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Clinical profile of bipolar patients with seasonal pattern: a systematic review

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Clinical profile of bipolar patients with seasonal pattern: a systematic review

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ABSTRACT

Background: Bipolar disorder(BD) is mainly characterised by (hypo)manic and depressive episodes, with recent studies showing that up to 25% of patients present a seasonal pattern(SP). The aim of this review is to uncover if BD patients with SP display a distinct clinical profile.
Methods: A systematic review was conducted on the clinical presentation of BD patients with and without SP, by querying PubMed and Web of Science.
Results: Sixteen papers were included, involving more than 13,000 BD patients. BD patients with SP were found to have an earlier age of onset of the disorder, be predominantly BD type-II, have an higher recurrence of mood episodes and have possibly a worse outcome than BD patients without SP.
Limitations: Only two search engines and articles in English were queried, some studies present small sample sizes and some limitations of the methodology applied to evaluate seasonality.
Conclusion: Even though it's soon to present any definitive conclusion, this review highlights some evidence that point to a distinct clinical profile in BD patients with SP.

Keywords: Bipolar Disorder; Season; Mania, Depression; Clinical Profile.

1. INTRODUCTION

Bipolar disorder(BD) is a severe mood disorder mainly characterised by (hypo)manic and depressive episodes. In recent years, a seasonal pattern (SP) of these episodes has been observed in some populations of BD patients, more specifically a predominance of (hypo)mania episodes in months with the highest amount of daylight hours, and a predominance of depressive episodes in months with the lowest amount daylight hours (Geoffroy et al,. 2014). Although this relationship hasn't been estabilished for all regions and populations (Bauer et al., 2009), it has gained sufficient recognition to be granted a disease specifier in the Bipolar Disorder's Chapter of DSM-V, with recent studies reporting a prevalence of almost 25% of BD patients having SP **(**Goikolea et al., 2007).

Scientific studies examining the clinical characteristics of BD patients with SP and BD patients without SP have been performed but no systematic review of this theme has been undertaken to date. Therefore, the aim of this study was to summarize the findings from published studies over the last 10 years concerning this issue and attempt to reach a conclusion of whether or not SP in BD patients implies a distinct clinical profile.

2. MATERIAL AND METHODS

The methodological approach used in this review was based in PRISMA's guidelines, available at "prisma-statement.org". Two authors (NM & MM) conducted a search of Pubmed and Web of Science's databases for publications released between January 1st 2010 and January 30th 2020 that were related to seasonality in BD. The query used was: bipolar disorder AND season; bipolar disorder AND seasonality; season AND mania; bipolar depression AND mania; bipolar disorder AND clinical. Manual searches were also conducted, using reference lists from identified articles.

In a first phase selection, repeated articles were sorted out, and the remaining articles were selected by title, having as inclusion criteria the combination of the terms "bipolar", "bipolar disorder", "mania", "bipolar depression, "season", "seasonality", "seasonal pattern", "clinical".

In a second phase, the selected articles were individually read and submitted to the following inclusion criteria: 1) any type of article, excluding reviews, meta-analysis and editorial notes; 2) population mainly composed of patients with bipolar disorder (both types); 3) the outcome is associated with seasonality as it relates to bipolar disorder; 4) the outcome pertains to the anamnesis of mood episodes in BD patients.

The articles in which the outcome would intentionally relate to other psychiatric disorders other than BP and those written in languages other than English were excluded.

The data retrieved from each article included study type, country, population, methodology and key findings.

3. RESULTS

3.1. LITERATURE SEARCH

From the initial search, 146 articles were selected. After the first phase selection, 48 articles followed to the second phase selection, resulting in 16 final articles that were included in this review(Fig.1).

From all articles, 7 were from Europe (3 - France; 1- Austria; 1- Finland; 1- Italy; 1- Spain), 5 from Asia (4- South Korea; 1- Israel; 1 - Taiwan) and 3 from the Middle East (3 - Turkey).

The study types included 8 cross-sectional studies, 5 case-control studies and 3 longitudinal studies.

3.2. POPULATION

A great portion of the studies included both types of bipolar patients, although some included only bipolar type I patients due to insufficient number of bipolar type II subjects for statistical significance. In one study, patients with Major Depressive Disorder(MDD) were also included.

