



Universiteit
Leiden
The Netherlands

The relationship between perceived stress and the course of bipolar disorder in adults recently diagnosed with bipolar disorder type I or II

Blankman, Simone

Citation

Blankman, S. (2026). *The relationship between perceived stress and the course of bipolar disorder in adults recently diagnosed with bipolar disorder type I or II.*

Version: Not Applicable (or Unknown)

License: [License to inclusion and publication of a Bachelor or Master Thesis, 2023](#)

Downloaded from: <https://hdl.handle.net/1887/4293425>

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



The relationship between perceived stress and the course of bipolar disorder in adults recently diagnosed with bipolar disorder type I or II

Simone Blankman

Master thesis Psychology
Institute of Psychology
Clinical Psychology Master Program
Faculty of Social and Behavioural Sciences – Leiden University
Date: 23.12.2024
Student number: 2796503
Supervisor and first examiner: Dr. Manja Koenders

Contents

Abstract	3
Layman’s abstract.....	4
Introduction	5
Definition, prevalence and onset of bipolar disorder	5
Perceived stress	5
Perceived stress and the course of bipolar disorder	6
Research objective, implications and clinical relevance	6
Method	8
Design.....	8
Participants	8
Measures.....	8
Procedure.....	9
Ethics.....	9
Statistical analyses.....	9
Results	10
Sample characteristics	10
Perceived stress and depression severity.....	12
Perceived stress and the amount of depressive episodes six months after baseline.....	12
Perceived stress and mania severity	12
Perceived stress and the amount of manic episodes six months after baseline.....	12
Discussion	13
References	17

Abstract

Background: Bipolar disorder is a chronic psychiatric disorder characterized by recurrent mood episodes alternated with periods of remission. Major life events appear to have an important role in the course of the disorder. However, little is known about the influence of daily perceived stress. In the few studies that did focus on this, a positive association has been found between perceived stress and depression severity and number of mood episodes.

Aim: To investigate whether perceived stress is associated with the course of bipolar disorder in patients recently diagnosed with bipolar disorder type I or II.

Methods: Data was obtained from the longitudinal naturalistic Bipolar Netherlands Cohort (BINCO) Study ($N = 64$). Measurements included the Quick Inventory Depressive Symptomatology, Young Mania Rating Scale, Perceived Stress Scale and the WHO-Composite International Diagnostic Interview- Bipolar Disorder. Analyses included linear regression analyses and ANOVA's.

Results: The amount of perceived stress at baseline was found to be associated with an increase in depression severity at baseline. However, perceived stress was not found to be associated with the severity nor the number of episodes of depression or mania six months after baseline.

Conclusions: The study's findings could imply the effectiveness of stress-management in treating patients with bipolar disorder. Future research should be done using a bigger sample, to make results more generalizable. Also, more research may clarify the difference between perceived stress and life events, and the role of the kindling hypothesis.

Keywords: bipolar disorder, perceived stress, depression, mania, longitudinal cohort

Layman's abstract

Bipolar disorder is a chronic psychiatric disorder characterized by recurrent manic or depressive episodes alternated with periods of no mood episodes. Major life events, like the death of a loved-one, seem to play an important role in the course of the disorder. They seem to be able to trigger or sustain manic or depressive episodes. However, not much attention has been drawn to the influence of daily stress that patients experience (i.e. perceived stress). In the few studies that did focus on this, perceived stress seems to be associated with higher self-reported depression and higher amount of mood episodes. This study investigates if perceived stress is associated with the course of bipolar disorder in patients recently diagnosed with bipolar disorder type I or II. The course of bipolar disorder is defined by the severity of depressive and manic symptoms, and the amount of depressive and manic episodes. Data from the longitudinal naturalistic BINCO study (Bipolar Netherlands Cohort Study) was used. The amount of perceived stress at baseline was found to have an influence in the increase in the severity of depressive symptoms at baseline. However, perceived stress was not found to have an influence in depression or mania severity after six months, or in the amount of depressive and manic episodes after six months. This study's findings could show the effectiveness of stress-management in treating patients with bipolar disorder. More research should be done on this topic, using more participants to make results more generalizable to a bigger population. Also, more research may clarify the difference between perceived stress and life events, and the role of the kindling hypothesis.

