 35.6 | $\chi^2(2)=0.079$, p=0.961 |
| Paid work | 10 | 33.3 | 12 | 40.0 | 8 | 26.7 | |
| Female | 6 | 23.1 | 13 | 50.0 | 7 | 26.9 | $\chi^2(2)=3.006$, p=0.222 |
| Male | 16 | 43.2 | 12 | 32.4 | 9 | 24.3 | |
| ADHD[a] | 6 | 46.2 | 4 | 30.8 | 3 | 23.1 | $\chi^2(2)=1.693$, p=0.429 |
| Oppositional defiant disorder[a] | 1 | 33.3 | 1 | 33.3 | 1 | 33.3 | $\chi^2(2)=0.152$, p=0.927 |
| Behavioral disorder[a] | 1 | 25.0 | 1 | 25.0 | 2 | 50.0 | $\chi^2(2)=1.047$, p=0.592 |
| Externalizing disorders[a] | 6 | 42.9 | 4 | 28.6 | 4 | 28.6 | $\chi^2(2)=1.387$, p=0.500 |

(9.4 years of age, SD=2.2 years) compared to the GIT (14.9 years of age, SD=1.4 years) and the GIA (24.3 years of age, SD=5.0; F[2,61]=99.738,p=0.001). The average age of the first depressive episode in the group EIMT of the first hippomanic/manic episode was younger compared to the onset age of the group EIT. The GIMT subjects reported an onset dysfunction age of 12.2 years with regard to the group GIT and GIA of 16.5 and 23.9 years, respectively (F[2,60]=35.549, p=0.0001).

As for the average time between the beginning of the illness and care seeking, the GIMT subjects reported a higher average interval compared to the group GIT and GIA (8.1 years of age, SD=6.9 years and 8.2 years of age, SD=6.2 years, respectively (F[2,61]=3.201,p=0.048). Regarding the score obtained of EEPE-AA, it was found that there were significant differences for all average compared, therefore obtaining higher scores for the GIMT in all subscales (Table 4).

Figure 1 displays the comparison made between the total score obtained in each onset age group, both for the depressive episode and for the hippomanic/manic episode. Finally, by a linear regression model and a structural equation analysis (Figures 1 and 2) we found that the age at the moment of the interview had an influence on the ADHD diagnosis throughout life. Patients with a retrolectively obtained ADHD diagnosis have a higher score in the EEPE-AA (appendix 1). A younger onset age of the first depression episode was associated with a younger onset age of the first hippomanic and/or manic episode (p<0.0001). In addition, a lower grade in the EEPE–AA predicted an older onset age of the first depressive episode (p=0.013).

## DISCUSSION

The approach in the psychopathology study throughout life, taking into account the onset age, proposes an analysis method that allows getting closer, in a more accurate way, to different risks according with the onset of the disease. It

**Table 2.** Comparison of clinical and clinimetric variable averages from the onset age of the first depressive episode

| | First depressive episode Starting | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Earlier onset | | | Early onset | | | Adulthood onset | | | |
| Variable | N | $\bar{X}$ | SD | N | $\bar{X}$ | SD | N | $\bar{X}$ | SD | Significance |
| Age | 22 | 9.8 | 1.9 | 25 | 16.5 | 3.6 | 16 | 23.4 | 7.7 | F(2,60)=5.827, p=0.005 |
| Starting age of dysfunction | 21 | 13.4 | 3.3 | 25 | 18.4 | 4.9 | 16 | 23.1 | 6.6 | F(2,59)=17.351, p<0.001 |
| Time elapsed between the beginning of the illness and care seeking | 22 | 12.4 | 8.8 | 25 | 7.8 | 5.9 | 16 | 7.7 | 7.0 | F(2,60)=2.896, p=0.063 |
| EEPE AA* Inattention | 22 | 12.5 | 5.5 | 25 | 9.4 | 4.8 | 16 | 9.1 | 4.1 | F(2,60)=3.135, p=0.051 |
| EEPE AA* Hyperactive | 22 | 10.8 | 5.2 | 25 | 9.0 | 5.4 | 16 | 6.9 | 4.3 | F(2,60)=2.653, p=0.079 |
| EEPE AA* Oppositional defiant | 22 | 4.0 | 2.5 | 25 | 3.4 | 2.7 | 16 | 2.3 | 2.0 | F(2,60)=2.334, p=0.106 |
| EEPE AA* Dissocial-predatory | 22 | 7.6 | 3.8 | 25 | 6.2 | 3.6 | 16 | 5.5 | 2.5 | F(2,60)=1.989, p=0.146 |
| EEPE AA* Dissocial-non-predatory | 22 | 3.5 | 2.7 | 25 | 3.4 | 2.8 | 16 | 2.6 | 2.9 | F(2,60)=0.631, p=0.536 |
| EPE AA* Total | 22 | 38.5 | 16.7 | 25 | 31.5 | 17.0 | 16 | 26.4 | 13.1 | F(2,60)=2.749, p=0.072 |

*Assessment scale of externalizing problems for adolescents and young adults.

