Universiteit
Leiden
The Netherlands

Tangled up in mood : predicting the disease course of bipolar disorder

Koenders, Manja

Citation
Koenders, M. (2016, April 7). *Tangled up in mood : predicting the disease course of bipolar disorder*. Retrieved from https://hdl.handle.net/1887/38787

Version:	Corrected Publisher's Version
License:	Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden
Downloaded from:	https://hdl.handle.net/1887/38787

Note: To cite this publication please use the final published version (if applicable).

Cover Page

Universiteit Leiden

The handle http://hdl.handle.net/1887/38787 holds various files of this Leiden University dissertation.

Author: Koenders, Manja
Title: Tangled up in mood : predicting the disease course of bipolar disorder
Issue Date: 2016-04-07

CHAPTER 1

General introduction

"Circular insanity varies in intensity and in duration as a whole and in each of its phases, whether it be among various patients or among various episodes in the same patient. At times, the circle is complete in 3 weeks or a month; sometimes it takes many months or years. Still, whether the course is slow or rapid, the tempo of the disorder does not alter its essential nature: the disease remains the same in its general features as well as in its principal details"

— Falret JP, 1854. Memoire sur la folie circulaire. Bulletin de l'Académie de Médecine, 19: 382-415 (1)

This text originates from the 19th century psychiatrist Jean-Pierre Falret, who was one of the first to extensively describe 'la folie circulaire', or what we today know as bipolar disorder (BD). This description of the disorder illustrates that 130 years ago the notion already existed that the disease course of BD is characterized by both recurrences within patients and a strong variability between patients. The circularity in Falret's description of the disorder refers to the circular occurrence of both manic and depressed mood episodes. However, clinically it seems evident that this circularity is not only restrained to the bipolar mood episodes, but seems to include all facets of the lives of bipolar patients. Typical patterns in the life course of bipolar patients are those of increasing (subjective) professional or interpersonal achievements in periods of hypomania and a typical decline of all these facets when mania becomes more severe or when depression arises. This erosion of important

life domains as a consequence of the disorder presumably will enhance the risk for relapse into new mood episodes. However, to what extent the disorder and adverse environmental factors negatively interact with each other is unknown, since most previous research mainly focused on unidirectional associations between the disorder and the psychosocial environment. Thus, the effect of environmental factors, such as life stress and support, on the disease course has been studied, but the opposite direction, the effect of the disorder on the psychosocial environment, is hardly investigated within BD samples. With the growing interest and need for effective psychosocial interventions for bipolar patients (2, 3), a better understanding of the complex interactions between the illness and associated psychosocial factors is of great importance. The major purpose of this thesis is to find a more refined model for the complex associations between the bipolar mood course and several (environmental) factors. This aim is based on the assumption that, in order to obtain more understanding of the complexity of BD and its mood course, one should use other approaches than cross-sectional and unidirectional methods.

1.1 Bipolar disorder

BD is a common mood disorder, which is characterized by periods of major depression alternated with periods of hypomania (BD II) or mania (BD I) (see Figure 1.1). Depression is characterized by low mood, lack of energy, lack of interest, changes in sleep and appetite, and negative thoughts about the self, the world and the future. Mania can be perceived as the total opposite of depression, leading to a supra-normal state with increased energy, little need for sleep, racing thoughts, elevated mood, and positive perceptions of the self, the world and the future (4). When the manic state does not lead to functional impairment and lasts at least 4 days we speak of a hypomanic state. When functioning is impaired and symptoms last for 7 days we speak of a manic state.

