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# COULD BIPOLARITY BE INFLUENCED BY STRESSFUL LIFE EVENTS? A REFLECTION BASED ON A CASE REPORT

**Alice Bries, Christine Reynaert & Nicolas Zdanowicz**

*Medicine Faculty, Université Catholique de Louvain, Psychopathology and Psychosomatic Unit*
*Hospital Universitary Center Mont-Godinne, Yvoir, Belgium*

## *SUMMARY*

***Introduction:*** *Bipolar disorder (BPD) has over the last fifteen years been considered as a biological disease with genetic bases, possibly triggered by stress factors. On the basis of a clinical case, we will question this theory.*

***Subject and methods:*** *Mrs. X, a patient with a history of domestic violence, has two manic episodes that corresponded with conjugal difficulties. This would lead us to believe that stressful life events may have triggered the onset and the relapse of the illness of our patient. To confirm this , we made a literature review with the keywords bipolar disorder, stress, family functioning and domestic violence on three databases: PubMed, PsycInfo and PsycArticles.*

***Results:*** *Studies show that BPD has likely genetic and biological origins. It is also established in the literature that stressful life events influence the course of the disease, with for example the "Kindling" effect. However, there is very few data regarding the precise nature of these events. It is also established that the family interactions are affected by the BPD. Nonetheless, little is known about the influence of the family's interactions on the onset of the disease.*

***Conclusions:*** *Our clinical case raises the question of the stress factors that may influence the onset and the course of BPD. It also raises the question of the possible link between BPD and domestic violence and the question of theeffect of stressors on the genetic and biological factors, introducing a more psychodynamic view of BPD. Further research on this subject should allow us to expand the treatment to more comprehensive care.*

***Key words:*** *bipolar disorder - stress factor - family functioning - domestic violence*

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## INTRODUCTION

Over the last fifteen years, researchers have been essentially focused on the biological aspects of bipolar disorders, such as genetic predisposition or inflammatory factors. In our clinical practice, we met a patient with manic episodes that seemed to be triggered by life events. By searching in the literature, we found that the relation between stress and manic or depressive episodes among the bipolar patients had already been observed by Kraepelin (1921). Several studies conducted in the past two decades have focused on the environmental factors playing a role in the precipitation of mania or depression among the bipolar population and have strongly documented existing associations. For example, in a large literature review, Johnson and Roberts indicated that life stress appears to exert an important effect on the course of bipolar illness (Johnson & Roberts 1995). In an experimental study, Milkowitz and Goldstein demonstrated that high expressed emotion (critical, hostile, or emotionally over-involved attitudes) among the relatives of patients suffering from bipolar disease are associated with high rates of patients sufferring from a relapse (Miklowitz et al. 1988). Others researches seem to confirm an existing link between stress and the bipolar disorder. However, varying methodology of these studies and their varying results make proper conclusions difficult to establish. Furthermore, the nature of these psychosocial factors remains unclear. In the light of all these considerations, we will describe our clinical case. Then, we will glance through the findings that may be relevant in understanding our case to finally discuss our patient and her story and focus on possible implications for further research.

## SUBJECT AND METHODS

### Subject: a clinical vignette

Mrs. X is a patient without any personal psychiatric history. Regarding her family, she has no psychiatric history by the side of her mother; the psychiatric history of her father's ancestors is unclear. Mrs. X got married at 21, and has three children and two grandchildren in good health. She reports a conflictual relationship with her husband for the past twenty years and describes amongst other things, episodes of physical violence and sexual assaults by her husband. She tried several times to break-up with him but never succeeded. At the time we met her; Mrs. X was 49 and seemed fully integrated in society. She came into our consulting service for hypomanic symptoms developed soon after her husband had left for another woman. We followed her progress as an outpatient at a frequency of once or twice a month, we also prescribed her medication (Olanzapine, 5 to 10 milligram a day depending on her symptoms) and six month later, Mrs. X was clear of any hypomanic, manic or depressive symptoms. Because of the diagnostic uncertainty of bipolar disorder (no personal or family history of psychiatric disorder, symptoms limited to hypomania) we did not initiate thymoregulators at that

time. In April 2013, a year and a half later, Mrs. X was admitted to our service with clear evidence of mania according to DSM IV-tr. Because of the severity of her condition, hospitalization became rapidly necessary. During our interviews with Mrs. X, it turned out that her husband had come back home a few weeks before her relapse and that the couple had decided to get back together again. Currently, this patient is receiving thymoregulator medication.