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**Table 3.** Comparison of clinical and sociodemographic variable percentages from the onset age of the first manic episode

| | First manic episode | | | | | | |
|---|---|---|---|---|---|---|---|
| | Starting | | | | | | |
| | Earlier onset | | Early onset | | Adulthood onset | | |
| Variable | N | % | N | % | n | % | Significance |
| BD I | 10 | 19.6 | 25 | 49.0 | 16 | 31.4 | $\chi^2(2)=2.842$, p=0.241 |
| BD II | 4 | 30.8 | 3 | 23.1 | 6 | 46.2 | |
| 18 years old or younger | 6 | 33.3 | 12 | 66.7 | | | $\chi^2(2)=12.241$, p=0.002 |
| 19 years old or older | 8 | 17.4 | 17 | 37.0 | 21 | 45.7 | |
| Without paid work | 6 | 17.6 | 17 | 50.0 | 11 | 32.4 | $\chi^2(2)=1.327$, p=0.515 |
| With paid work | 8 | 26.7 | 11 | 36.7 | 11 | 36.7 | |
| Female | 6 | 23.1 | 13 | 50.0 | 7 | 26.9 | $\chi^2(2)=1.127$, p=0.569 |
| Male | 8 | 21.1 | 15 | 39.5 | 15 | 39.5 | |
| ADHD[a] | 7 | 53.8 | 4 | 30.8 | 2 | 15.4 | $\chi^2(2)=10.118$, p=0.006 |
| Oppositional defiant disorder[a] | 3 | 100.0 | 0 | 0.0 | 0 | 0.0 | $\chi^2(2)=13.371$, p=0.001 |
| Behavioral disorder[a] | 3 | 75.0 | 1 | 25.0 | 0 | 0.0 | $\chi^2(2)=7.163$, p=0.028 |
| Externalizing disorders[a] | 7 | 50.0 | 5 | 35.7 | 2 | 14.3 | $\chi^2(2)=10.526$, p=0.005 |

[a] Diagnosed obtained by K SADS PL.

bears mention that early identification and the intervention of the initial stages of any mental childhood- or adolescent-onset disorder, such as the BD, could allow modifying the clinical course that is very likely to be torpid and difficult to manage. In general, earlier-onset BD is an illness with substantial deterioration, in the psychosocial field for instance, having a high suicidal risk, a significant transmission in relatives to the first degree of blood and a long course of the disorder in which the typically described cycles, followed by well-being periods are seldom observed.

The main objective of this study was to assess —on a type I and II BD adolescent and adult sampling, who attend a third level of care hospital— the association of the onset age, both for the first depressive episode and for the first hippomanic/manic episode, with the presence of symptoms related to the externalizing disorders (ADHD, ODD and TC). Based on these objectives, our data confirm our primary hypothesis, since subjects who started their symptomatology by 13 years of age had a higher average score in the instrument EEPE–AA compared to the adolescent-onset group (between 13 and 18 years of age) and to the adult-onset group (19 years of age or older).

The study of the relationship between the bipolar disorder and the externalizing disorders, especially the attention deficit-hyperactivity disorder, has been conducted for over 20 years, from the Biederman's reports at the end of the last century,[8] where he proved that the ADHD is a risk factor for the BD presentation also considering an earlier onset. The association between the externalizing disorders, especially the ADHD and the affective disorders as for their earlier-onset age, has different implications regarding health, treatment response and a poorer prognosis.

**Table 4.** Comparison of clinical and clinimetric variable averages from the onset age of the first hippomaniac or maniac episode