3.3. METHODOLOGY APPLIED

Regarding SP of mood and behaviour, the most frequently used instrument was the Seasonal Pattern Assessment Questionnaire (SPAQ), including one study that used SPAQ+, the italian version of SPAQ. The second most frequent instrument were seasonality criteria of symptoms as detailed in DSM-IV. One study used empirical mode decomposition on its population to assess seasonality. Five studies did not specify the instrument used.

3.4. CLINICAL PRESENTATION OF BIPOLAR PATIENTS WITH SEASONAL PATTERN

3.4.1. GENDER

Gender was the most recurrent variable in the studies included in this review. Two studies that compared BD patients with and without SP found no significant statistical differences in terms of gender **(**Geoffroy et al., 2015; Altınbaş et al., 2019), while another study concluded that a possible effect of gender, if existent, would be small(Fellinger et al., 2019).

On the other hand, one study found that manic episodes with SP were more associated with the male gender (Hochman et al., 2016). This supports the findings of another study that estabilished that male patients experienced a higher seasonality for manic than depressive episodes, while female patients experienced a higher seasonality for depressive than manic episodes (Yang et al., 2013). Regrettably, one study found an association between SP and depressive episodes, in males, but not manic episodes (Geoffroy et al., 2013).

Continuing with this contraditory tendency, one study associated SP in BD-II patients with the female gender (Kim et al., 2015) and another study associated SP in BD-II patients with the male gender (Geoffroy et al., 2013).

Some final discoveries regarding gender were a significant presence of rapid cycling and lifetime history of eating disorders in women with SP (Geoffroy et al., 2013), as well as an association between seasonality and premenstrual syndrome(PMS) (Choi et al., 2011) and seasonality and premenstrual dysphoric disorder(PMDD), in BD-II women (Choi et al., 2011; Kim et al., 2015).

3.4.2. AGE

Most findings regarding age point towards an earlier age of onset in BP patients with SP, compared to BP patients without SP (Yang et al., 2013; Geoffroy et al., 2015, 2017), with one study finding the strongest SP pattern for manic and mixed episodes in women aged between 15 and 35 years, in comparison to older age groups (Fellinger et al., 2019).

However, one study found no statistical difference in terms of age of onset between BD patients with and without SP (Altınbaş et al., 2019).

3.4.3. EDUCATION LEVEL

Two studies evaluated whether there was association between the patient educational level and SP of mood and behaviour, finding no statistical differences between the studied groups (Geoffroy et al., 2015; Altınbaş et al., 2019).

3.4.4. BD-I vs BD-II

All the studies comparing seasonality between BP-I and BP-II patients showed a significantly higher frequency of SP in patients in BP-II patients (Geoffroy et al., 2013, 2015, 2017; Kim et al., 2015). One of these works showed that the global seasonality score(GSS) on the SPAQ was significantly higher in BD-II patients, while also associating seasonality in BP-II patients with female gender, predominance of depressive episodes and premenstrual dysphoric disorder (PMDD)(Kim et al., 2015).

3.4.5. FAMILY HISTORY

Only one research studied the association between family history and SP, finding a higher Global Seasonality Score (GSS) in BP patients with positive family history of BP (Brambilla et al., 2012).

3.4.6. MOOD AND BEHAVIOUR

Several studies surveyed the differences in mood and behaviour in BP patients with or without SP, during manic and/or depressive episodes. One common finding among these was an higher prevalence of mood episodes in patients with SP (Geoffroy et al., 2013, 2015, 2017), particularly depressive episodes (Geoffroy et al., 2013; Yang et al., 2013; Altınbaş et al., 2019).

BD patients with SP were also more likely to meet criteria for rapid cycling, have a lifetime history of eating disorders (particularly in women) (Geoffroy et al., 2013), and have evening-preference as well as irregularity of weekday bed-rise time (Baek et al., 2016). Related to these last two findings, another study found that BP patients with SP are more likely to have poor sleep quality (Keskin et al., 2016).