We found this case interesting for several reasons. Firstly, the presentation of the bipolar disease of Mrs. X is uncommon, because of the late onset and because of the lack of psychiatric family history. Secondly, the existence of stress factors is well documented in this case. Finally, the relapse occurred soon after a stressful life event. This clinical story leads us to ask ourselves about a potential link between the bipolar disorder and domestic violence, and, in a larger way, between the disease and stressful life events. We note that we have observed in our service a few other patients with a similar history of bipolar disorder and domestic violence.

### Methods

We performed a systematic review with two methods to obtain relevant studies. First, we searched the three Internet-based databases PubMed, PsycInfo and PsycArticles with the term bipolar disorder (a/c) combined with each of the following terms: stress (a/c), family functioning and domestic violence's. We placed a date limitation (all the articles published over the last twenty years i.e. after 1994) and a limitation for journal articles. We selected all the relevant articles bytheir titles in the databases, choosing those that could be relevant to our subject. Second, we searched relevant articles in reference lists from collected papers. We have to remember that the goalof this article is not to do a extended literature review; we are trying to explore new leads about the bipolar disorder in order to raise new questions about its relation with stressful live events.

## RESULTS

For the purposes of clarity, we will distinguish three major subjects in our findings: the role ofstressful life events in the onset and the relapse in the bipolar disorder, the links between biological theories, and the family way of functioning.

### Stressful life events and bipolar disorder

Regarding the possible link between stressful life events and bipolar disorder, several studies were performed.

In a large literature review, Johnson and Roberts demonstrated in 1995 that bipolar patients appear more likely to experience stressful life events before episodes than non-psychiatric controls and that life events appear to be more prevalent before relapse in bipolar patients, as opposed to other time periods in their life (see Johnson & Roberts 1995, for a review). However, they revealed a large variety of methodological issues in the broader literature. Moreover, certain studies did not confirm the hypothesis that stressful events may influence the bipolar disease (Chung et al. 1986, McPherson et al. 1993). Johnson and Roberts noticed also that the role of stressor severity, the timing and the type of event needed to be clarified. In others studies a link was found between stressful life events and recurrence of both manic or depressive episodes among bipolar patients (Hammen & Gitlin 1997, Malkoff-Schwartz 1998, Reilly-Harrington et al. 1999, Beyer et al. 2008, Hosang et al. 2012). Some authors found also more stressful events before the first episode than before relapses (Hammen et al. 1997, Horesh & Iancu 2010), but the causal link remains difficult to establish in particular because many stressful events experienced by bipolar patients could be a consequence of their illness or prodromal symptoms rather than a cause (Johnson & Robert 1995, Hosang et al. 2012).

Some researchers have focused on childhood adversity to predict the course of the bipolar disease. Post and his colleagues demonstrated that patient with bipolar illness who have a history of early extreme adversity, versus those without, show an earlier onset of illness, faster cycling frequencies, increased suicidality, more Axis I and Axis II comorbidities, and longer illness in more than 2 years of prospective follow-up (Post et al. 2001). These findings are consistent with those of Dienes and her colleagues in 2006 (Dienes et al. 2006), but they were not fully confirmed in some others studies, such as the one of Henry in 2002 that suggest that childhood exposure to adversity may hasten the onset of the illness but that individuals with a history of adversity appeared later "steeled" to the effects of stress (Henry 2002). Wals and her colleagues also demonstrated in a sample of bipolar offspring that the association between stressful life events and the onset of mood disorders disappeared after adjustment of prior anxious/depressive symptoms, demonstrating that prior anxious/depressive symptoms seem to increase the risk for both occurrence of dependent stressful life events and mood disorders onset or recurrence (Wals et al. 2005).

