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Similarities between emotional dysregulation in adults suffering from ADHD and bipolar patients

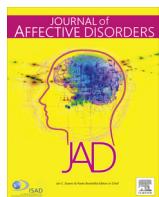
Richard-Lepouriel, Hélène; Etain, Bruno; Hasler, Roland; Bellivier, Frank; Gard, Sébastien; Kahn, Jean-Pierre; Prada, Paco Boris; Nicastro, Rosetta; Ardu, Stefano; Dayer, Alexandre; Leboyer, Marion; Aubry, Jean-Michel; Perroud, Nader Ali; Henry, Chantal

How to cite

RICHARD-LEPOURIEL, Hélène et al. Similarities between emotional dysregulation in adults suffering from ADHD and bipolar patients. In: *Journal of affective disorders*, 2016, vol. 198, p. 230–236. doi: 10.1016/j.jad.2016.03.047

This publication URL: <https://archive-ouverte.unige.ch/unige:89042>

Publication DOI: [10.1016/j.jad.2016.03.047](https://doi.org/10.1016/j.jad.2016.03.047)



Review article

Similarities between emotional dysregulation in adults suffering from ADHD and bipolar patients



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ARTICLE INFO

Article history:

Received 7 December 2015

Received in revised form

2 February 2016

Accepted 12 March 2016

Available online 15 March 2016

Keywords:

Psychiatry

ADHD

Mood disorders

Emotion

Affective lability

Affective intensity

ABSTRACT

Background: Emotional dysregulation in subjects with attention deficit and hyperactivity disorder (ADHD) is a topic of growing interest among clinicians and researchers. The present study aims at investigating components of emotional dysregulation in adults ADHD compared to subjects suffering from bipolar disorder (BD).

Methods: A total of 150 adults ADHD, 335 adults BD subjects and 48 controls were assessed using the Affective Lability Scale (ALS) and the Affect Intensity Measure (AIM), measuring respectively emotion lability and emotion responsiveness.

Results: ADHD and BD subjects scored significantly higher on the ALS compared to controls ($p=0.0001$). BD subjects scored above ADHD ones ($3.07 (\text{SD}=0.66)$ vs. $2.30 (\text{SD}=0.68)$; $p < 0.0001$). The average total scores achieved on the AIM were significantly different for the three groups ($p=0.0001$) with significantly higher scores for ADHD subjects compared to BD ones ($3.74 (\text{SD}=0.59)$ vs. $3.56 (\text{SD}=0.69)$; $p < 0.0001$).

Limitations: Suspected cases of ADHD in the BD and control groups were derived from the Wender Utah Rating Scale (WURS). This study is a retrospective one.

Conclusion: Our study thus highlights the importance of emotional dysregulation in adults suffering from ADHD, showing that they display higher emotional intensity than bipolar disorder subjects and controls. Although the current diagnostic criteria of ADHD do not contain an emotional dimension, a better recognition of the significance of emotional responsiveness in ADHD patients can improve the care afforded to these patients, beyond the inattentive and hyperactive/impulsive components.

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1. Introduction

Attention deficit hyperactivity disorder (ADHD) is a disabling neurodevelopmental disorder. It is estimated that 2.5–5% of the general adult population suffer from this disorder (Fayyad et al., 2007; Ginsberg et al., 2014; Kessler et al., 2006; Simon et al., 2009). The diagnosis is harder to establish for adults than it is with children since it shares numerous symptoms with other psychiatric pathologies (Ginsberg et al., 2014). Emotional dysregulation can be defined by excessive expression and experience of emotions with rapid and poorly controlled shift in emotions and abnormal allocation of attention to emotional stimuli. Emotional dysregulation is frequently encountered in ADHD patients (Robinson et al., 2008) and is also common in other disorders such as bipolar disorder (BD) or borderline personality disorder (BPD). Furthermore, the emotional dysregulation, and other related dimensions such as impulsiveness, might explain the high rate of comorbidity between ADHD and these two disorders. Indeed, among patients suffering from BPD, approximately 16% also suffer from ADHD and more than 40% had ADHD symptoms during childhood (Philipsen et al., 2008). Additionally, approximately 20% of subjects suffering from BD also suffer from ADHD (Perroud et al., 2014; Wingo and Ghaemi, 2007). Some authors even suggested the existence of a common diathesis rendering subjects vulnerable to BD and ADHD (Baud et al., 2011).

Emotional dysregulation has been extensively studied among patients suffering from BD and is marked essentially by emotional hyper-responsiveness (Henry et al., 2012; Henry et al., 2008), poor recognition and acceptance of emotions and difficulties in adapting behaviours to experienced emotions (Van Rheezen et al., 2015). During manic or mixed episodes, patients show a very high degree emotional hyper-responsiveness. During depressive phases, two types of patients are identified: those who show emotional hypo-responsiveness and those who show emotional hyper-responsiveness; with the latter being probably more at risk of experiencing mixed episodes (Henry et al., 2012). This emotional dysregulation continues during euthymic phases and is related with an increase in the frequency of relapses (M'Bailara et al., 2009). Moreover, the severity of symptoms during manic, mixed or depressive episodes is correlated with the severity of the pre-existing emotional dysregulation during euthymic phases (Van Rheezen et al., 2015). Finally, patients with impulsiveness issues are more at risk of relapsing into an hypomanic or manic mode, whereas patients who lack strategies to regulate their emotions are more at risk of relapsing into a depressive mode (Van Rheezen et al., 2015).

Concerning ADHD, clinicians and researchers are increasingly interested in the issue of emotional dysregulation (Shaw et al., 2014). Indeed, besides the two traditional domains of attention deficits and hyperactivity/impulsivity, more and more researchers support the view of a third dimension characterized by poor emotional regulation (Shaw et al., 2014).