Introduction

Definition, prevalence and onset of bipolar disorder

Bipolar disorder (BD) is a chronic psychiatric disorder characterized by recurrent mood episodes alternated with periods of remission (Rowe et al., 2024). Individuals with bipolar disorder can experience depressive and/or (hypo)manic episodes. A depressive episode is characterized by a sad, empty or irritable mood, as well as somatic and cognitive changes that significantly affect the individual's capacity to function. A manic episode is defined as a distinct period during which an individual experiences an abnormally, persistently elevated, expansive or irritable mood and continuous increased energy or activity. For an episode to be defined as a manic episode, it should last for at least a week and be sufficiently severe to cause significant impairment in the functioning of the individual. A hypomanic episode can consist of the same symptoms as a manic episode. However, the duration of an episode should be between four to seven consecutive days and the episode should not be severe enough to cause significant impairment in the individual's functioning (American Psychiatric Association, 2013). Bipolar disorder consists of the subtypes bipolar disorder type I, bipolar disorder type II, cyclothymic disorder, rapid cycling and bipolar disorder not otherwise specified. The two subtypes that are relevant for this study are bipolar disorder type I and bipolar disorder type II. These two types of bipolar disorder share a lot of similarities in their symptoms and illness severity, except for the fact that patients with bipolar disorder type II do not experience full-blown manic episodes, but only hypomanic episodes (American Psychiatric Association, 2013). In between of the mood episodes, patients with bipolar disorder can also experience periods of remission. These periods are called euthymia and are characterized by a lack of mood disturbances, a cheerful, calm, active and interested feeling and a resistance to stress (Fava & Bech, 2016).

According to a meta-analysis, the estimated lifetime prevalence of bipolar disorder type I is 1.1% and the estimated 1-year prevalence is 0.7%. The estimated lifetime prevalence of bipolar disorder type II is 1.6% with a 1-year prevalence of 0.5% (Clemente et al., 2015). For bipolar disorder type I, the mean age at onset of the first depressive, manic or hypomanic episode is approximately 18 years. Bipolar disorder type II generally has a slightly later onset, with a mean age of approximately mid-20's (American Psychiatric Association, 2013).

Perceived stress

Psychological stress occurs when a person feels that demands from his or her environment exceed his or her adaptive capacity. Psychological stress is mostly divided into two types. On one hand there is the occurrence of environmental events that are seen as

exceeding one's ability to cope, for example negative life events. On the other hand there is perceived stress, defined as individual responses to these events that are indicative of this overload (Cohen et al., 2007). In other words, perceived stress is the amount of stress individuals experience as a result of environmental events.

Perceived stress can have a large influence on people's lives. It can negatively affect general health as well as mental health. Perceived stress can for example be associated with dizziness, headaches, stomach aches and the risk of hypertension (Li et al., 2023; Thorsén et al., 2022). For mental health, perceived stress has been found to be associated with a higher prevalence of depression and anxiety (Bergdahl & Bergdahl, 2002; Cristóbal-Narváez et al., 2020).

Perceived stress and the course of bipolar disorder

Previous research on bipolar disorder has shown that life stress has an important role in the course of the disorder. It can for example trigger and sustain manic or depressive episodes for patients who suffer from it (Gershon et al., 2013). Most of the research in this field focuses on acute stressors and major life events. Negative life events (like the loss of a loved one or going through a divorce) have been found to be predictors of an increase in depressive symptoms, higher chances of relapsing and an increase in the duration of episodes (Gershon et al., 2013). However, not only negative life events can influence the course of bipolar disorder. It was found that positive life events (like getting married or having a baby) predicted functional impairment due to symptoms of mania and the severity of manic episodes (Koenders et al., 2014).

Although a lot of attention has been drawn to the influence of life events on the course of bipolar disorder, not a lot of attention has been drawn to the perceived stress patients experience on a daily basis, and the influence this could have on the course of the disorder. It has for example been shown that chronic stress, in this case related to peer relationships, significantly predicted less improvement in symptoms of mania for adolescents with bipolar disorder (Kim et al., 2007). Also, perceived stress has been found to be correlated with higher self-reported depression, higher amount of mood episodes, higher suicidality and a lower reported quality of life in patients with bipolar disorder (Rowe et al., 2024).