| | First manic episode | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Starting | | | | | | | | | |
| | Earlier onset | | | Early onset | | | Adulthood onset | | | |
| Variable | N | $\bar{X}$ | SD | N | $\bar{X}$ | SD | N | $\bar{X}$ | SD | Significance |
| Age | 14 | | 8.5 | 28 | 14.9 | 1.4 | 22 | **24.3** | **5.0** | F(2,61)=99.7, p=0.0001 |
| Onset of the first depressive episode | 14 | 10.9 | 4.7 | 28 | 14.0 | 3.0 | 21 | **23.4** | **5.3** | F(2,60)=25.321, p= 0.0001 |
| Starting age of dysfunction | 14 | 12.2 | 4.7 | 28 | 16.5 | 3.6 | 21 | **23.9** | **4.6** | F(2,60)=35.549, p=0.0001 |
| Time elapsed between the beginning of the illness and care seeking | 14 | 13.6 | 9.1 | 28 | 8.1 | 6.9 | 22 | **8.2** | **6.2** | F(2,61)=3.201, p=0.048 |
| EEPE AA* Inattention | 14 | 13.5 | 5.8 | 28 | 11.0 | 4.2 | 22 | **7.3** | **4.2** | F(2,61)=8.195, p=0.001 |
| EEPE AA* Hyperactive | 14 | 12.1 | 5.4 | 28 | 10.2 | 4.9 | 22 | **5.3** | **3.5** | F(2,61)=11.336, p=0.0001 |
| EEPE AA* Oppositional defiant | 14 | 5.2 | 2.6 | 28 | 3.6 | 2.4 | 22 | **1.7** | **1.4** | F(2,61)=11.9, p=0.0001 |
| EEPE AA* Dissocial-predatory | 14 | 8.6 | 4.0 | 28 | 7.0 | 2.8 | 22 | **4.2** | **2.9** | F(2,61)=9.339, p=0.0001 |
| EEPE AA* Dissocial-non-predatory | 14 | 4.1 | 2.8 | 28 | 3.8 | 2.9 | 22 | **1.8** | **2.1** | F(2,61)=4.947, p=0.01 |
| EEPE AA* Total | 14 | 43.6 | 17.6 | 28 | 35.7 | 14.3 | 22 | **20.3** | **11.7** | F(2,61)=12.958, p=0.0001 |

*Assessment scale of externalizing problems for adolescents and young adults.

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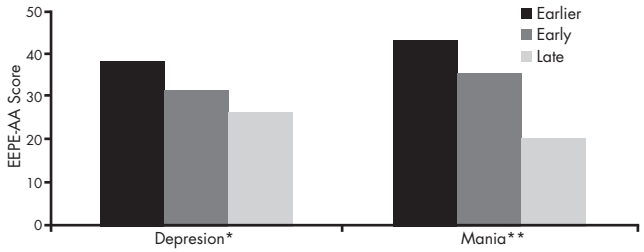


**Figure 1.** Comparison of total EEPE AA scores and groups sorted out by onset age of the affective symptoms.
* Depression, F (1,62)=0.215, p = 0.645; ** Hippomania/mania, F (2, 61) = 12.958 p = 0.0001.

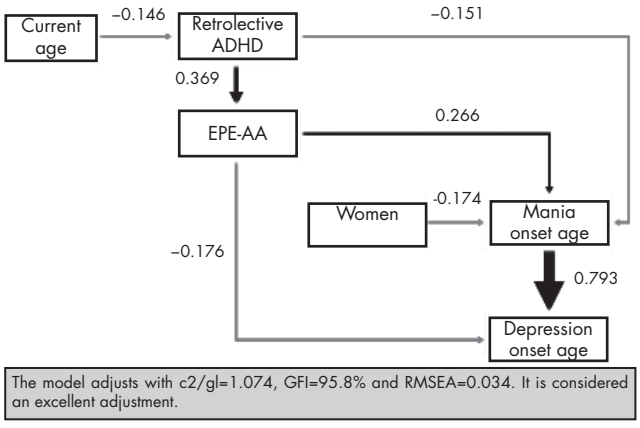


**Figure 2.** BD onset age and symptoms of externalizing disorders: predictive model (refer to Appendix 1)

The importance of the study of the onset age and its association with the bipolar-type affective disorders lies in the course and prognosis implications of individuals who could be affected by such disorder. In general, in our sampling of patients the time elapsed between the beginning of the illness and care seeking was slightly over nine years, not having found subtype bipolar disorder differences. One of the strengths and contributions of our study was the analysis made from the perspective of the depressive and the hypomanic/manic episode. For both perspectives there were two data we must stand out and which help pinpoint the need of a change in the conceptualization perspective of the BD as a childhood-onset and non-adult-onset disorder. The first datum is that the early onset of a depressive or hippomanic/manic episode was associated with an earlier onset of the complementary episode, either hippomanic/manic or depressive, respectively. The second datum, even more worrying, was that for the earlier-onset group the care seeking age for this reason was, in average, 12 years after the beginning of the affective symptomatology, six years older compared to the two remaining groups and two more years if evaluated from the perspective of the first hypomanic/manic episode. Different studies, as the one reported by Chong,[27] show that the onset age is associated to the treatment search. Therefore, the younger the onset age the less likely is to receive treatment.