Although several scales are available to measure emotional dysregulation, no consensus has been reached to define the best measurement to be used in research settings. However, as the Affective Lability Scale (ALS) (Harvey et al., 1989) and the Affect Intensity Measure (AIM) (Flett et al., 1988; Larsen and Diener, 1985, 1986; Mathieu et al., 2014) are the most commonly used scales to assess emotional dysregulation in borderline and in bipolar patients, diseases in which emotional dysregulation is particularly salient (Marwaha et al., 2014), we decided to choose these scales for our study to assess this dimension. Although these two scales examine different aspects of emotional dysregulation, responsiveness for the AIM and lability for the ALS, they are strongly correlated: the higher the lability, the higher the responsiveness, and inversely (Henry et al., 2008). For patients suffering from ADHD, emotional lability, as measured by the ALS, has only been studied by one group (Skirrow and Asherson, 2013; Skirrow et al., 2014), while the degree of emotional responsiveness measured by the AIM has never been examined (Marwaha et al., 2014). Our aim is therefore to assess emotional dysregulation among subjects suffering from ADHD, by comparison with subjects suffering from BD and control subjects, with a focus on two dimensions: emotional lability (ALS) and emotional responsiveness (AIM). Furthermore, we are also keen to test the internal validity of these two scales for ADHD sufferers.

2. Method

2.1. Participants

One hundred and fifty subjects suffering from ADHD were recruited in the Psychiatric Specialties Service of Geneva's University Hospitals (Switzerland), in an ambulatory unit specialized for adult ADHD that offers assessing and medical care. Patients are referred to this unit by general practitioners and private or hospital psychiatrists for diagnostic assessment and possibly care. Patients are assessed by psychiatrists specialized in adult ADHD according to the criteria of the DSM-IV-TR (American Psychiatric Association, 2000) and on collected clinical and anamnestic data. Anamnestic data refers to medical histories, family history, onset of the disorder and previous treatments usually collected during the interview with patient. The patients also fill in self-reported questionnaires, the Adult ADHD Self-Report Scale (ASRS v1.1) (Adler et al., 2006; Kessler et al., 2005) and the Wender Utah ADHD Rating Scale (WURS) (Romo et al., 2010; Ward et al., 1993) and undergo structured clinical interviews, the Diagnostic Interview for ADHD in adults (DIVA 2.0) and the French version of the Diagnostic Interview for Genetic Studies (DIGS) (Nurnberger et al., 1994; Preisig et al., 1999). The DIVA 2.0 was used to ascertain the number of attentional and/or impulsive/hyperactive symptoms according to DSM-IV criteria and help in deciding whether or not

to retain ADHD diagnosis. The ASRS v1.1 includes 18 items for the assessment of ADHD severity. It has proved to be relatively reliable to detect ADHD subjects and is useful as a screening tool. The participants score each item on a 0–4 Likert scale, based on their observations during the six previous months. Concerning the WURS, we have used the short version which includes 25 items. Subjects with a score > 46 are considered as having ADHD during childhood. The DIGS is used in this study to establish the comorbidity diagnoses and only axis-1 comorbidities were considered. However, since our centre is also specialized in the diagnosis and treatment of BPD sufferers, ADHD patients with a borderline comorbidity were excluded from the study (Prada et al., 2014).

The group of subjects suffering from BD includes 235 subjects recruited in France for a research protocol investigating the genetic and environmental susceptibility factors to bipolar disorders. The diagnoses of BD were established by either psychiatrists or psychologists. The patients with BD were euthymic when included in the study. Euthymic state was defined by the treating psychiatrist's clinical examination and confirmed by 1) a score < 12 on the Montgomery–Åsberg Depression Scale (Montgomery and Åsberg, 1979) and a score < 6 on the Bech Mania Scale (Bech et al., 1978). All participants answered the French version of the DIGS. The patients also filled in the WURS.

The control group includes 48 subjects recruited among dentistry students and doctors at the University of Geneva.

The Ethics Committees in each centre approved the study and all participants gave their written informed consent.

2.2. Measurements

Emotional dysregulation was studied through two dimensions, lability and responsiveness, respectively measured by:

ALS - Affective Lability Scale: emotional lability was measured with the French version of the ALS (Guile et al., 2009; Oliver and Simons, 2004), in its extended form (54 items). In this self-questionnaire, respondents are asked to describe their emotions with a 0–3 score (not at all characteristic to very characteristic). The items are grouped in six sub-dimensions that examine variations from normal mood to depression (11 items), euphoria (12 items), anxiety (7 items), anger (7 items), from anxiety to depression (8 items) and from depression to elation (9 items). The score of each sub-dimension is the sum for each item divided by the number of items. The gross total is the sum of the scores for each question and the total score is equal to the sum of scores for each item divided by 54. With adult respondents and in its French version, the ALS shows high internal coherence (section alpha between 0.73 and 0.89, and intersection correlations between 0.64 and 0.81) as well as acceptable test-retest reliability (section correlations between 0.48 and 0.86) (Guile et al., 2009).

AIM – Affect Intensity Measure: it is a self-questionnaire that includes 40 items that examine the emotional intensity experienced by the subject in various situations. The emotions are either positive or negative. The items are scored from 1 to 6. The AIM has high internal coherence (alpha coefficient = 0.90–0.94) and a time reliability for three months of 0.81 (test-retest reliability).

2.3. Statistical analysis

Analytic and descriptive statistics were done using STATA 13.0 software (Statacorp, 2013). The distribution of ALS scores was not normal, and we therefore carried out non parametric Kruskall-Wallis tests to draw comparisons between the three groups, and Mann Whitney tests to draw group-to-group comparisons. The distribution of scores of the AIM being normal, we conducted a one-way analysis of covariance (ANCOVA) for the comparison of

the three groups and a Hotelling test for the group-to-group comparison, taking gender into account. Similarly, we conducted sensitivity analyses by excluding ADHD sufferers with a bipolar disorder comorbidity, and bipolar disorder sufferers with a WURS > 46.

For the ADHD group, we also carried out multilinear regressions to identify the factors associated with ALS and AIM. The factors included in the multivariate regression model were the type of ADHD, age, gender, marital status, socio-professional category and the presence of axis-1 comorbidities.

The internal consistency of these scales was assessed with an alpha Cronbach measurement. For all the analyses, the alpha risk was of 0.05.

3. Results

3.1. Description of the sample

The sample included 533 subjects: 150 subjects had a main diagnosis of ADHD, 335 had a main diagnosis of BD, and 48 were control subjects (see Table 1).