Research objective, implications and clinical relevance

It is important to find out more about the possible relationship between perceived stress and the course of bipolar disorder, because perceived stress has been shown to be significantly associated with mood problems, for example with depression (Bergdahl & Bergdahl, 2002). A second reason why it is so important, is simply that very little research has

been done on the influence of perceived stress on the course of bipolar disorder. Major life events (both positive and negative) can of course cause a lot of stress for people, but the exact same life event can cause a lot of stress in one person, and very little in another. This is why it is important to look into the influence that perceived stress can have on the course of bipolar disorder. If a relationship exists between these two variables, we might need to put more focus on coping with stress on a daily basis in the treatment of patients with bipolar disorder. This might lead to a better course of the disorder, with for example less relapse, a shorter duration of episodes and a lower severity of symptoms. It might also lead to patients feeling better in general, when they have learned to better cope with stress.

For this reason, the objective of this study is to find out if perceived stress has an influence on the course of bipolar disorder. The study focuses on the question: ‘Is there a relationship between perceived stress and the course of bipolar disorder in adults recently diagnosed with bipolar disorder type I or II?’ Following from the scientific background, firstly it is hypothesized that perceived stress at baseline will be positively associated with the severity of depression at baseline as well as with the severity of depression and the amount of depressive episodes six months after baseline. This hypothesis is based on several findings. One study found that perceived stress is positively correlated with higher self-reported and interviewer-rated depression (Rowe et al., 2024). Another study has shown that greater depression severity across 24 months of follow-up was predicted by the severity of overall chronic stressors in adults with bipolar disorder (Gershon et al., 2013). Also, the relationship between depression and stress has been shown to be bidirectional, meaning that the depression can also cause the patient to perceive more stress (Phillips et al., 2015). Secondly it is hypothesized that perceived stress at baseline will be positively associated with both the severity of mania as well as with the amount of manic episodes six months after baseline. This hypothesis is founded on various discoveries. A study found that higher levels of chronic stress predicted less improvement in mania in people with bipolar disorder (Kim et al., 2007). Another study found that perceived stress was a significant predictor of the total number of mood episodes (including manic episodes) in adults with bipolar disorder at six-month follow-up (Rowe et al., 2024).

In this study, perceived stress is defined as the amount of stress a patient has experienced in the last month, as reported on the Perceived Stress Scale (Cohen et al., 1983b). The course of bipolar disorder is defined as the severity of mania as reported on the Young Mania Rating Scale (Young et al., 1978), the severity of depression as reported on the Quick Inventory Depressive Symptomatology (Rush et al., 2003), and the amount of manic and

depressive episodes as reported on the Composite International Diagnostic Interview (World Health Organization, 1990).

Method

Design

The BINCO study (Bipolar Netherlands Cohort Study) of which this study is a part, is a longitudinal naturalistic study with a prospective cohort design, with measurements at baseline, six months and a year.

Participants

Participants of the BINCO study are Dutch speaking adults (older than 18 years old) recently (< 1 year) diagnosed with bipolar disorder type I or II, who were at the start of their specialized outpatient treatment in facilities in Rotterdam, Leiden or the Hague, The Netherlands. The BINCO study included 93 participants. Three people decided after enrollment not to participate after all, and one person was excluded based on language. For the current study, a smaller subgroup is used, consisting of 64 participants.

Measures

To measure participants' severity of depression, the Quick Inventory Depressive Symptomatology (QIDS) is used (Rush et al., 2003). The QIDS comprises 16 items, which assess sleep, mood, weight, concentration, guilt, suicidal ideation, interest, fatigue and psychomotor changes based on self-report. The total score ranges from 0 to 27 and is composed of the score on the nine different domains. Higher scores indicate more severe depression. The QIDS has been found to have highly acceptable reliability and validity, with a Cronbach's α ranging from 0.81 to 0.92 (Trivedi et al., 2004). The Young Mania Rating Scale (YMRS) is administered to measure participants' severity of mania (Young et al., 1978). The YMRS consists of 11 items. Each of these items focuses on a different aspect of mania, such as elevated mood, increased motor activity-energy, sleep, irritability, sexual interest and speech patterns. The total score for the YMRS ranges from 0 to 60, with higher scores indicating more severe mania. The YMRS has been found to have good reliability and validity, with a Cronbach's α ranging from 0.70 to 0.90 in various studies (Mohammadi et al., 2018). The WHO-Composite International Diagnostic Interview- Bipolar Disorder (CIDI bipolar disorder) is administered to assess the amount of depressive and manic episodes the participants have experienced during the six months after baseline (World Health Organization, 1990). Specifically, sections E and F, focusing on mania, hypomania, and major depressive episodes are used. The Dutch version of the CIDI (Ter Smitten et al., 1998), with confirmed reliability (Wittchen, 1994), was used in this study. For the analyses that use the

CIDI, the participants will be divided into groups. For the CIDI depression, the participants will be divided into three groups. Group 1 will consist of participants who experienced no depressive episodes six months after baseline, group 2 of participants who experienced one depressive episode, and group 3 of participants who experienced 2 through 7 depressive episodes. This way of dividing the groups was chosen because of the equality of the group sizes. For the CIDI mania, the participants will be divided into two groups. Group 1 will consist of participants who experienced no manic episodes six months after baseline, and group 2 of participants who experienced 1 through 6 manic episodes. Again, this way of dividing the groups was chosen because of the equality of the group sizes.