Two reasons that could probably have influence in this wide range between the onset age of the symptomatology and the seeking care, would be: 1. the family character of the affective disorders in those who start at earlier ages, that is to say, that more than a first-degree relative would be affected by the same disorder or by the same spectrum of disorders, which in turn could contribute to a higher recognition threshold, and 2. the non-suspicion and thus the non-detection by the first-level or contact health care providers de primer, which makes necessary to improve the education and health systems where civil society is involved, introducing early detection and treatment objectives in high risk groups as well as a psychopathology vision throughout life where most of it starts in childhood. Geller *et al*.[28] have been able to prove the early detection importance and its implication in the prognosis, because subjects with childhood-onset BD present, when reaching adulthood, very similar characteristics than adults with BD with a chronic course, without periods of time with no symptomatology, difficult to manage and with resistance to psychopharmacological treatments established.

Another reason to be able to introduce the onset age in the comprehensive evaluation of our patients is that the onset age can be, for any psychiatric disease, a marker of etiological and genetic heterogeneity.[29] For this reason, the study of the onset age has been useful for different perspectives, for example, the assessment of phenotypes of certain disorder to help with the diagnosis, the determination of the etiology or the prognosis of the disorder being studied and, possibly, with the prevention and treatment of the disorder, in this case, the bipolar disorder. Studying a bipolar disorder from this perspective implies relating it with other concepts such as the "*cohort or secular effect*". In this regard, some epidemiological reports have indicated that subjects with bipolar disorder who were born in or after 1940 have earlier onset ages compared to subjects who were born by 1940.[30,31]

The dimensional and symptomatological evaluation of the externalizing disorders in subjects with bipolar disorder from our study indicated a significant connection between them and the first hypomanic/manic episode. The association of symptoms related to the attention deficit-hyperactivity disorder, the oppositional defiant disorder and the behavioral disorder in subjects with a bipolar disorder who started their first hypomanic/manic episode during childhood was more evidently proved. This datum stresses the importance of the ADHD as a factor of poor prognosis and of earlier-onset age of the comorbid psychopathology, in this case the bipolar disorder.

There age two major limitations of this study that should be mentioned. First, not having included the unspecified bipolar disorder (UBD) or BD NE (in Spanish). Notwithstanding DSM-IV defines the BD NOS (in Spanish) ambiguously, Birmaher *et al*.[32] defined in the COBY study -one of the most extensive and significant longitudinal studies within the re-

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search area of the pediatric bipolar disorder- with a greater accuracy the BD NE as the presence of clinically relevant BD symptoms that do not completely gather the criteria according to the DSM-IV for BD I and BD II. In this study only 8% (n=263) of the sampling had a BD II at the moment of the evaluation and 35% had a BD NE. Subjects with BD II had a later onset of their affective disorder and had lower comorbid ADHD indexes than subjects with BD I and BD NE ($p< 0=0.05$). The importance to consider the BD NE comes from the fact that many earlier or early onset cases relate to this type of BD and then they may go unnoticed, even showing a BD I comparable dysfunction level. Second, it was not possible to clinimetrically prove that all patients were in euthymia, although evaluators at the beginning of the interview had to clinically prove if patients were able to continue the interview, otherwise they were discarded.

Finally, considering said limitations and strengths, the main implication of our study, which was confirmed, is to point out the importance of the externalizing disorders, especially regarding the ADHD, as a predictor of an earlier-onset age of other mental disorders, in this case, of the bipolar disorder.

## CONCLUSIONS

The study of the BD from the perspective of the onset age offers an interesting vision allowing integrating elements of the development stage being studied. Papers prepared by different researchers show that there is a unique course of subjects with a childhood-onset bipolar disorder, being more serious and chronic. The incorporation of externalizing disorders, especially the ADHD, as risk factors, reinforces the need for having a longitudinal and dynamic vision of psychopathology throughout life. Our study, with its aforementioned limitations, could prove —from a cross-perspective— that there are clinical characteristics, such as the greatest presence of externalizing disorders associated with a minor onset age of the bipolar disorder.