There were significantly more men in the ADHD group than in the BD group ($\text{Chi}^2(1)=18.16$; $p < 0.0001$). The marital status was significantly different in the ADHD and the BD groups ($\text{Chi}^2(5)=30.10$; $p < 0.0001$). The subjects in the ADHD group were significantly younger than the subjects in the BD group (Mann-Whitney test: $z=-5.36$; $p < 0.0001$). There was no significant difference according to the socio-professional category ($\text{Chi}^2(3)=7.61$; $p=0.06$). There was a significant difference between control subjects, ADHD subjects and BD subjects according to gender ($\text{Chi}^2(2)=18.39$; $p < 0.0001$) and age (Kruskal-Wallis test: $\text{Chi}^2(2)=31.53$; $p=0.0001$).

Among subjects with ADHD, 72 subjects (48.0%) had a mixed type of ADHD, 48 subjects (32.0%) had an inattentive type of ADHD and 7 subjects (4.7%) had a hyperactive-impulsive type of ADHD. For 23 subjects (15.0%), the DIVA scale was not filled in: the ADHD diagnosis was established following the clinical interview, with no retrospective means of determining the type of ADHD.

Table 1
Socio-demographic characteristics of ADHD, BD and control subjects.

	ADHD		BD		Control		Total
	n	%	n	%	n	%	
Gender							
Man	99	66	151	45.1	23	47.9	273
Marital status							
Single	72	51.4	96	29.2			
Married	46	32.9	174	52.9			220
Separated	10	7.1	10	3.0			20
Divorced	12	8.6	43	13.1			55
Widower	0	0.0	5	1.5			5
Not filled-in	0	0.0	1	0.3			1
Socio-professional category							
Active	73	48.7	201	60.0			
Unemployed/Students/Retirees	65	43.3	114	34.0			179
Disability benefits/Disabled	12	8.0	17	5.1			29
Not filled-in	0	0	3	9.0			3
Presence of comorbidities	101	67.3	101	30.2			202
Age	37.7	11.5	44.0	12.1	39.5	11.2	

m=mean.

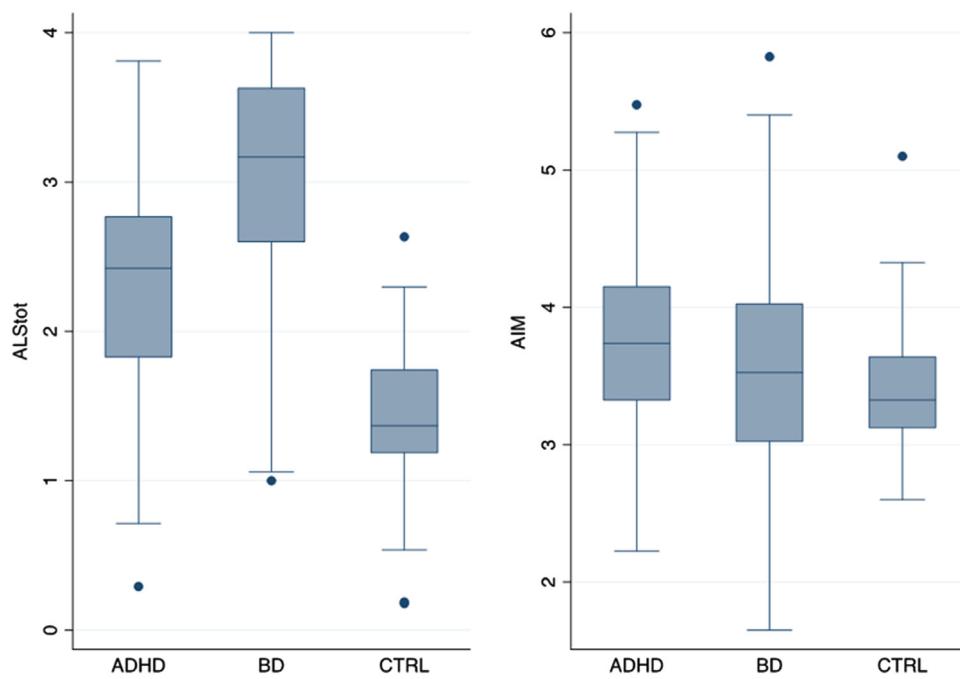


Fig. 1. Box plots of ALS and AIM scores in ADHD, BD and control subjects.

3.2. ALS-AIM

Neither age nor gender were associated with the ALS (respectively $p=0.71$ and $p=0.06$). The average total score achieved on the ALS was significantly different for the three groups (control group (3): $m=1.45$ ($SD=0.49$), ADHD(1): $m=2.30$ ($SD=0.68$) and BD group(2): $m=3.07$ ($SD=0.66$); Kruskall-Wallis test: $\chi^2(2)=191.3$; $p=0.0001$). These average values were significantly different between each group taken two-by-two (Mann-Whitney test: 1vs2, $z=-10.30$ $p<0.0001$; 1vs3, $z=7.11$ $p<0.0001$; 2vs3, $z=10.47$ $p<0.0001$) (Fig. 1).

The average scores achieved for each dimension of the ALS were significantly different for the three groups (Table 2).

The average values for each dimension were also significantly different for each group taken two-by-two ($p<0.0001$).

Age was not associated with the AIM ($p=0.14$). Gender was associated with the AIM ($p<0.0001$): women had significantly higher scores at the AIM. ANCOVA and Hotelling tests were therefore adjusted for gender. The average total scores achieved on the AIM were significantly different for the three groups [control group (3): $m=3.40$ ($SD=0.51$), BD group (2): $m=3.56$ ($SD=0.69$) and ADHD group (1): $m=3.74$ ($SD=0.59$) (ANCOVA: $F(2, 532)=10.02$; $p=0.0001$)].

Table 2

Average scores for the different dimensions of the ALS and difference between groups.