Lastly, the Perceived Stress Scale (PSS) is used to measure the amount of stress a patient has experienced in the last month (Cohen et al., 1983b). The PSS consists of 10 items, each of which can be given a score ranging from 1 to 5. The total score ranges from 10 to 50, with a higher score indicating a higher level of perceived stress in the last month. The PSS has been proven to possess satisfactory reliability and validity, with a Cronbach's α typically ranging from 0.78 to 0.91 (Cohen et al., 1983a).

Procedure

Before enrollment, patients were informed about the research protocol, provided written informed consent, and underwent clinical assessments, including the World Health Organization's (WHO) Composite International Diagnostic Interview- Bipolar Disorder (CIDI bipolar disorder) (World Health Organization, 1990). As incentives for participation, participants received a book after the first measurement and a 30 euro gift card after the third measurement.

Ethics

The study has been approved by the medical ethical committee of the Leiden University Medical Centre (LUMC) in 2016, with the approval number P15.210 and was carried out in accordance with the Declaration of Helsinki.

Statistical analyses

To analyze the data in this study, IBM SPSS Statistics version 29 is used (IBM Corp., 2022). A Bonferroni correction will be applied to account for multiple testing, setting the p -value at .01. Three separate linear regression analyses and two One-Way ANOVA's will be conducted to address the research question. A cross-sectional linear regression will be performed to examine the relationship between the independent variable perceived stress (PSS score) (x) and the dependent variable depression severity (QIDS score) (y) at baseline. For the two prospective analyses, two regressions will assess the relationship between the

independent variable perceived stress at baseline (x) and the two dependent variables depression symptom severity (QIDS score) (y) and mania symptom severity (YMRS score) (y) six months later, controlling for baseline symptom severity. Finally, a One-Way ANOVA will be used to explore the relationship between perceived stress at baseline (x) and the difference between the groups of participants with different amounts of depressive episodes six months after baseline (group 1: 0 episodes, group 2: 1 episode, group 3: 2-7 episodes). Another One-Way ANOVA will be used to explore the relationship between perceived stress at baseline (x) and the difference between the groups of participants with different amounts of manic episodes six months after baseline (group 1: 0 episodes, group 2: 1-6 episodes).

For the linear regression analyses, the assumptions of linearity, homoscedasticity, multicollinearity and normality of the residuals will be tested. Linearity will be tested by using a scatterplot of the standardized z-scores of the predicted values and the residuals. Homoscedasticity will be tested by using a scatterplot of the unstandardized predicted values and the unstandardized residuals. The assumption of multicollinearity will be tested with the Variance Inflation Factor (VIF). Lastly, the normality of the residuals is tested by using a histogram plot of the standardized residuals. All of the assumptions of the linear regression analyses have been met in this study.

For the One-Way ANOVA's, the assumptions of normality of the dependent variable within groups and homogeneity of variances (homoscedasticity) will be tested by using a normality plot of the dependent and independent variables and by checking the Shapiro-Wilk and Kolmogorov-Smirnov tests and the Levene's Test of Equality of Variances. The assumption of normality of the dependent and independent variables within groups was met for both of the ANOVA's. For the ANOVA of perceived stress and the amount of depressive episodes six months after baseline, the assumption of homoscedasticity was also met. This assumption initially wasn't met for the ANOVA of perceived stress and the amount of manic episodes six months after baseline. Therefore, the ANOVA was run again, this time including a Welch test.