The life time prevalence of BD is estimated around 1% for BD I and between 1%–2% for BD II (5–7). The highly disabling character of the disorder is well reflected by the fact that it is responsible for the loss of more disability-

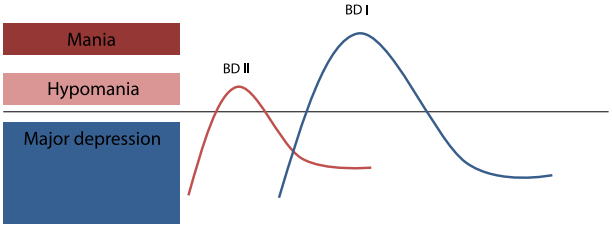

Figure 1.1 | Bipolar type I and II disorder.

adjusted life-years (DALYs) than all forms of cancer or major neurologic disorders such as Alzheimer's and other dementias (8). Further, BD is associated with premature mortality, both resulting from higher prevalence proportions of several medical conditions like cardiovascular disease and diabetes mellitus, as well as from suicide (9). Suicide rates are estimated to be 20 to 30 times higher than for the general population (10), with up to one half of the BD patients attempting to commit suicide during their life (11).

Both the high recurrence rates of mood episodes and the relatively early age of onset of the disease are responsible for the high burden of BD. The natural course of BD is characterized by a constant risk of recurrence, even when patients receive optimal treatment, according to official practice guidelines (12, 13). Over 90% of patients with BD relapse into new mood episodes during their lifetime (14). The recurrence risk in BD is about twice as large as in major depression and the risk of having mood episodes remains relatively high for at least 30 to 40 years after onset (15). Moreover, while symptomatic recovery is reached by 90% of the patients within 2 years after a severe episode, only 30% attain full functional recovery (16).

Furthermore, the average age of onset is estimated around age 25 years (17) with a majority of the patients reporting an age of onset before the age of 20 years (18). This indicates that BD is a disease of young adults, striking them in a critical period in their lives and affecting both personal and professional development.

1.2 The longitudinal bipolar mood course and its (psychosocial) predictors

Because of the high recurrence rates in bipolar patients, monitoring of the longitudinal disease course is highly valuable both in clinical and research settings. Monitoring of the course provides the opportunity to evaluate treatment efficacy and the effects of a variety of factors on increasing or decreasing symptom severity. Systematically monitoring of the longitudinal bipolar mood course originates from 1921 when Kraepelin developed a scheme for charting fluctuations in manic and depressive mood (19). This scheme was modified over the subsequent years and resulted in the The National Institute of Mental Health's Life Chart Method (NIMH LCM)(20). This method includes both a retrospective technique using monthly ratings (21) and a prospective version using daily ratings (20). A systematic analysis of the literature showed that over the last decades both retrospective and prospective NIMH life chart data have been used in over a 100 scientific papers, illustrating the wide use of this tool (Chapter 2).

The systematic monitoring of the bipolar disease course in large longitudinal cohort studies (e.g. 22, 23, 24) led to valuable information about the bipolar disease course and its possible predictors. It appeared that individual patients vary strongly in cycling pattern and severity and polarity of episodes. Some of this variability is associated with the different BD I and II subtypes. For instance, BD II is associated with a more chronic course with more frequent episodes compared to BD I (25–27). However, the BD subtype classification does not fully reflect the wide variety in course patterns among BD patients (26–28). Therefore numerous studies attempted to find correlates or predictors of the longitudinal bipolar mood course. These studies showed that the strongest predictors of the future disease course are disease characteristics itself, such as the predominant polarity of previous episodes (29), the previous number of episodes (30), and the number of residual mood symptoms (12). However, also environmental factors such as stressful life events (31) and lack of social support are associated with a more unfavourable disease course. In prospective studies, the occurrence of negative life events (31–33) and low social support support (34) are predominantly as-

sociated with more depressive symptomatology, and less with increases in manic symptomatology. It remains however unclear whether there is truly no association between environmental stress and mania or whether it is due to the mainly cross-sectional designs of previous studies. The short follow-up times and the infrequent occurrence of manic symptomatology in the bipolar samples that were included may explain the lack of an association of environmental factors with manic symptoms. A study by Johnson et al. (31) showed that mania is not trigged by negative events, but specifically by goal attainment life events. This may indicate that manic versus depressive symptoms are trigged by different environmental factors.