	ADHD		BD		Control subjects		Chi2 (2df)	<i>p</i>
	<i>m</i>	<i>SD</i>	<i>m</i>	<i>SD</i>	<i>m</i>	<i>SD</i>		
ALS-A	2.28	0.76	3.11	0.72	1.40	0.58	183.62	<0.0001
ALS-AD	2.44	1.29	3.07	0.82	1.30	0.50	152.90	<0.0001
ALS-Ang	1.97	0.84	3.29	0.69	1.26	0.51	257.19	<0.0001
ALS-E	2.36	0.65	2.93	0.71	1.63	0.54	133.50	<0.0001
ALS-D	2.46	0.71	2.95	0.67	1.62	0.56	126.13	<0.0001
ALS-B	2.26	0.75	3.09	0.73	1.47	0.49	180.16	<0.0001

A = anxiety; AD = anxiety to depression; Ang = anger; E = euphoria; D = depression; B = depression to elation.

3.3. Sensitivity analyses

We then conducted sensitivity analyses considering ADHD subjects without BD ($n=139$), BD subjects with a WURS score ≤ 46 ($n=289$) and control subjects with a WURS score ≤ 46 ($n=44$). The average total score achieved on the ALS was significantly different for the three groups (ADHD group (1): $m=2.28$ ($SD=0.69$), BD group (2): $m=3.16$ ($SD=0.62$) and control group (3): $m=1.43$ ($SD=0.51$); Kruskall-Wallis test: $\chi^2(2)=199.71$; $p<0.0001$). These average values were significantly different between each group taken two-by-two (Mann-Whitney test: 1vs2, $z=-11.07$, $p<0.0001$; 1vs3, $z=10.25$ $p<0.0001$; 2vs3, $z=6.74$, $p<0.0001$). With regard to the scores achieved on the AIM, the average values were significantly different for the three groups [ADHD group (1): $m=3.74$ ($SD=0.60$), BD group (2): $m=3.46$ ($SD=0.65$) and control group (3): $m=3.40$ ($SD=0.51$) (ANOVA: $F(2, 472)=16.62$; $p<0.0001$)]. These average values were significantly different for the ADHD group and the BD group (Hotelling test: $F(2, 82)=16.73$; $p<0.0001$) and for the ADHD group and the control group (Hotelling test: $F(2, 195)=11.29$; $p<0.0001$). However, there was no significant difference between the BD group and the control group (Hotelling test: $F(2, 380)=1.09$; $p=0.33$).

3.4. ALS, AIM and ADHD subtypes

Seventy-one subjects (56.7%) had mixed type of ADHD, 48 subjects (38.1%) had attentional type of ADHD and 7 subjects (5.6%) had impulsive/hyperactive type of ADHD. Subjects with a mixed type of ADHD had a total average score at the ALS of 2.37 ($SD=0.70$). Subjects with an inattentive type of ADHD have a total average score at the ALS of 2.30 ($SD=0.61$). Subjects with a hyperactive-impulsive type of ADHD have a total average score at the ALS of 1.91 ($SD=0.45$). There was no significant difference between the average values of these three groups (Kruskall-Wallis test: $\chi^2(2)=3.82$; $p=0.148$).

Subjects with a hyperactive-impulsive type of ADHD have a total average score at the AIM of 3.29 ($SD=0.38$). Subjects with an inattentive type of ADHD have a total average score at the AIM of

3.55 ($SD=0.55$). Subjects with a mixed type of ADHD had a total average score at the AIM of 3.92 ($SD=0.60$). These three average values were significantly different (ANOVA: $F(2, 126)=9.00$; $p < 0.0001$).

Finally, severity of ADHD as measured by the ASRS v1.1 significantly correlated with AIM and ALS scores (Pearson's $r=0.46$; $p < 0.0001$ and Pearson's $r=0.64$; $p < 0.0001$ respectively).

3.5. Internal consistency

The Cronbach's alpha for the AIM was excellent with a value 0.90. The Cronbach's alpha was also good to excellent for each of the ALS subscales with values comprised between 0.81 and 0.91 and excellent for the ALS total score with an alpha=0.96.

4. Discussion

Using two self reports we have shown that adults ADHD patients displayed emotional dysregulation with a higher mood lability and responsiveness in comparison to control following the same pattern of emotional dysregulation than that in BD patients. Moreover, in comparison to BD patients, ADHD patients exhibited a higher responsiveness score.

To our knowledge, there is no study that has compared adult ADHD patients with BD patients from the perspective of emotional dysregulation (Marwaha et al., 2014). Our results show that emotional dysregulation in ADHD is nearly as important in terms of emotional lability and greater in terms of emotional responsiveness than in BD. In other words, ADHD subjects essentially differ from BD subjects on the perceived emotional intensity, but not on emotional instability.

Two previous studies relied on the ALS for ADHD subjects (Skirrow and Asherson, 2013; Skirrow et al., 2014). In these two studies ADHD subjects showed significantly higher ALS scores than control subjects for three sub-dimensions that were irritability, frustration and anger. In our study, those scores are significantly different for all of the six sub-dimensions. Many studies have previously demonstrated that emotional dysregulation is higher among patients who suffer from ADHD than non ADHD patients (Shaw et al., 2014), including when anxiety or depression comorbidities are absent (Reinherr et al., 2005). Some authors (Baud et al., 2011; Skirrow et al., 2012) have also described similarities between ADHD and mania symptoms, especially in terms of irritability and thymic lability. One study compared the emotional dynamics among children suffering from ADHD without BD comorbidity and among children suffering from ADHD with BD comorbidity. In this study, children with ADHD showed chronic emotional dysregulation, whereas children with BD showed strong emotional dysregulation during thymic episodes, which was reduced during euthymic periods (Rosen and Epstein, 2010). Our study, by using the AIM, shed light on the mechanisms underlying emotional dysregulation in ADHD subjects suggesting that beyond emotional lability, components of emotional responsiveness are at play.

Furthermore, we were able to observe that the presence of axis-1 comorbidities (with the exception of BD) was associated with higher scores on the ALS and AIM scales. Previous studies (Sobanski et al., 2010; Surman et al., 2013; Vidal et al., 2014) have shown similar results, without differentiating between BD and other axis-1 comorbidities. These two scales therefore seem useful to assess the weight of comorbidities in emotional dysregulation among ADHD sufferers. The type of ADHD was not linked to ALS scores, except for the Anger and Depression/Elation sub-dimensions. However, the type of ADHD was associated with AIM scores: the mixed form was more closely linked to high scores at the AIM

than the inattentive or hyperactive-impulsive types. Other studies have also shown that emotional responsiveness is more important in mixed forms in adults (Reinherr et al., 2005) and children (Jensen and Rosen, 2004; Maedgen and Carlson, 2000). This is probably linked to severity of ADHD as in our study subjects with a mixed type had higher severity of ADHD compared to those suffering from inattentive type (data not shown). In this perspective, severity of ADHD was strongly correlated to AIM and ALS scores. Individuals with ADHD and emotional dysregulation were significantly more impaired in peer relationships, family life, occupational attainment, and academic performance than those with ADHD alone (Wehmeier et al., 2010).