Two studies focused on seasonality of manic episodes and had two different findings. The first one showed that seasonal hypomanic episodes were more associated with irritable, impulsive and careless behaviour (“irritable/risk taking”) than active, elated, self-confident behaviour (“active/elated”) (Bae et al., 2014). The second of these studies found that manic episodes with SP were associated with the presence of psychotic features (Hochman et al., 2016).

One investigation studying the relationship between BD and Obsessive-Compulsive Disorder(OCD) discovered higher seasonality in BD patients with comorbid OCD (Ozdemiroglu et al., 2015).

One study performed a series of neuropsychological tests on BD-I patients and revealed that patients with SP performed worse with regards to visuoconstructional functions, visuospatial reasoning, auditory attention, working memory and verbal memory (Rajajärvi et al., 2010).
Finally, one paper associated seasonality with a higher rate of suicide attempts in BD-I patients (Kim et al., 2015).

3.4.7. METABOLIC SYNDROME

One study in this review tried to determine whether BD with SP was associated with increased risk of Metabolic Syndrome(MetS) and its subcomponents. Although no significant difference in prevalence of MetS was found between groups, BD patients with SP had higher systolic blood pressure, higher fasting glucose and increased risk of obesity (Geoffroy et al., 2017).

3.4.8. PREDICTOR

One study concluded that the presence of psychotic features during a manic episode as well as male gender were predictors of manic episodes with SP (Hochman et al., 2016).
On another note, SP in BD patients was found to be a strong predictor of dropout/irregular follow-up (Ezquiaga et al., 2014).

4. DISCUSSION

The results found in this systematic review shine a light on the clinical profile of BD patients with SP and how it contrasts in some aspects with the profile of BD patients without SP (Table 1). It is however impossible to draw definitive conclusions from all outcomes evaluated in this work.
The literature is not consensual when it comes to the role of gender in the SP of BD patients. In fact, studies directly contradicted each other, with some of them defending that a specific gender had an influence in SP (Geoffroy et al., 2013; Yang et al., 2013; Kim et al., 2015; Hochman et al., 2016), while others reported that gender had no influence on the matter (Geoffroy et al., 2015; Altınbaş et al., 2019; Fellinger et al., 2019). Even among studies that reported influence of gender, an agreement couldn't be made as to the manner in which gender influenced SP (Geoffroy et al., 2013; Yang et al., 2013; Kim et al., 2015; Hochman et al., 2016). Some findings without apparent conflict, were the presence of significant rapid cycling, eating disorders, PMS and PMDD in BD women with SP (Choi et al., 2011; Geoffroy et al., 2013; Kim et al., 2015), which may suggest a specific interaction between the female gender and seasons. With these results, the influence of gender in the SP of BD patients remains for the most part unattainable, and so further research is needed to unravel the influence of gender on seasonality.
When it comes to the age of onset, most studies agree that BP patients with SP have an earlier onset of the disorder than those without SP (Yang et al., 2013; Geoffroy et al., 2015, 2017), with only one study reporting no significant differences between groups **(**Altınbaş et al., 2019). Given the small population of Altınbaş et al.'s study (2019) and the fact that it only included BD-I patients, it seems reasonable to give preponderance to the other 3 studies and infer that BD patients with SP have an earlier age of onset of their condition.
Concerning educational level, no differences were found between groups (Geoffroy et al., 2015; Altınbaş et al., 2019), implying a lack of influence of education in the presence of SP in BD. It is known that low educational levels can bring on the emergence of mood disorders (Kivimäki et al., 2020) but so far an association between education and SP of these disorders remains elusive.
Regarding whether SP is more present in BD-I or BD-II, all studies gave the same answer. SP is more present in BD-II patients (Geoffroy et al., 2013, 2015, 2017; Kim et al., 2015). BD-II patients usually present evening-preference (Melo et al., 2017) and are therefore at increased risk of being affected by changes in circadian rhythms that occur with the change of seasons, which might be one of the reasons behind the significant presence of SP in this group.
Only one study tried to estabilish a relation between SP and family history of mood disorders, with its findings advocating that BD patients with family history of BD achieved higher GSS and therefore presented a SP more frequently (Brambilla et al., 2012). This suggests the possibility of a genetic component underlying the fluctuation of mood and behaviour throughout seasons, which concurs with recent findings from genetic studies of seasonality (Byrne et al., 2015).
A plethora of papers focused on mood and behaviour differences between BD patients with and without SP. One common finding was an higher prevalence of mood episodes in patients with SP (Geoffroy et al., 2013, 2015, 2017), which seems to be supported by the fact that BP patients with SP were more likely to meet criteria of rapid-cycling (Geoffroy et al., 2013). These recurrent episodes