In the last decades, cognitive impairment has also been linked to BD in several studies. Ample evidence indicated that bipolar patients suffer from cognitive impairment, even in euthymic state (35). Attention problems, slowing of processing speed, deficits in visual and working memory, and executive disfunctioning were the most consistent observations (36). A growing number of studies found evidence for the hypothesis that cognitive impairments persist in the euthymic state (37–39), giving rise to the idea that cognitive impairments may represent a trait or an endophenotype of the disorder (40). Although it is widely suggested that cognitive performance is affected by mood symptoms, studies investigating this association are rather scarce and limited by cross-sectional design and small sample sizes. The few longitudinal studies that have been performed show that especially depressive symptomatology was associated with poorer cognitive functioning in bipolar patients, whereas no specific associations were found with mania (41, 42). We hypothesize that the failure to find effects of manic mood on cognitive performance might be due to the fact that these association are non-linear instead of linear (43). This means that mild manic symptoms might increase cognitive performance until they become increasingly severe and cognitive performance will decline, following a reversed U-shaped association. This is in line with findings suggesting that low levels of manic symptoms are related to reports of mental alertness, goal directed activity, increased self-confidence and increased self-efficacy in non-clinical samples (44, 45). In Chapter 5 of the current thesis these specific association between depressed and manic mood and cognitive performance will be investigated.

1.3 Causation and the bipolar disease course

As the previous sections illustrate, BD research has focused primarily on the identification of predictors of relapse into new mood episodes. The assumption is that once the triggers are identified, it will be possible to target these triggers with (psychotherapeutic) treatment strategies. This suggests that clear cause-and-effect mechanisms can be identified. However, how to approach causality in general, and in psychology or behavioural sciences specifically, is still debated among philosophers and scientists (46, 47). In BD the assumed multifactorial etiology and chronicity of the disorder makes it highly difficult to define a starting point of both the disorder itself and of the recurrent episodes. Consequently, cause and effect are equally complex to disentangle. Especially interactions between the social environment and symptomatology are highly dynamic and are more likely to be bidirectional or circular than unidirectional.

Moreover, in the unipolar depression literature there is ample evidence that suggests that the depressed person creates its own unfavorable psychosocial environment, which is known as the 'stress generation theory' (48, 49). Moreover, this generation of life stressors may also play an important role in the maintenance and recurrence of depressive episodes. Although it seems plausible that such a mechanism may even more strongly apply to BD, because of its chronic and recurrent character, it has hardly been studied in bipolar samples. To our knowledge, only one small prospective study (50) to date investigated reciprocal associations of life events in BD. However, because of the small sample size and short follow-up time, these results should be interpreted with caution. Other longitudinal studies on the association between psychosocial factors like social support and life events, only tested whether psychosocial factors preceded increases of bipolar symptomatology, but failed to test for the opposite temporal direction. Thus, although bidirectional associations between environmental stressors and the course of BD are assumed to exist, this issue received very little scientific attention within bipolar samples. In our view, this means that the complexity of the interaction between the BD and its environment has not been fully acknowledged in theoretical and statistical models that were tested in previous studies. We

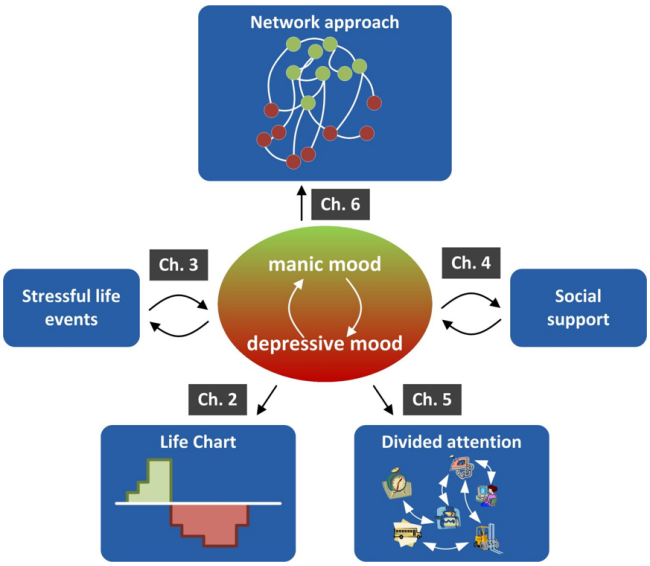

Figure 1.2 | Schematic representation of chapter content.

assume that there exists an ongoing vicious cycle in which bipolar mood symptoms are triggered by adverse life events and low social support, and the mood symptoms in turn will lead to the occurrence of more adverse events and erode the social support system (Figure 1.2) (Chapter 3 and 4).