It should be noted that gender was not linked to ALS scores, however, it bears a significant relation to higher AIM scores: women had significantly higher scores at the AIM. This data confirms the study of Robison et al. (2008).

The poor emotional regulation strategies for ADHD patients have possible significant consequences in terms of global functioning and quality of life. Interpersonal relations (at work, in social situations or with relatives) are poor, often confrontational, and marked by a large degree of incomprehension. ADHD patients have thus greater professional instability, fewer work perspectives, and a lower financial income than control subjects (Biederman and Faraone, 2006; Doshi et al., 2012; Ginsberg et al., 2014). Regarding family and attachment relations, those difficulties generate higher divorce rates than the general population. Babinski et al. (2011) have also demonstrated that young girls with ADHD have a tendency towards confrontational relationships with their mothers, fewer romantic relations and more depressive symptoms than control subjects. This emotional dysregulation can also lead to high-risk behaviours, possibly through poor management of emotions such as anger, especially while driving: ADHD subjects are more likely of being involved in serious accidents, speeding violations or other infractions of traffic regulations than control subjects (Chang et al., 2014; Fried et al., 2006). Our results thus suggest that emotional dysregulation is stronger in severely affected subjects and should thus be considered when assessing and treating these patients.

Our study highlighted the interest to assess dimensions such as emotional dysregulation in disorders, which have some close clinical characteristics leading to some confusion in differentiating both diagnosis (Wingo and Ghaemi, 2007). To our knowledge and to date, there was no study comparing adult ADHD patients to bipolar disorder ones from the perspective of emotional dysregulation (Marwaha et al., 2014). This approach is also interesting to better understand the mechanisms which could be involved in such disturbances. Disorders with a high emotional dysregulation could have common genes or environmental factors for the determinism of the disease (Baud et al., 2011; Skirrow et al., 2012).

Some studies (Etain et al., 2008; Marwaha et al., 2016) showed that BD type 1 subjects with a history of childhood trauma had higher affective instability than those without such a history. ADHD is considered as a neurodevelopmental disorder with symptoms such as impulsivity and attention deficits often arising early in the life of an individual and sometimes disrupting the crucial link with the caregivers ultimately leading to childhood trauma. Indeed, ADHD subjects report more history childhood maltreatment such as emotional abuses or neglects than controls and this might be one of the reasons why some of these subjects display, as adults, emotional dysregulation (Becker and McCloskey, 2002; Flisher et al., 1997; Prada et al., 2014). In this perspective, emotional dysregulation in adults suffering from ADHD may represent a clinical trace of childhood maltreatment such as it is also evoked in borderline patients. Future researches should focus on this issue and try to link this dimension to biological traces of childhood maltreatment such as epigenetic ones (Perroud et al., 2016).

Neuroimaging studies have found that emotional lability and responsiveness could result from the automatic activity of the amygdala and with the regulation of such activity, relying on a prefrontal network including the lateral prefrontal cortex, the anterior cingulate cortex and the orbitofrontal cortex (Purper Ouakil et al., 2014; Villemonteix et al., 2015). Specifically for ADHD, some authors describe an altered connectivity between regions dedicated to emotional regulation and morphological alterations of the amygdala in children with ADHD (Kasperek et al., 2015). In a study by Posner et al., (2011), subjects suffering from ADHD show a left amygdala hyperactivity that is more important than control subjects. Brotman et al., (2010) have demonstrated that, faced with emotional stimuli, children suffering from ADHD have greater amygdala hyperactivity than children suffering from bipolar disorder. In BD, there are an increased right parahippocampal gyrus and subgenual cingulate gyrus effective connectivity (Houenou et al., 2011) and reduced activation of the parahippocampal gyrus in response to emotional stimuli (Almeida et al., 2009). In this perspective, in a recent review, Broome et al. (2015) suggested that the dysfunction of amygdala as well as connectivity between key brain regions are essential to understand the emotional dysregulation beyond and above diagnostic categories. Better understanding of the neuroanatomical background of emotional dysregulation may shed light on the heterogeneous expression of this dimension (lability vs. responsiveness) in ADHD and BD subjects. Based on these assumptions, ultimately, emotional dysregulation could be considered as a marker or precursor of the disorder and thus be one of the dimension to be looked at during development as an early risk factor for ADHD and BD (Broome et al., 2015).

As suggested by the Research Domain Criteria (RDoC) project, it is necessary to develop transnosographic dimensional studies rather than starting with symptom-based definitions of disorders to better understand mental illnesses (Cuthbert and Insel, 2013). Dimensions are considered in terms of disruptions of the normal-range operation of one specific neural circuit resulting in dysfunctions of varying degrees (Marwaha et al., 2014). As suggested by Broome and al. (2015), emotional dysregulation meets the requirement of RDoC. In our study, we have chosen two main aspects of emotional dysregulation, lability and responsiveness, since these two characteristics allow gathering most of emotional symptoms and could be linked with specific limbic circuit. This approach gives information on the possible overlap between brain dysfunctions between ADHD and BD, explaining the high rate of comorbidities and also the difficulty for differential diagnosis between these two pathologies.