Others authors have compared patients with and without family/genetic history of affective illness regarding stressful life events. They noticed that patients with high constitutional vulnerability have an earlier age of onset and need less stress factors to become ill (Johnson et al. 2000).

Finally, some researchers examined the role of life events separately in mania and depression. In 2000 and 2008, Johnson found in two separate studies that goal attainment life events significantly increase manic but not depressive symptoms over time (Johnson at al. 2000, 2008). On the contrary, Meier found in 2008 that expressed emotion and chronic stress were a polarity-

specific predictor of depressive recurrence, although episodic stress was a predictor of both manic and depressive recurrence (Meier 2008).

In summary, several studies found an existing link between stressful life events and the onset and the course of the bipolar disorder, especially among patients without genetic vulnerability. It is however difficult to establish a formal link of causality because of the large variability of methodology of studies and their various results, but also because stressful events may be a consequence, rather than a cause, of the illness. Some authors found a polarity-specific interaction.

## The links with biological theories

We choose to introduce here two theories integrating biological and psychosocial findings, but have to bear in mind that there are other biopsychosocial theories of bipolar disorder.

Firstly, Post and his colleagues introduced in 1984 the concepts of behavioral sensitization and the "Kindling" effect to construct a model where environmental events might be translated into biological processes (Post et al. 1984, 1986, Post 1992). Behavioral sensitization is based on the principle that repeated and intermittent exposure to psychomotor stimulants increase vulnerability to their effects, even at progressively smaller levels of ingestion. According to Post, in bipolar disease, both environmental agents such as life stress and affective episodes could become conditioned at a physiological level, with as a finality "episodes triggering episodes". The Kindling effect is analogous to behavioral sensitization at an electrophysiological level. Neurophysiologists have indeed demonstrated that repeated and intermittent electrophysiological stimulation to certain brain regions could induce seizures and that those, with repetition, could become spontaneous over time. In such a model, in the bipolar disease, the events needed to induce the onset of the disease should be more stressful than those before a relapse. Some studies have found results congruent with this theory (Hammen et al. 1997, Johnson et al. 2000, Horesh & Iancu 2010, Bender 2013), some other studies in different settings did not find the same results (Hlastala et al. 2000, Henry 2002).

The second biopsychosocial view we would like to introduce here is based on Depue's theory which link a dysregulation of the BAS (behavioral activation system) to mania (Depue et al. 1987, Depue & Iacono 1989). This came from the fact that Depue and his colleagues observed that manic symptoms where quite similar to the BAS-regulated behaviors, such as inflated self-esteem, decreased need for sleep or flight of ideas and increased talkativeness. We would expect mania to be triggered by events that involved BAS activity if there is a link, namely in the cues of reward. Once more, some studies seem to confirm this theory by finding a link between specifically goal-attainment life events, rather than positive life events, in manic episodes (Johnson et al. 2000, Johnson et al. 2008, Molz et al. 2013) but we have not fully explained yet the physiological mechanisms of the BAS system and its relation with bipolar disorder.

## Family functioning and bipolar disease

Several studies were conducted about the family functioning of bipolar patients. In a literature review, Ramana and Bebbington showed in 1995 a link between EE - high expressed emotion (critical, hostile, or emotionally overinvolved attitudes among relatives), AS – negative affective style (negative parent-to-patient verbal interactional behaviors) and the symptoms among the bipolar population. Especially, Miklowitz and his colleagues found that, in families scored negatively on both measures (EE and AS), the relapse rate rose to 94% (Miklowitz et al. 1988). Priebe also found that patients living with high EE relatives were less stable (Priebe et al. 1989, see Ramana & Bebbington 1995, for a review). Additionally, Cohen, Weinstock and Miller's prospective studies indicate that individuals with bipolar disease who have supportive close family members experience less depressive symptomatology over time (Cohen et al. 2004, Weinstock & Miller 2010). Decrease in parents-reported conflicts also predicted decrease in adolescent's manic symptoms over a 2-years study (Sullivan et al. 2012). In 2007, Kim and his colleagues also found that among the various domains of life stress, family relationships seem to be associated with the greatest frequency of stressful events and the higher level of chronic stress (Kim et al. 2007).