Results

Sample characteristics

The total sample at baseline consisted of 64 participants, out of which 28 identified as male (43.8%) and 36 identified as female (56.3%). The participants' age ranged from 20 to 62 years old, with an average of $M = 33.7$ years old ($SD = 10.5$). The participants' score on the Perceived Stress Scale ranged from 24 to 40, with an average of $M = 32.1$ ($SD = 3.8$). The

participants' QIDS score on baseline ranged from 1 to 22, with an average of $M = 9.2$ ($SD = 5.4$). The participants' QIDS score six months after baseline had a range from 1 to 27, with an average of $M = 10.0$ ($SD = 6.9$). The participants' average score on the YMRS six months after baseline was $M = 0.5$ ($SD = 2.0$), ranging from 0 to 12. The average amount of depressive episodes participants experienced in the last six months was $M = 1.3$ ($SD = 1.4$), ranging from 0 to 7. The amount of manic episodes participants experienced in the last six months ranged from 0 to 6, with an average of $M = 1.0$ ($SD = 1.6$). All of the sample characteristics are described in table 1.

Table 1.

Sample characteristics

		<i>N</i>	%	Min	Max	<i>M</i>	<i>SD</i>
Gender	Male	28	43.8				
	Female	36	56.3				
Level of Education	Secondary vocational education	2	3.1				
	High School	30	46.9				
	Higher vocational education	16	25.0				
	Higher professional education	16	25.0				
BD subtype	BD type I	19	29.7				
	BD type II	43	67.2				
	Unknown	2	3.1				
Age		64		20	62	33.7	10.5
PSS score		64		24	40	32.1	3.8
QIDS score baseline		64		1	22	9.2	5.4
QIDS score six months after baseline		49		1	27	10.0	6.9
YMRS score six months after baseline		50		0	12	0.5	2.0
Depressive episodes		48		0	7	1.3	1.4
Manic episodes		46		0	6	1.0	1.6

Perceived stress and depression severity

The results showed a significant cross-sectional association between perceived stress and the severity of depression at baseline ($R^2 = .108$, $\beta = .328$, $SE = .173$, $F(1,62) = 7.481$, $t = 2.735$, $p = .008$). Prospectively, there was no association between baseline perceived stress and the severity of depression six months after baseline ($R^2 = .027$, $\beta = .165$, $SE = .241$, $F(1,49) = 1.374$, $t = 1.172$, $p = .247$). Also after correction for depression severity at baseline, no significant association between perceived stress and the severity of depression at six months was found ($R^2 = .197$, $\beta = .082$, $SE = .261$, $F(2,46) = 5.639$, $t = .597$, $p = .554$). The results described in this section are presented in table 2.

Perceived stress and the amount of depressive episodes six months after baseline

The results showed no significant association between perceived stress and the amount of depressive episodes six months after baseline. No differences were found between the group with no depressive episodes, the group with one episode and the group with several episodes ($F(2,45) = .494$, $p = .613$, $\eta^2 = .022$). The results described in this section are presented in table 3.

Perceived stress and mania severity

The results of the analysis showed no significant prospective association between perceived stress and the severity of mania six months after baseline ($R^2 = .05$, $\beta = -.224$, $SE = .068$, $F(1,50) = 2.634$, $t = -1.623$, $p = .111$). Also after correction for mania severity at baseline, no significant association between perceived stress and the severity of mania at six months was found ($R^2 = .143$, $\beta = -.283$, $SE = .075$, $F(2,47) = 3.931$, $t = -2.099$, $p = .041$). The results described in this section are presented in table 2.

Perceived stress and the amount of manic episodes six months after baseline

The results showed no significant association between perceived stress and the amount of manic episodes six months after baseline. No differences were found between the group with no manic episodes and the group with several manic episodes ($F(1, 33.259) = .007$, $p = .934$, $\eta^2 = .000$). The results described in this section are presented in table 3.

Table 2.*Perceived stress and depression and mania severity results*

	<i>N</i>	Bèta (β)	<i>p</i>
Depression cross-sectional	64	.328	.008
Depression prospective	51	.165	.247
Depression prospective after correction	49	.082	.554
Mania prospective	52	-.224	.111
Mania prospective after correction	50	-.283	.041

Table 3.*Perceived stress and the amount of depressive and manic episodes results*

	<i>N</i>	<i>F</i>	<i>p</i>
Depressive episodes six months after baseline	48	.494 (2, 45)	.613
Manic episodes six months after baseline	46	.007 (1, 33.259)	.934

Discussion

The objective of this study was to find out if perceived stress was associated with the course of bipolar disorder. Firstly, it was hypothesized that perceived stress at baseline would be positively associated with the severity of depression at baseline as well as with the severity of depression and the amount of depressive episodes six months after baseline. Secondly, it was hypothesized that perceived stress at baseline would be positively associated with both the severity of mania as well as with the amount of manic episodes six months after baseline.