Our study has several limitations. Suspected cases of ADHD in the BD and control groups were derived from the WURS scores. Although there is a good sensitivity/specificity for both scales, we cannot exclude the possibility that ADHD subjects were present in these two populations. Another limit to our study is the impossibility to draw group comparisons in terms of socio-demographic features, except for the socio-professional category. However, we have no strong hypotheses indicating that gender or marital status influence ALS or AIM scores, beyond the pathology itself. The significant number of axis-1 comorbidities is another limitation factor, especially in the ADHD group. With sensitivity analyses, we are able to exclude any comorbidity between ADHD and BD, and can therefore conclude that emotional dysregulation measured among ADHD subjects is not the result of a bipolar component. Another limitation of this study is the fact that we did not control for current mood state and our results should thus be interpreted with this caveat in mind. However, the bipolar subjects were euthymic at the time of inclusion in the study as were controls. This was unfortunately not the case for ADHD subjects and thus some might have been depressed at the time of their assessment. However, it has been shown that emotional reactivity is

normally reduced during depressive episodes, to both positively and negatively valenced stimuli (Bylsma et al., 2008). In this perspective, our findings showing higher emotional dysregulation in ADHD subjects compared to controls and bipolar subjects could have been undermined by not controlling for the current mood state. The retrospective design of our study as well as the self-report assessment of emotional dysregulation are other limitations that need to be raised. Finally, the relative small sample size of our study might hamper some of the results such as the value of Chronbach's alpha. Replication in an independent and bigger sample is thus needed. However, this study is the first to compare emotional dysregulation in adults suffering from ADHD to those suffering from BD and we thus believe that our findings are of importance in a clinical point of view.

In conclusion, although current diagnostic criteria of ADHD do not contain an emotional component, our results suggest that emotional dysregulation is a core feature of ADHD and that increased emotional dysregulation could define a distinct sub-group of ADHD patients with mixed characteristics and with a poorer outcome. This dimension should be systematically assessed in ADHD patients and treatment should target this component.

Acknowledgements and fundings

We thank patients with BD, ADHD and controls who agreed to participate in this study. We thank the staff at the inclusion sites in Paris-Créteil (JR Richard for his assistance concerning the ethical procedures), Bordeaux (L. Zanouy) and Nancy (O. Wajsbrodt-Elgrably and RF. Cohen).

We also would like to thank Sophie Blin, Gérald Bouillault, Jean-Jacques Kunckler, Venus Kaby, Karen Dieben, and Caroline Waeber for their help in recruiting and assessing ADHD patients.

This work was supported by INSERM (Institut National de la Santé et de la Recherche Médicale) AP-HP (Assistance Publique des Hôpitaux de Paris), the ITMO Neurosciences.

Cognitive Sciences, Neurology and Psychiatry, the foundation Fondamental (*fondation de coopération scientifique*). This research was also supported by the Investissements d'Avenir program managed by the ANR under reference ANR-11-IDEX-0004-02.

References

- DIVA 2.0: Entretien diagnostique pour le TDAH chez l'adulte (DIVA). (www.diva-center.eu/Content/Downloads/DIVA_2_FRANCAIS.pdf).
- Adler, L.A., Spencer, T., Faraone, S.V., Kessler, R.C., Howes, M.J., Biederman, J., Seznik, K., 2006. Validity of pilot adult ADHD Self- Report Scale (ASRS) to rate adult ADHD symptoms. *Ann. Clin. Psychiatry* 18, 145–148.
- Almeida, J.R., Mechelli, A., Hassel, S., Versace, A., Kupfer, D.J., Phillips, M.L., 2009. Abnormally increased effective connectivity between parahippocampal gyrus and ventromedial prefrontal regions during emotion labeling in bipolar disorder. *Psychiatry Res.* 174, 195–201.
- American Psychiatric Association, 2000. *DSM-IV-TR: diagnostic and statistical manual of mental health disorders*, 4th ed. American Psychiatric Association, Washington, DC, Text revision ed.
- Babinski, D.E., Pelham Jr., W.E., Molina, B.S., Gnagy, E.M., Waschbusch, D.A., Yu, J., Maclean, M.G., Wymbs, B.T., Sibley, M.H., Biswas, A., Robb, J.A., Karch, K.M., 2011. Late adolescent and young adult outcomes of girls diagnosed with ADHD in childhood: an exploratory investigation. *J. Atten. Disord.* 15, 204–214.
- Baud, P., Perroud, N., Aubry, J.M., 2011. Bipolar disorder and attention deficit/hyperactivity disorder in adults: differential diagnosis or comorbidity. *Rev. Med. Suisse* 7, 1219–1222.
- Bech, P., Rafaelsen, O.J., Kramp, P., Bolwig, T.G., 1978. The mania rating scale: scale construction and inter-observer agreement. *Neuropharmacology* 17, 430–431.
- Becker, K.B., McCloskey, L.A., 2002. Attention and conduct problems in children exposed to family violence. *Am. J. Orthopsychiatry* 72, 83–91.
- Biederman, J., Faraone, S.V., 2006. The effects of attention-deficit/hyperactivity disorder on employment and household income. *MedGenMed* 8, 12.
- Broome, M.R., He, Z., Iftikhar, M., Eyden, J., Marwaha, S., 2015. Neurobiological and behavioural studies of affective instability in clinical populations: a systematic review. *Neurosci. Biobehav. Rev.* 51, 243–254.
- Brotman, M.A., Rich, B.A., Guyer, A.E., Lunsford, J.R., Horsey, S.E., Reising, M.M., Thomas, L.A., Fromm, S.J., Towbin, K., Pine, D.S., Leibenluft, E., 2010. Amygdala activation during emotion processing of neutral faces in children with severe mood dysregulation versus ADHD or bipolar disorder. *Am. J. Psychiatry* 167, 61–69.
- Bylsma, L.M., Morris, B.H., Rottenberg, J., 2008. A meta-analysis of emotional reactivity in major depressive disorder. *Clin. Psychol. Rev.* 28, 676–691.

