

OBJECTIVE

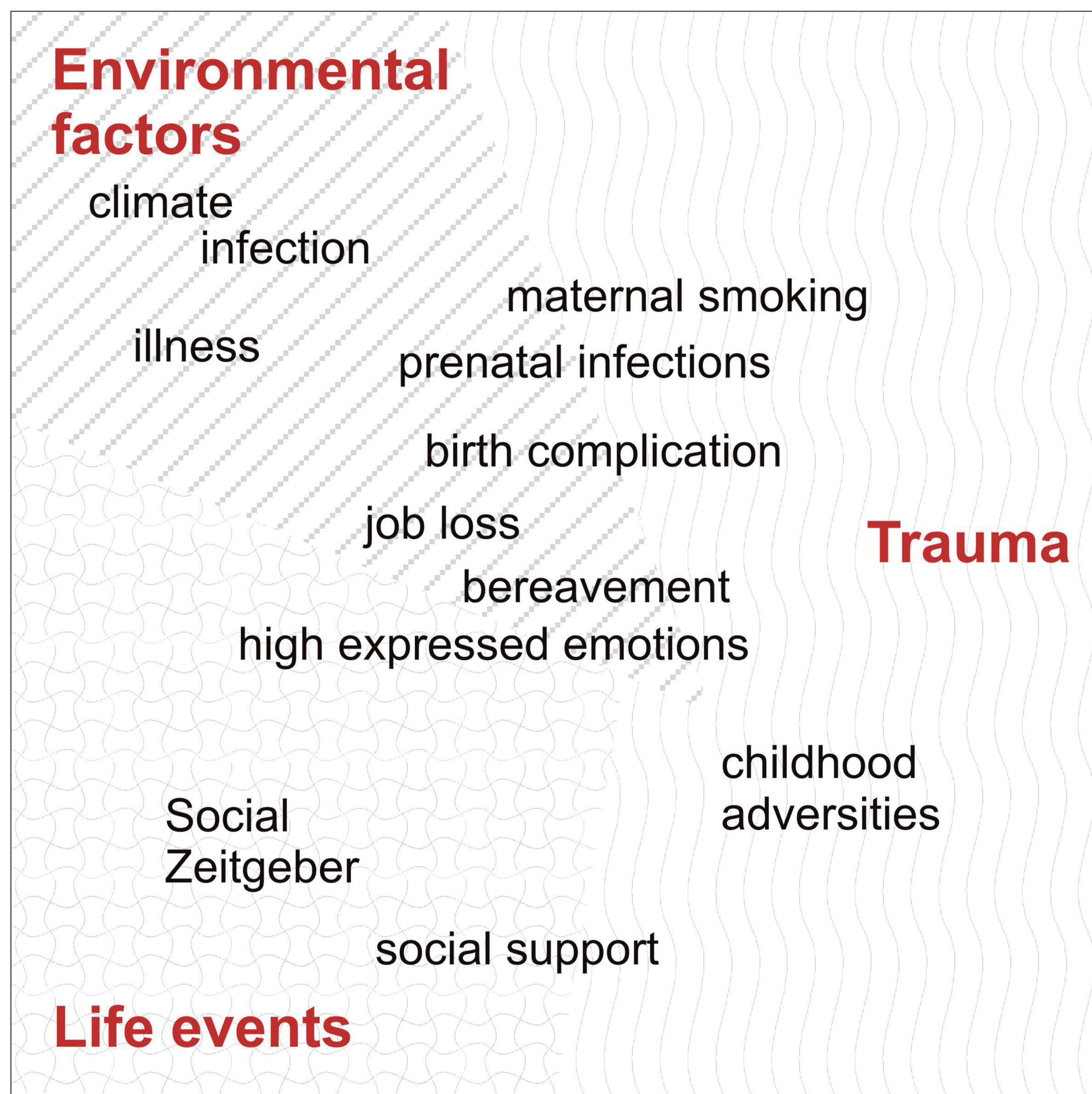
The etiology and clinical course of bipolar disorder (BD) is considered to be determined by genetic and environmental factors. Although the kindling hypothesis emphasizes the impact of environmental factors on initial onset, their connection to the outcome and clinical course has been poorly established. Hence there have been numerous research efforts to investigate the impact of environmental factors on the clinical course of illness. Our aim is to outline recent research on the impact of environmental determinants on the clinical course of BD.

METHODS

Publications (between 2000 and January 2016) dealing with the association between environmental factors, life events and the clinical course of BD. Publications in the reference lists of suitable papers have been taken into consideration as well. A narrative overview was performed on eligible publications.

RESULTS

The different aspects influencing the clinical course of BD can be categorized following various approaches. The complexity and mutual interference of the different categories lead to inconsistent categorization in the literature. Therefore, we abandoned the effort to develop a larger classification of the different categories. (Graphik)



Infections Maternal exposure to influenza is associated with an increased risk of BD and psychotic features (1,2). The hypothesis that gestational viral infections increase susceptibility to BD couldn't be supported by Pang et al. and Mortensen et al. (3,4). They all found a higher seroprevalence in BD with an OR between 2.17 and 3 (5–7).

Maternal smoking Two studies showed an increased risk for BD due to maternal smoking during pregnancy (8,9). Until now there have not been any systematic research protocols dealing with the impact of maternal smoking during pregnancy on the clinical course of BD.

Birth complications There is one study which suggests an association with 2.5-fold higher risk of BD in onset born by planned cesarean section (10). Born preterm was associated with a higher risk of BD in one study (11).

Climate Overall mania has its peaks in spring and summer and a third peak in mid of winter while depression shows high occurrence in winter and spring (12,13).

Childhood trauma The prevalence of posttraumatic stress disorder (PTSD) in BD ranges from 16 to 39% (14–16). Childhood trauma in the broader sense is considered to be evident in almost 50% of patients with BD (17). The association between childhood trauma and BD in onset and its influence on the clinical course are consistent findings (16,18–20). Childhood trauma influences the clinical course by provoking an earlier age of onset, childhood trauma increases the likelihood of a rapid cycling course, the occurrence of psychotic features, the number of life time mood episodes and the risk for suicide ideation and attempts and increases substance misuse.

Life events Numerous researchers have shown that certain life events influence the age of onset and the clinical course of BD (21–30). The type of stressful life events differs in triggering mania or depression. The literature emphasizes that positive life events and goal attainment are more likely to be followed by mania (23,25,31,32). Others support the point of view that negative as well as positive life events are able to trigger both depression and mania (31,33–35). An increased life event load stands for a higher risk for the first episode as well as subsequent episodes (24,26,36). Life events prior to subsequent episodes were discussed to be caused by the illness itself (24,26,32). Post's kindling theory emphasizes that external triggers such as life events have a greater impact on the first episode than on subsequent episodes.

Social Support The rate of relapse is higher in patients with low social support (37–40). Furthermore the results show that having a partner at onset of illness has a positive effect on the course of illness especially on the remission between episodes (38).

CONCLUSION

The findings suggest an association between environmental factors and the clinical course of BD. Due to various methodological limitations the results should be considered cautiously. Systematic longitudinal long term follow-up trials are needed to produce robust results. In the future new therapeutic concepts could be derived from the findings.

Genetic associations between bipolar disorder and childhood trauma

Candidate genes	Age of onset	Suicidality
BDNF val66met	✓	
5-HTTLPR SLC6A4	✓	✓
TLR2	✓	
SNPs near genes coding for calcium channel related proteins	✓	
CLOCK		✓

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