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## APPENDIX 1
## Description of the interactive model of the study variables

| Dependent variable | Independent variable | Standard Beta | Z | P | Comments |
|---|---|---|---|---|---|
| Retrolective ADHD Dx | Age | -0.146 | 1.163 | 0.122 | Young patients are more likely to present ADHD Dx |
| EPE-AA | Retrolective ADHD Dx | 0.369 | 3.128 | 0.001 | Patients with ADHD Dx have a greater score in EPE-AA |
| Hippomania/mania onset age | Sex | -0.174 | 1.425 | 0.077 | Women are associated with a younger age for mania onset |
| Hippomania/mania onset age | Retrolective ADHD Dx | -0.151 | 1.146 | 0.126 | Retrolective ADHD Dx is associated with a younger age for mania onset |
| Hippomania/mania onset age | EEPE-AA | 0.206 | 1.565 | 0.059 | A higher score in EPE-AA is associated with an older age for mania onset |
| Depression onset age | Mania onset age | 0.793 | 9.998 | 0.0001 | Mania and depression onset ages are associated very significantly |
| Depression onset age | EEPE-AA | -0.176 | 2.216 | 0.013 | A lower score in EPE-AA is associated with an older age for depression onset |

*It bears mentioning that in this model the role of non-significant relationships is as covariates. The model adjusts with $\chi^2$/gl=1.074, GFI=95.8% y RMSEA=0.034. Therefore, it is considered an excellent adjustment.

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# APPENDIX 2
# Assessment scale of externalizing problems for adolescents and young adults

(Scale developed in the Instituto Nacional de Psiquiatría RFM, Mexico, 2002) Palacios Cruz L et al.

Name: _____ Age: _____

File: _____ Date: _____

Diagnosis (completed bye the physician): _____

_____

**Instructions:**
Please read carefully each sentence and check off the answer that best represents the frequency which you have acted. That is to say, answer how often you have acted according to the way each sentence is asked **throughout your life**: never, occasionally or frequently. There are **no correct or incorrect answers** in this instrument. The information hereby gathered shall be kept confidential by your physician. Please, ensure to answer the whole scale.

| | | Never | Occasionally | Frequently |
|---|---|---|---|---|
| 1 | I've had problems to finish my homework | | | |
| 2 | I've been acted as if I had an engine inside | | | |
| 3 | I've started physical fights | | | |
| 4 | I've had concentration problems | | | |
| 5 | I've been concentrating in games | | | |
| 6 | I've argued with adults | | | |
| 7 | I've followed the rules at home and at school | | | |
| 8 | You've told that you don't seem to listen when someone is talking you; that is, you don't pay attention to what people say | | | |
| 9 | I've had exploded; I lose control | | | |
| 10 | I've been organized | | | |
| 11 | I've got angry for insignificant things | | | |
| 12 | I've finished what I've started | | | |
| 13 | I am among those who really talk a lot | | | |
| 14 | I've been upset because people have ordered me to do things; I've refused to obey despite they've been right | | | |
| 15 | I've despaired when waiting my turn | | | |
| 16 | I've thrown tantrums | | | |
| 17 | I've had trouble to follow directions | | | |
| 18 | I've meddled or interrupted someone else's conversations or games | | | |
| 19 | I've been someone who doesn't pay attention and/or forgets where I've put some things (keys, wallet, books) | | | |
| 20 | I've found it hard to remain seated (i.e. when eating or at school) | | | |
| 21 | I've been very noisy | | | |
| 22 | I've blame others for my mistakes intentionally, knowing that I was responsible | | | |
| 23 | I've pestered people just for it | | | |
| 24 | I've acted before thinking instead of thinking before acting; therefore, I don't think what I do or say | | | |
| 25 | I've been resentful and vengeful when someone has teased me | | | |

| | | | | |
|---|---|---|---|---|
| 26 | I've lost things easily | | | |
| 27 | I've interrupted others when they speak; thus, I don't wait until they finish because of my impatience for participating or replying | | | |
| 28 | I've been able to follow directions without difficulty | | | |
| 29 | I've been very intrepid; I don't consider danger | | | |
| 30 | I've run away from home without permission; I've arrived home after some hours or even days | | | |
| 31 | I've been involved in trouble with the police | | | |
| 32 | I've been a liar | | | |
| 33 | I've skipped classes or left my school | | | |
| 34 | I've threatened others in order to intimidate them or simply because I enjoy that they are afraid of me | | | |
| 35 | I've stolen and slipped away unnoticed | | | |
| 36 | I've stolen face-to-face | | | |
| 37 | I've destroyed other people's things intentionally, in revenge | | | |
| 38 | I've caused fires or burnt another person's property just for teasing | | | |
| 39 | HI've used knives, switchblades or pistols to hurt someone | | | |
| 40 | I've pay attention at school without problems | | | |
| 41 | I've exceeded sexually; I've gone beyond my partner's desire | | | |
| 42 | I've smoked | | | |
| 43 | I've been drunk | | | |
| 44 | I've used drugs | | | |

PLEASE VERIFY THAT ALL QUESTIONS ARE ANSWERED

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