- Chang, Z., Lichtenstein, P., D'Onofrio, B.M., Sjolander, A., Larsson, H., 2014. Serious transport accidents in adults with attention-deficit/hyperactivity disorder and the effect of medication: a population-based study. *JAMA Psychiatry* 71, 319–325.
- Cuthbert, B.N., Insel, T.R., 2013. Toward the future of psychiatric diagnosis: the seven pillars of RDoC. *BMC Med.* 11, 126.
- Doshi, J.A., Hodgkins, P., Kahle, J., Sikirica, V., Cangelosi, M.J., Setyawan, J., Erder, M.H., Neumann, P.J., 2012. Economic impact of childhood and adult attention-deficit/hyperactivity disorder in the United States. *J. Am. Acad. Child Adolesc. Psychiatry* 51, 990–1002, e1002.
- Etain, B., Henry, C., Bellivier, F., Mathieu, F., Leboyer, M., 2008. Beyond genetics: childhood affective trauma in bipolar disorder. *Bipolar Disord.* 10, 867–876.
- Fayyad, J., De Graaf, R., Kessler, R., Alonso, J., Angermeyer, M., Demetsky, K., De Girolamo, G., Haro, J.M., Karam, E.G., Lara, C., Lepine, J.P., Ormel, J., Posada-Villa, J., Zaslavsky, A.M., Jin, R., 2007. Cross-national prevalence and correlates of adult attention-deficit hyperactivity disorder. *Br. J. Psychiatry* 190, 402–409.
- Flett, G.L., Bator, C., Blankstein, K.R., 1988. Affect intensity and components of emotional style. *Person. Individ. Differ.* 9, 185–186.
- Flisher, A.J., Kramer, R.A., Hoven, C.W., Greenwald, S., Alegria, M., Bird, H.R., Canino, G., Connell, R., Moore, R.E., 1997. Psychosocial characteristics of physically abused children and adolescents. *J. Am. Acad. Child Adolesc. Psychiatry* 36, 123–131.
- Fried, R., Petty, C.R., Surman, C.B., Reimer, B., Aleardi, M., Martin, J.M., Coughlin, J.F., Biederman, J., 2006. Characterizing impaired driving in adults with attention-deficit/hyperactivity disorder: a controlled study. *J. Clin. Psychiatry* 67, 567–574.
- Ginsberg, Y., Quintero, J., Anand, E., Casillas, M., Upadhyaya, H.P., 2014. Under-diagnosis of attention-deficit/hyperactivity disorder in adult patients: a review of the literature. *Prim. Care Companion CNS Disord.*, 16.
- Guile, J.M., Chapdelaine, C., Desrosiers, L., Cornez, C., Bouvier, H., Breton, J.J., 2009. Preliminary reliability study of the affective lability scale adapted for adolescents in a francophone clinical population. *J. Can. Acad. Child Adolesc. Psychiatry* 18, 293–306.
- Harvey, P.D., Greenberg, B.R., Serper, M.R., 1989. The affective lability scales: development, reliability, and validity. *J. Clin. Psychol.* 45, 786–793.
- Henry, C., Phillips, M., Leibenluft, E., M'Bailara, K., Houenou, J., Leboyer, M., 2012. Emotional dysfunction as a marker of bipolar disorders. *Front. Biosci.* 4, 2722–2730.
- Henry, C., Van den Bulke, D., Bellivier, F., Roy, I., Swendsen, J., M'Bailara, K., Siever, L.J., Leboyer, M., 2008. Affective lability and affect intensity as core dimensions of bipolar disorders during euthymic period. *Psychiatry Res.* 159, 1–6.
- Houenou, J., Frommberger, J., Carde, S., Glasbrenner, M., Diener, C., Leboyer, M., Wessa, M., 2011. Neuroimaging-based markers of bipolar disorder: evidence from two meta-analyses. *J. Affect. Disord.* 132, 344–355.
- Jensen, S.A., Rosen, L.A., 2004. Emotional reactivity in children with attention-deficit/hyperactivity disorder. *J. Atten. Disord.* 8, 53–61.
- Kasperek, T., Theiner, P., Filova, A., 2015. Neurobiology of ADHD from childhood to adulthood: findings of imaging methods. *J. Atten. Disord.* 19, 931–943.
- Kessler, R.C., Adler, L., Ames, M., Demler, O., Faraone, S., Hiripi, E., Howes, M.J., Jin, R., Seznik, K., Spencer, T., Ustun, T.B., Walters, E.E., 2005. The world health organization adult ADHD self-report scale (ASRS): a short screening scale for use in the general population. *Psychol. Med.* 35, 245–256.
- Kessler, R.C., Adler, L., Barkley, R., Biederman, J., Conners, C.K., Demler, O., Faraone, S.V., Greenhill, L.L., Howes, M.J., Seznik, 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.
- Larsen, R.J., Diener, E., 1985. A multitrait-multimethod examination of affect structure: hedonic level and emotional intensity. *Person. Individ. Differ.* 6, 631–636.
- Larsen, R.J., Diener, E., 1986. Affective intensity and reactions to daily life events. *J. Person. Soc. Psychol.* 51, 803–814.
- M'Bailara, K., Demotes-Mainard, J., Swendsen, J., Mathieu, F., Leboyer, M., Henry, C., 2009. Emotional hyper-reactivity in normothymic bipolar patients. *Bipolar Disord.* 11, 63–69.
- Maedgen, J.W., Carlson, C.L., 2000. Social functioning and emotional regulation in the attention deficit hyperactivity disorder subtypes. *J. Clin. Child Psychol.* 29, 30–42.
- Marwaha, S., Gordon-Smith, K., Broome, M., Briley, P.M., Perry, A., Forty, L., Craddock, N., Jones, I., Jones, L., 2016. Affective instability, childhood trauma and major affective disorders. *J. Affect. Disord.* 190, 764–771.
- Marwaha, S., He, Z., Broome, M., Singh, S.P., Scott, J., Eyden, J., Wolke, D., 2014. How is affective instability defined and measured? A systematic review. *Psychol. Med.* 44, 1793–1808.
- Mathieu, F., Etain, B., Daban, C., Raymond, R., Raust, A., Cochet, B., Gard, S., M'Bailara, K., Desage, A., Kahn, J.P., Wajsbrodt-Elgrabi, O., Cohen, R.F., Azorin, J.M., Leboyer, M., Bellivier, F., Scott, J., Henry, C., 2014. Affect intensity measure in bipolar disorders: a multidimensional approach. *J. Affect. Disord.* 157, 8–13.
- Montgomery, S.A., Asberg, M., 1979. A new depression scale designed to be sensitive to change. *Br. J. Psychiatry* 134, 382–389.