For the first hypothesis, only the first part was confirmed. In this study, perceived stress at baseline was found to be positively associated with the severity of depression at baseline, but not with the severity of depression and the amount of depressive episodes six months after baseline (after controlling for baseline mood severity). This means that the amount of stress participants experienced at the baseline measurement only increased the

severity of their depressive symptoms at the same measurement time. However, we cannot be certain about the direction of the association, meaning that it could also be that the severity of depressive symptoms at baseline influenced the amount of perceived stress at baseline, instead of the other way around. The amount of perceived stress at baseline had no association with the severity of depressive symptoms six months later, or with the amount of depressive episodes participants experienced six months later.

For the second hypothesis, it was found that perceived stress at baseline was not associated with both the severity of mania as well as with the amount of manic episodes six months after baseline (after controlling for baseline mood severity). For this finding as well, this means that the amount of stress participants experienced at baseline had no association with the severity of their manic symptoms six months later, or with the amount of manic episodes they experienced six months later.

These findings are slightly contradictory to the scientific findings discussed in the introduction, like the study that found that the severity of overall chronic stressors in adults with bipolar disorder predicted greater depression severity across 24 months of follow-up (Gershon et al., 2013), or the study that found that perceived stress was a significant predictor of the total amount of mood episodes (including manic episodes) in adults with bipolar disorder at six-month follow-up (Rowe et al., 2024). These two studies have some aspects in common with the current study. For example, the study by Gershon et al. (2013) also found stressors to only be associated with depression, and not with mania. The study by Rowe et al. (2024) used measures that were similar to the measures used in the current study. However, both of these studies found significant results at follow-up, unlike the current study. The most notable distinction between these two studies and the current one appears to be the number of participants. The current study had a much smaller sample in comparison to the other two studies. Therefore, it could be that the difference in findings is (partially) due to lack of statistical power in the current study.

Another potential explanation of the unexpected findings of the current study could be the kindling hypothesis. The kindling hypothesis theorizes that later episodes of a mood disorder are less likely to be influenced by psychosocial stressors in comparison to earlier episodes. The stressors are thought to have a larger effect on the onset of earlier episodes of a mood disorder. However, with every episode a person experiences, the effect psychosocial stressors have on the onset of a mood episode is thought to become smaller (Post, 1992). A study that researched the effect of the kindling hypothesis in bipolar disorder, found that in individuals who experienced more lifetime mood episodes, more life stress related to minor

events was needed to set off a new depressive episode (Weiss et al., 2015). This could be an explanation as to why perceived stress at baseline had no effect on the severity of depression and the amount of depressive episodes six months after baseline. Perhaps higher levels of perceived stress would have been needed to influence the severity of depression and the amount of depressive episodes after six months. This theory is supported by the data. In the current study, the past number of depressive episodes ranged from 1 to 96, with an average of $M = 16.8$ and a standard deviation of $SD = 20.2$. The past number of manic episodes ranged from 0 to 500, with an average of $M = 27.2$ and a standard deviation of $SD = 76.0$. In comparison, in the study by Gershon et al. (2013) the average number of past depressive episodes was $M = 7.4$ with a standard deviation of $SD = 11.5$ and the average number of past manic episodes was $M = 9.4$ with a standard deviation of $SD = 12.8$. This shows that the participants in the current study have relatively higher amounts of past manic and depressive episodes, which could support the kindling hypothesis as being a partial explanation for the current findings.

The current study, despite of being part of a well-designed larger study, has some limitations. First off, the current study only used a small part of the total sample of the larger study. The total sample size of the current study was 64. In some analyses, the sample was even smaller, because of missing cases on certain variables. Perhaps, the current study did not have enough power to be able to find any valid results. Also, the BINCO-study is a longitudinal study that took part during the COVID-19 pandemic. This led to some complications, for example some participants not being able to show up to the research location for follow-up appointments, which led to drop-out and missing cases. Potentially, this could be the reason for some of the missing cases in certain variables, which lead to a relatively small sample size in the current study. Another limitation of the current study is that most of the questionnaires were based on self-report. Some were administered through interviews, but still relied on the participants' own answers. This way, the answers to the questions on the questionnaires are relatively subjective. On the other hand, it might be the only way to administer variables like stress and symptom severity, since there are little to no objective ways to measure these.

Despite its limitations, the current study also has some strong points. All of the measures that were used in the current study had good reliability and validity. The statistical analyses that were conducted were carefully chosen to match the aim of the research question and the hypotheses. Also, all of the assumptions for the analyses were met.

