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Cognitive functioning in bipolar disorder

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Bipolar disorders are severe illnesses, chronic and lifelong. In Europe, many psychiatrists would wait until the second or even the third episode before they prescribe prophylactic treatment. Interruption of prophylactic pharmacotherapy is more the rule than the exception (Maj, 1999), and even in the context of sophisticated psychoeducational programmes the rate of non-compliance is close to 40% (Colom et al., 2000).

Bipolar disorders are associated with high rates of recurrences and impairment: treatment, therefore, has to be early and lifelong. Impairment and suicide risk are not exclusive of the most severe forms of the disorder: bipolar II and other apparently milder clinical presentations may indeed carry on high relapse rates and disability. One important source of impairment is cognitive dysfunction: contrary to Kraepelin's belief, many bipolar patients show neuropsychological disturbances which may be associated to poor occupational and social functioning.

CHRONIC ILLNESS AND Milder FORMS

Since there is a complete chapter and several commentaries on therapies for bipolar disorder, we will just put emphasis on how important it is to share this information with our patients. The younger ones are generally very reluctant to admit the chronicity of their illness and to be compliant with pharmacotherapy for long periods. Denial is a common problem among bipolar patients, but the attitude of the treating physician is crucial to help the patient deal with it. Non-adherence is common in the management of bipolar disorder (Colom et al., 2005). In this regard, psychoeducation is an efficacious intervention to prevent recurrences in pharmacologically treated patients (Colom et al., 2003).

Psychoeducation has demonstrated to reduce the number of relapsed patients and the number of recurrences per patient, and increased the time to manic, hypomanic, mixed and depressed recurrences (Colom et al., 2003). The role of the family is essential as well. The family should be involved in the therapeutic process to help the patient understand and work actively towards achieving complete remission and effective prevention of new episodes (Reinares et al., 2004). Moreover, psychoeducational intervention on caregivers of bipolar patients may improve the caregiver's knowledge of the illness and reduce their distress as well as altered beliefs regarding disruptions that may be due to the illness. Overall, the treatment should be vigorous and sustained, in order to achieve not only syndromal recovery, but functional recovery and prevention of recurrences (Tohen et al., 2000).

Impairment is not only a consequence of psychosis, mania or hospitalizations. Many patients with bipolar II subtype suffer the consequences of an extremely high recurrence rate. Several studies have reported that bipolar II disorder is less severe than bipolar I with regard to symptom intensity, but is more severe with respect to episode frequency (Vieta et al., 1997). The incidence of rapid cycling is, consistently, higher in bipolar II disorder (Akiskal, 1996). Comorbidity rates, often a supplementary source of impairment, are also higher (Vieta et al., 2000), and so is suicide risk (Rihmer et al., 1990). Since underdiagnosis and misdiagnosis are more the rule than the exception in bipolar II disorder (Akiskal, 1996), it is unclear whether these high relapse, suicide, and comorbidity rates are related to inadequate treatment. The regular use of mood-stabilisers and psychoeducation may reverse the higher cyclicality and suicidality of bipolar II compared to bipolar I (Vieta et al., 1997; 1999; Colom et al., 2003).

COGNITIVE IMPAIRMENT IS AN ISSUE IN BIPOLAR DISORDER

Cognitive impairment has been believed to make a big difference in the outcome of schizophrenia versus bipolar disorder. However, there is a growing body of evidence that

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about one third of bipolar patients show persistent and clinically significant neuropsychological disturbances. Compared to schizophrenic patients, cognitive impairment is observed in a lesser degree in bipolar patients. Nevertheless, the pattern of cognitive dysfunctions is similar in both groups (Martínez-Arán et al., 2002a; Balanza-Martínez et al., 2005; Daban et al., 2006) and seem to persist in the long-term (Balanza-Martínez et al., 2005). Recently, Tabares-Seisdedos et al. (2006) observed that mutations in genes involved in the molecular diagnosis of lissecephaly and neuronal migration alterations seem to predict the severity of prefrontal cognitive deficits in schizophrenic and bipolar patients, regardless the diagnosis. In bipolar disorder, cognitive dysfunctions may involve changes in the fluency of thought, verbal memory, sustained and selective attention and executive functions (Martínez-Arán et al., 2000; Daban et al., 2006). Bipolar II patients also have cognitive deficits, showing an intermediate level of performance between bipolar I patients and healthy controls (Torrent et al., 2006). Cognitive disturbances, and especially those related to verbal memory, may have a great impact on occupational and social functioning, and on quality of life as well (Martínez-Arán et al., 2004a,b, 2007). Probably, we can find different subgroups regarding the severity of cognitive impairment in bipolar patients. In this regard, bipolar patients with previous history of bipolar symptoms seem to be more impaired than patients without such a history on verbal memory tasks (Martínez-Arán et al., in press). The negative impact of cognitive deficits on the functional outcome of the patients should be further studied (fig. 1). There is some evidence that the presence of subthreshold symptoms is closely related to cognitive disability (Martínez-Arán et al., 2002a,b). This leads again to the need of lifelong effective treatment and achievement of full remission as the main goal of therapy. Clinicians should take into account cognitive complaints in order to detect, early, objective cognitive impairment (Martínez-Arán et al., 2005). Cognitive impairment