1.4 Network approach

In addition to a bidirectional approach to longitudinal bipolar data there is a novel approach in psychopathology research, called the network approach. Within this approach the symptoms of the disorders and their associations are proposed as the central focus of attention and as the source of more profound understanding of psychiatric diseases (51). One of the important aims of this approach is to study psychiatric disorders less categorical than they are now presented by the diagnostic boundaries of the diagnostic handbooks (4).

For example, in a recent study Goekoop et al. (52) the authors show that within an unselected group of psychiatric patients, symptoms of a wide vari-

ety of disorders are all interconnected, with particular groups of symptoms clustering together into 6 distinct psychiatric syndromes. In the bipolar field, we also become more aware of the fact that diagnostic categories do not always reflect what we observe in the clinical reality. For instance, the fact that the 'mixed specifier' category is incorporated in the new DSM 5 reflects the need for less strict distinction between manic and depressed mood states. Within a network approach, one would be able to study in what way manic and depressed symptoms are interconnected, and possibly reinforce one another.

Additionally the way symptoms are interconnected and mutually reinforce one another might provide more insight in how specific course patterns in bipolar patients evolve, apart from all sorts of external factors that might affect the disease course (Chapter 6).

1.5 Aims and outline of this thesis

Given the severe disease course in terms of chronicity, recurrence rate, and high burden of BD it seems likely that the associations between psychological factors and the disease course are complex and reciprocal in nature. However, most previous research used unidirectional approaches when studying the association between the disorder and the psychosocial environment. Therefore the overall aim of the current thesis is to critically investigate previously reported associations between psychological factors and the bipolar disease course from a novel theoretical and statistical angle. We investigated this in the context of the 'Bipolar Stress Study'. This cohort contains 173 BD I and II patients who were followed over a 2-year period. Previously, Spijker et al. presented the first findings from this study (53–55), mostly focusing on genetic and biological vulnerabilities in BD patients. In the current dissertation, the focus is on the psychosocial vulnerabilities associated with the longitudinal mood course. For this aim, mood, positive and negative life events and levels of social support were measured repeatedly over a 2-year period, which allows for the testing of potential bidirectional associations within the longitudinal mood course. Figure 1.2 summarizes the associations that will be investigated within the different chapters of the current thesis.

In Chapter 2 the complexity of interpreting longitudinal mood data obtained from the prospective NIMH life chart method will be addressed. In this systematic review we will give an overview of different methods to handle the data and calculate different outcome measures. Subsequently, the aims of chapter 3 and 4 is to critically examine the issue of bidirectionality in the bipolar disease course. In Chapter 3 bidirectional associations between positive and negative life events and the longitudinal course of manic and depressive symptomatology are investigated, including differences in these associations between bipolar I and II patients. In Chapter 4 temporal, bidirectional associations between longitudinal manic and depressive symptomatology and different forms of social support are examined.

In Chapter 5 we will address one part of the dispute about whether cognitive impairments are considered as trait characteristic of BD or rather as a consequence of state dependent mood symptoms. Therefore we will thoroughly investigate divided attention (DA) performance variability over time within patients, and the association of this performance with the fluctuating mood states. We will also assess potential non-linear relationships between level of manic symptoms and cognitive performance.

In Chapter 6 we will focus on the phenomenon that regardless of which factors triggered new mood episodes, the longitudinal course displays rather consistent patterns of time. As previously mentioned, the previous mood course is one of the strongest predictors for the future polarity and severity of the disease course (12, 56, 57). This means that when a patient displays a specific course pattern in the early stage of the disease, it is more likely that the patient will also display this pattern in the future. The potential existence of this vulnerability for developing specific symptom patterns is acknowledged within the previously described network approach of psychopathology (51). By using this approach we aim to identify specific symptom patterns for bipolar patients with different longitudinal course types.