Although most of the expected results did not turn out to be significant, the current study did find that the amount of perceived stress at baseline is associated with an increase in the severity of depressive symptoms at baseline. This finding can be important in clinical practice. It could mean that patients with bipolar disorder or unipolar depression experience an increase in depressive symptoms when they are experiencing high levels of stress. This could mean that focusing on stress-management can be an effective step in treating patients with bipolar disorder or unipolar depression. This is supported by a study that found that Mindfulness-based Cognitive Therapy (MBCT), which focuses on mindfulness-based stress reduction, was successful in reducing symptoms of depression and anxiety in patients with bipolar disorder (Williams et al., 2008).

For future research, it could be important to look into the effects of perceived stress on the course of bipolar disorder in a bigger sample. This might lead to results that are more generalizable to the bigger population. It could also be useful to do a study in which both perceived stress and stress related to life events are studied in relation to the course of bipolar disorder. This way, a clear distinction could be made between these different types of stress, and their influence on bipolar disorder. Also, more research should be done on the kindling hypothesis, and its effects on the course of bipolar disorder. More specifically, it would be good to look into the question if the effects of the kindling hypothesis influence the role of stress in the course of bipolar disorder.

References

- American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). <https://doi.org/10.1176/appi.books.9780890425596>
- Bergdahl, J., & Bergdahl, M. (2002). Perceived stress in adults: Prevalence and association of depression, anxiety and medication in a Swedish population. *Stress and Health, 18*(5), 235–241. <https://doi.org/10.1002/smi.946>
- Clemente, A. S., Diniz, B. S., Nicolato, R., Kapczinski, F. P., Soares, J. C., Firmo, J. O., & Castro-Costa, É. (2015). Bipolar disorder prevalence: A systematic review and meta-analysis of the literature. *Brazilian Journal of Psychiatry, 37*, 155–161. <https://doi.org/10.1590/1516-4446-2012-1693>
- Cohen, S., Janicki-Deverts, D., & Miller, G. E. (2007). Psychological Stress and Disease. *JAMA, 298*(14), 1685–1687. <https://doi.org/10.1001/jama.298.14.1685>
- Cohen, S., Kamarck, T., & Mermelstein, R. (1983a). A Global Measure of Perceived Stress. *Journal of Health and Social Behavior, 24*(4), 385–396. <https://doi.org/10.2307/2136404>
- Cohen, S., Kamarck, T., & Mermelstein, R. (1983b). *Perceived Stress Scale* [Dataset]. <https://doi.org/10.1037/t02889-000>
- Cristóbal-Narváez, P., Haro, J. M., & Koyanagi, A. (2020). Perceived stress and depression in 45 low- and middle-income countries. *Journal of Affective Disorders, 274*, 799–805. <https://doi.org/10.1016/j.jad.2020.04.020>
- Fava, G. A., & Bech, P. (2016). The Concept of Euthymia. *Psychotherapy and Psychosomatics, 85*(1). <https://doi.org/10.1159/000441244>
- Gershon, A., Johnson, S. L., & Miller, I. (2013). Chronic stressors and trauma: Prospective influences on the course of bipolar disorder. *Psychological Medicine, 43*(12), 2583–2592. <https://doi.org/10.1017/S0033291713000147>
- IBM Corp. (2022). *IBM SPSS Statistics* (Version 29) [Computer software].

- Kim, E. Y., Miklowitz, D. J., Biuckians, A., & Mullen, K. (2007). Life Stress and the Course Of Early-Onset Bipolar Disorder. *Journal of Affective Disorders*, *99*(1–3), 37.
<https://doi.org/10.1016/j.jad.2006.08.022>
- Koenders, M. A., Giltay, E. J., Spijker, A. T., Hoencamp, E., Spinhoven, P., & Elzinga, B. M. (2014). Stressful life events in bipolar I and II disorder: Cause or consequence of mood symptoms? *Journal of Affective Disorders*, *161*, 55–64.
<https://doi.org/10.1016/j.jad.2014.02.036>
- Li, D., Rong, C., & Kang, Q. (2023). Association between perceived stress and hypertension in Chinese adults: A population-based survey. *Journal of Human Hypertension*, *37*(4), 321–326. <https://doi.org/10.1038/s41371-022-00684-y>
- Mohammadi, Z., Pourshahbaz, A., Poshtmashhadi, M., Dolatshahi, B., Barati, F., & Zarei, M. (2018). Psychometric properties of the Young Mania Rating Scale as a mania severity measure in patients with bipolar I disorder. *Journal of Practice in Clinical Psychology*, *6*(3), 175–182.
- Phillips, A. C., Carroll, D., & Der, G. (2015). Negative life events and symptoms of depression and anxiety: Stress causation and/or stress generation. *Anxiety, Stress and Coping*, *28*(4), 357–371. <https://doi.org/10.1080/10615806.2015.1005078>
- Post, R. M. (1992). Transduction of psychosocial stress into the neurobiology of recurrent affective disorder. *The American Journal of Psychiatry*, *149*(8), 999–1010.
<https://doi.org/10.1176/ajp.149.8.999>
- Rowe, A.-L., Perich, T., & Meade, T. (2024). Childhood cumulative trauma, social support and stress as predictors of illness outcomes and quality of life in bipolar disorder. *The Australian and New Zealand Journal of Psychiatry*, *58*(4), 334–344.
<https://doi.org/10.1177/00048674231209225>