- Nurnberger Jr., J.I., Blehar, M.C., Kaufmann, C.A., York-Cooler, C., Simpson, S.G., Harkavy-Friedman, J., Severe, J.B., Malaspina, D., Reich, T., 1994. Diagnostic interview for genetic studies. Rationale, unique features, and training. NIMH Genetics Initiative. *Arch. Gen. Psychiatry* 51, 849–859, discussion 863–844.
- Oliver, M.N.I., Simons, J.S., 2004. The affective lability scales: development of a short form measure. *Person. Individ. Differ.* 37, 1279–1288.
- Perroud, N., Cordera, P., Zimmermann, J., Michalopoulos, G., Bancila, V., Prada, P., Dayer, A., Aubry, J.M., 2014. Comorbidity between attention deficit hyperactivity disorder (ADHD) and bipolar disorder in a specialized mood disorders outpatient clinic. *J. Affect. Disord.* 168, 161–166.
- Perroud, N., Zewdie, S., Stenz, L., Adouan, W., Bavamian, S., Prada, P., Nicastro, R., Hasler, R., Nallet, A., Piguet, C., Paoloni-Giacobino, A., Aubry, J.M., Dayer, A., 2016. Methylation of serotonin receptor 3A in ADHD, borderline personality, and bipolar disorders: link with severity of the disorders and childhood maltreatment. *Depression Anxiety* 33, 45–55.
- Philipsen, A., Limberger, M.F., Lieb, K., Feige, B., Kleindienst, N., Ebner-Priemer, U., Barth, J., Schmahl, C., Bohus, M., 2008. Attention-deficit hyperactivity disorder as a potentially aggravating factor in borderline personality disorder. *Br. J. Psychiatry* 192, 118–123.
- Posner, J., Nagel, B.J., Maia, T.V., Mechling, A., Oh, M., Wang, Z., Peterson, B.S., 2011. Abnormal amygdala activation and connectivity in adolescents with attention-deficit/hyperactivity disorder. *J. Am. Acad. Child Adolesc. Psychiatry* 50, 828–837, e823.
- Prada, P., Hasler, R., Baud, P., Bednarz, G., Ardu, S., Krejci, I., Nicastro, R., Aubry, J.M., Perroud, N., 2014. Distinguishing borderline personality disorder from adult attention deficit/hyperactivity disorder: a clinical and dimensional perspective. *Psychiatry Res.* 217, 107–114.
- Preisig, M., Fenton, B.T., Matthey, M.L., Berney, A., Ferrero, F., 1999. Diagnostic interview for genetic studies (DIGS): inter-rater and test-retest reliability of the French version. *Eur. Arch. Psychiatry Clin. Neurosci.* 249, 174–179.
- Purper Ouakil, D., Vacher, C., Villemonteix, T., 2014. Trouble déficit d'attention/ hyperactivité(TDA/H) et émotions: de la labilité émotionnelle au trouble bipolaire. *Ann. Med. Psychiatr.* 172, 309–312.
- Reimherr, F.W., Marchant, B.K., Strong, R.E., Hedges, D.W., Adler, L., Spencer, T.J., West, S.A., Soni, P., 2005. Emotional dysregulation in adult ADHD and response to atomoxetine. *Biol. Psychiatry* 58, 125–131.
- Robison, R.J., Reimherr, F.W., Marchant, B.K., Faraone, S.V., Adler, L.A., West, S.A., 2008. Gender differences in 2 clinical trials of adults with attention-deficit/hyperactivity disorder: a retrospective data analysis. *J. Clin. Psychiatry* 69, 213–221.
- Romo, L., Legauffre, C., Mille, S., Cheze, N., Fougeres, A.L., Marquez, S., Excoffier, A., Dubertret, C., Ades, J., 2010. Psychometric properties of the French version of the Wender Utah rating scale and Brown's Attention Deficit Disorders Scale for adults. *Encephale* 36, 380–389.
- Rosen, P.J., Epstein, J.N., 2010. A pilot study of ecological momentary assessment of emotion dysregulation in children. *J. ADHD Relat. Disord.* 1, 39–52.
- Shaw, P., Stringaris, A., Nigg, J., Leibenluft, E., 2014. Emotion dysregulation in attention deficit hyperactivity disorder. *Am. J. Psychiatry* 171, 276–293.
- Simon, V., Czobor, P., Balint, S., Meszaros, A., Bitter, I., 2009. Prevalence and correlates of adult attention-deficit hyperactivity disorder: meta-analysis. *Br. J. Psychiatry* 194, 204–211.
- 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., Banaschewski, T., Asherson, P., Buitelaar, J., Chen, W., Franke, B., Holtmann, M., Krumm, B., Sergeant, J., Sonuga-Barke, E., Stringaris, A., Taylor, E., Anney, R., Epstein, R.P., Gill, M., Miranda, A., Mulas, F., Oades, R.D., Roeyers, H., Rothenberger, A., Steinhausen, H.C., Faraone, S.V., 2010. Emotional lability in children and adolescents with attention deficit/hyperactivity disorder (ADHD): clinical correlates and familial prevalence. *J. Child. Psychol. Psychiatry* 51, 915–923.
- Statacorp, 2013. Stata Statistical Software: release 13. StataCorp LP, College station, TX.
- Surman, C.B., Biederman, J., Spencer, T., Miller, C.A., McDermott, K.M., Faraone, S.V., 2013. Understanding deficient emotional self-regulation in adults with attention deficit hyperactivity disorder: a controlled study. *Atten. Defict Hyperact. Disord.* 5, 273–281.
- Van Rheenen, T.E., Murray, G., Rossell, S.L., 2015. Emotion regulation in bipolar disorder: profile and utility in predicting trait mania and depression propensity. *Psychiatry Res.* 225, 425–432.
- 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.
- Villemonteix, T., Purper-Ouakil, D., Romo, L., 2015. La dysrégulation émotionnelle est-elle une des composantes du trouble déficit d'attention/hyperactivité ? *Encephale* 41, 108–114.
- Ward, M.F., Wender, P.H., Reimherr, F.W., 1993. The Wender Utah Rating Scale: an aid in the retrospective diagnosis of childhood attention deficit hyperactivity disorder. *Am. J. Psychiatry* 150, 885–890.
- Wehmeier, P.M., Schacht, A., Barkley, R.A., 2010. Social and emotional impairment in children and adolescents with ADHD and the impact on quality of life. *J. Adolesc. Health* 46, 209–217.
- 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.