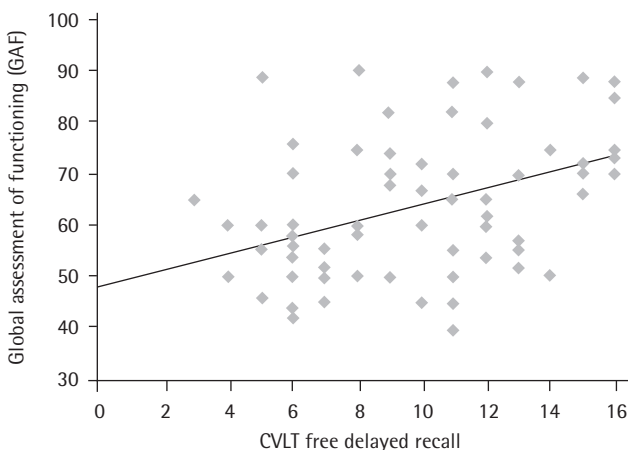


Figura 2 Verbal memory and functional outcome. *n* = 77 euthymic bipolar patients. Martínez-Arán et al., 2007.

should be considered more widely with regard to the long-term management of bipolar disorder. This may mean selecting combination therapies suitable for long-term prophylaxis, taking into account tolerability, side effects and interactions. On the other hand, cognitive remediation may be useful in the treatment of cognitive dysfunctions in bipolar disorder.

REFERENCES

1. Akiskal HS. The prevalent clinical spectrum of bipolar disorders: beyond DSM-IV. *J Clin Psychopharmacol* 1996;16(Suppl. 1): 4-14.
2. Balanza-Martínez V, Tabares-Seisdedos R, Selva-Vera G, Martínez-Arán A, Torrent C, Salazar-Fraile J, et al. Persistent cognitive dysfunctions in bipolar I disorder and schizophrenic patients: a 3 year follow-up study. *Psychother Psychosom* 2005;74:113-9.
3. Colom F, Vieta E, Martínez-Arán A, Reinares M, Goikolea JM, Benabarre A, et al. A randomized trial on the efficacy of group psychoeducation in the prophylaxis of recurrences in bipolar patients whose disease is in remission. *Arch Gen Psychiatry* 2003;60:402-7.
4. Colom F, Vieta E, Tacchi MJ, Sánchez-Moreno J, Scott J. Identifying and improving non-adherence in bipolar disorders. *Bipolar Disord* 2005;7(Suppl. 5):24-31.
5. Colom F, Vieta E, Corbella B, Martínez-Arán A, Reinares M, Benabarre A, et al. Clinical factors associated to treatment non-compliance in euthymic bipolar patients. *J Clin Psychiatry* 2000; 61:549-55.
6. Daban C, Martínez-Arán A, Torrent C, Sánchez-Moreno J, Goikolea JM, Benabarre A, et al. Cognitive functioning in bipolar patients receiving lamotrigine: preliminary results. *J Clin Psychopharmacol* 2006;26:178-181
7. Daban C, Martínez-Arán A, Torrent C, Tabares-Seisdedos R, Balanza-Martínez V, Salazar-Fraile J, et al. Specificity of cognitive deficits in bipolar disorder versus schizophrenia. A systematic review. *Psychother Psychosom* 2006;75:72-84.
8. Maj M. Lithium prophylaxis of bipolar disorder in ordinary clinical conditions: patterns of long-term outcome. In: Goldberg JF, Harrow H, editors. *Bipolar disorders: clinical course and outcome*. Washington: American Psychiatric Press, 1999; p. 21-37.
9. Martínez-Arán A, Penades R, Vieta E, Colom F, Reinares M, Benabarre A, et al. Executive function in patients with remitted bipolar disorder and schizophrenia and its relationship with functional outcome. *Psychother Psychosom* 2002a;71:39-46.
10. Martínez-Arán A, Vieta E, Colom F, Reinares M, Benabarre A, Torrent C, et al. Neuropsychological performance in depressed and euthymic bipolar patients. *Neuropsychobiology* 2002b;46: 16-21.
11. Martínez-Arán A, Vieta E, Colom F, Torrent C, Reinares M, Goikolea JM, et al. Do cognitive complaints in euthymic bipolar patients reflect objective cognitive impairment? *Psychother Psychosom* 2005;74:295-302.
12. Martínez-Arán A, Vieta E, Colom F, Torrent C, Sánchez-Moreno J, Reinares M, et al. Cognitive impairment in euthymic bipolar patients: implications for clinical and functional outcome. *Bipolar Disord* 2004b;6:224-32.