In 1995, Miklowitz compared the family's interactions of schizophrenic and bipolar patients. He found that bipolar patients, notably those with high AS relatives, often took a predominantly externalizing, "refusing" stance in interactions. These patients frequently opposed the opinions, criticisms, or suggestions expressed by relatives in a "symmetrical" relation process (Miklowitz & Goldstein 1995). This finding may make us think that family functioning among the bipolar population deals more with a "conflictual interaction"rather than domestic violence, for example. The studies with the terms bipolar disorder and domestic violence give results in this direction.

Furthermore, studies on the relatives of bipolar patients showed that caregivers reported significant difficulties in their relationships with the patients, with considerable impact on their own lives. Mania was a particularly distressing situation for the caregivers, with frequent observed violence from patients (Dore & Romans 2001, Perlick et al. 2005). Rowe and Morris' study in 2012 also found that manic symptoms were associated with increased observed hostility and poorer partner relationship adjustment only when depressive symptoms were also elevated (Rowe & Morris 2012).

In summary, authors found a relation between family functioning and bipolar disease, especially, high

EE and AS relatives increase the risk of relapses while supportive parents and partners decrease it. The observed violence among the families of bipolar patients seems to be associated with manic states, with a higher risk of conflictual interactions, especially when AS are high.

## DISCUSSION

In the light of all these findings, could we find an integrated manner to read our clinical case? Firstly, we could say that Mrs. X was exposed to acute stressful episodes due to the episodes of domestic violence but also because of both the break-up and the settlement. As we seen before, stressful events seem related to the onset and the relapses in bipolar disease. Additionally, our patient has a late-onset of bipolar disease and has no family history of affective disorder. This could be consistent with our findings. Furthermore, we can also question ourselves about the manner in which to interpret these events: could we consider the separation as an acute stressful event, or do we have to see it as a goal-attainment for Mrs. X, due to her prior attempts to split-up with her husband? This second interpretation could be consistent with the specific onset of a manic episode as described by Depue but seems yet less likely because it does not explain why Mrs. X also experienced a manic episode after she had decided to live together with her husband again. We could also see the conflictual relationship of Mrs. X as a chronic stress factor. As we seen earlier, extreme childhood adversity could predict the course of the bipolar disorder among children. This theory is possible, but cannot be fully confirmed here, because this link was specifically studied for childhood adversity, and as we know, children are in a particularly sensitive period of their lives. Moreover, we saw that some authors found a polarity-specific link between chronic stress and depressive episodes. In a manner that could integrate neurobiology, behavioral sensitization could be more consistent to explain this case in our point of view: Mrs. X could have been sensitized by chronic stress factors, with some acute stress factors triggering the onset and the relapse of her disease. The several studies that we presented here do not allow us to have such a view of bipolar disorder. Further long terms research may help us to see mood and its variations more as a continuum than as separated sequences.

Secondly, regarding the violence in the couple of Mrs. X, we could both see it as a cause and as a consequence of the bipolar disease. It seems realistic to consider a double link where the variations in her mood precipitated the violence of her husband and vice versa.

Finally, we have to introduce the limitations of our study. We have to notice first that we did not study all the psycho-social factors of our patient, presuming immediately a causal link between domestic violence and bipolarity. Additionally, the results we presented here are not the reflection of the entire literature about bipolar disease and are only focused on certain aspects of it. Finally, the terms we used in our research introduced a bias in the selection of the articles.

## CONCLUSION

It seems important to us to keep a global vision of our patients, integrating their histories and the clinical contexts. The approach of our article attempts also to bring back together biological and psychodynamic theories in a more integrated view of the bipolar disorder and may help us to see mood and its variations more as a continuum than as separated sequences. The causality link between domestic violence and bipolar disease remains difficult to understand and needs further research.

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*Correspondence:*
*Alice Bries, MD.*
*Université Catholique de Louvain, Psychopathology and Psychosomatics Unit, Mont-Godinne University Hospital*
*1 avenue du Docteur Gaston Thérasse, 5530 Yvoir, Belgium*
*E-mail: alice.bries@student.uclouvain.be*