- Rush, A. J., Trivedi, M. H., Ibrahim, H. M., Carmody, T. J., Arnow, B., Klein, D. N., Markowitz, J. C., Ninan, P. T., Kornstein, S., Manber, R., Thase, M. E., Kocsis, J. H., & Keller, M. B. (2003). The 16-Item Quick Inventory of Depressive Symptomatology (QIDS), clinician rating (QIDS-C), and self-report (QIDS-SR): A psychometric evaluation in patients with chronic major depression. *Biological Psychiatry*, *54*(5), 573–583. [https://doi.org/10.1016/s0006-3223\(02\)01866-8](https://doi.org/10.1016/s0006-3223(02)01866-8)
- Ter Smitten, M. H., Smeets, R. M. W., & Van den Brink, W. (1998). *Composite International Diagnostic Interview (CIDI), Version 2.1, 12-months (in Dutch)*.
- Thorsén, F., Antonson, C., Palmér, K., Berg, R., Sundquist, J., & Sundquist, K. (2022). Associations between perceived stress and health outcomes in adolescents. *Child and Adolescent Psychiatry and Mental Health*, *16*(1), 75. <https://doi.org/10.1186/s13034-022-00510-w>
- Trivedi, M. H., Rush, A. J., Ibrahim, H. M., Carmody, T. J., Biggs, M. M., Suppes, T., Crismon, M. L., Shores-Wilson, K., Toprac, M. G., Dennehy, E. B., Witte, B., & Kashner, T. M. (2004). The Inventory of Depressive Symptomatology, Clinician Rating (IDS-C) and Self-Report (IDS-SR), and the Quick Inventory of Depressive Symptomatology, Clinician Rating (QIDS-C) and Self-Report (QIDS-SR) in public sector patients with mood disorders: A psychometric evaluation. *Psychological Medicine*, *34*(1), 73–82. <https://doi.org/10.1017/S0033291703001107>
- Weiss, R. B., Stange, J. P., Boland, E. M., Black, S. K., LaBelle, D. R., Abramson, L. Y., & Alloy, L. B. (2015). Kindling of life stress in bipolar disorder: Comparison of sensitization and autonomy models. *Journal of Abnormal Psychology*, *124*(1), 4–16. <https://doi.org/10.1037/abn0000014>
- Williams, J. M. G., Alatiq, Y., Crane, C., Barnhofer, T., Fennell, M. J. V., Duggan, D. S., Hepburn, S., & Goodwin, G. M. (2008). Mindfulness-based Cognitive Therapy

(MBCT) in bipolar disorder: Preliminary evaluation of immediate effects on between-episode functioning. *Journal of Affective Disorders*, 107(1), 275–279.

<https://doi.org/10.1016/j.jad.2007.08.022>

Wittchen, H. U. (1994). Reliability and validity studies of the WHO--Composite International Diagnostic Interview (CIDI): A critical review. *Journal of Psychiatric Research*, 28(1), 57–84. [https://doi.org/10.1016/0022-3956\(94\)90036-1](https://doi.org/10.1016/0022-3956(94)90036-1)

World Health Organization. (1990). Composite International Diagnostic Interview.

Young, R. C., Biggs, J. T., Ziegler, V. E., & Meyer, D. A. (1978). A rating scale for mania: Reliability, validity and sensitivity. *The British Journal of Psychiatry: The Journal of Mental Science*, 133, 429–435. <https://doi.org/10.1192/bjp.133.5.429>