13. Martínez-Arán A, Vieta E, Reinares M, Colom F, Torrent C, Sánchez-Moreno J, et al. Cognitive function across manic or hypomanic, depressed, and euthymic states in bipolar disorder. *Am J Psychiatry* 2004a;161:262-70.
14. Martínez-Arán A, Vieta E, Torrent C, Sánchez-Moreno J, Goikolea JM, Salamero M, et al. Functional outcome in bipolar disorder: the role of clinical and cognitive factors. *Bipolar Disord* 2007;9:103-13.
15. Martínez-Arán A, Torrent C, Tabares-Seisdedos R, Salamero M, Daban C, Balanza-Martínez V, et al. Neurocognitive impairment in bipolar patients with and without history of psychosis. *J Clin Psychiatry*, in press.
16. Martínez-Arán A, Vieta E, Colom F, Benabarre A, Reinares M, Gastó C, et al. Cognitive dysfunctions in bipolar disorder: evidence of neuropsychological disturbances. *Psychother Psychosom* 2000;69:2-18.
17. Reinares M, Vieta E, Colom F, Martínez-Arán A, Torrent C, Comes M, et al. Impact of a psychoeducational family intervention on caregivers of stabilized bipolar patients. *Psychother Psychosom* 2004;73:312-9.
18. Rihmer Z, Barsi J, Arato M, Demeter E. Suicide in subtypes of primary major depression. *J Affect Disord* 1990;18:221-5.
19. Tabares-Seisdedos R, Escámez T, Martínez-Giménez JA, Balanza V, Salazar J, Selva G, et al. Variations in genes regulating neuronal migration predict reduced prefrontal cognition in schizophrenia and bipolar subjects from mediterranean Spain: a preliminary study. *Neuroscience* 2006;139:1289-300.
20. Tohen M, Hennen J, Zarate CM, Baldessarini RJ, Strakowski SM, Stoll AL, et al. Two-year syndromal and functional recovery in 219 cases of first-episode major affective disorder with psychotic features. *Am J Psychiatry* 2000;157:220-8.
21. Torrent C, Martínez-Arán A, Daban C, Sánchez-Moreno J, Comes M, Goikolea JM, et al. Cognitive impairment in bipolar II disorder. *Br J Psychiatry* 2006;189:254-9.
22. Vieta E. Diagnosis and classification of psychiatric disorders. In: Sussman N, editor. *Anticonvulsants in psychiatry. Round table series n.º 64*. London: The Royal Society of Medicine Press, 1999; p. 3-8.
23. Vieta E, Benabarre A, Colom F, Gastó C, Nieto E, Otero A, et al. Suicidal behavior in bipolar I and bipolar II disorder. *J Nerv Ment Dis* 1997;185:407-9.
24. Vieta E, Colom F, Martínez-Arán A, Benabarre A, Reinares M, Gastó C. Bipolar II disorder and comorbidity. *Compr Psychiatry* 2000;41:339-43.
25. Vieta E, Gastó C, Otero A, Nieto E, Vallejo J. Differential features between bipolar I and bipolar II disorder. *Compr Psychiatry* 1997;38:98-101.