tended to be depressive episodes (Geoffroy et al., 2013; Yang et al., 2013; Altınbaş et al., 2019). BD patients with SP were found to have a lower quality of sleep (Keskin et al., 2016), as well as evening-preference and irregular weekday bed-rise time (Baek et al,. 2016), which, as stated before, might be one of the reasons for their susceptibility to mood episodes when seasons change. Some authors investigated only the presentation of patients during (hypo)mania episodes and came to the conclusion that seasonal hypomanic episodes were more associated with irritable, impulsive and careless behaviour (Bae et al., 2014), which is more suggestive of a psychopatological condition (Angst et al., 2010) (as opposed to a normal'high') and that manic episodes with SP were associated with psychotic features (Hochman et al., 2016), which can imply that BD patients with SP have a more severe form of BD and a poorer outcome, as psychotic features in mania episodes are associated with greater symptom severity and higher morbidity in the long-term (Coryell et al, 2001). One study discovered that BD patients with comorbid OCD presented SP more frequently (Ozdemiroglu et al., 2015). The fact that this same study proved that BD+OCD patients present more rapid cycling (Ozdemiroglu et al., 2015) and that BD+OCD patients tend to be BD-II (Krüger et al., 2000), makes it reasonable to assume that OCD-BD comorbidity is associated with seasonality. Neuropsychological tests were undertaken on BD-I patients in one paper, with patients reporting SP ending up with worse test scores (Rajajärvi et al., 2010), again suggesting a worse strain of disorder. BD-I patients with SP were found to have an higher rate of suicide as compared to BD-I without SP (Kim et al., 2015). The same distinction wasn't present in BD-II patients as both groups (with and without SP) presented similar rates of suicide. The authors of this study reported that further evidence was necessary to explain these differences.

BD is associated with MetS (Vancampfort et al. 2015) and one study in this review seeked to find if SP in BD influenced the prevalence of MetS (Geoffroy et al., 2017). Even though no association between SP and MetS was found, BD patients with SP were reported to have had higher systolic blood pressure, higher fasting glucose and increased risk of obesity, all factors that can contribute to the development of MetS. Therefore, more studies on this subject are advised to strengthen the relationship between MetS and BD with SP.

Finally, one study found that male gender and psychotic features in a manic episode(without previously known SP) can serve as a predictor for SP (Hochman et al., 2016). As previously discussed, it's problematic to draw conclusions related to gender but the presence of psychotic features falls in line with other conclusions that might point to BD with SP being a more severe form of the disease and so it would be more probable for a patient with psychotic features during a mania episode to present SP later on. SP in BD patients was found to be a predictor for loss of follow-up (Ezquiaga et al., 2014), which can be explained by the highly recurrence of mood episodes present in these patients (Geoffroy et al,. 2014), which in turn makes it more difficult for them to maintain a regular attendance with a structured follow up.

5. LIMITATIONS

Some limitations need to be acknowledged. First, only two search engines were used and only studies written in English were included, therefore, it is possible that a significant quantity of relevant articles were left out. Second, several studies had small populations, some not including BD-II patients, which makes it difficult to extrapolate the results to a general population. Third, not all studies used the same methodology to acess seasonality, which can lead to some discrepancy when it comes to defining seasonal variance of presentation. In addition, most methods used to acess seasonality rely on information given by the patient of past events which can lead to recall bias.

6. CONCLUSION

We can begin to infer with a certain degree of certainty some clinical aspects of BD patients with SP, albeit not all outcomes presented a conclusive result. This condition seems to represent a bleak variant of BD, with an higher recurrence of mood episodes (especially depressive episodes), while being more prevalent in BD-II patients and presenting at an earlier age.

In conclusion, this review starts to paint a picture of the clinical profile of BD patients with SP.

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The authors have no financial relationships, or conflits of interest to disclose.

Fig. 1. Flowchart of Article Selection Process

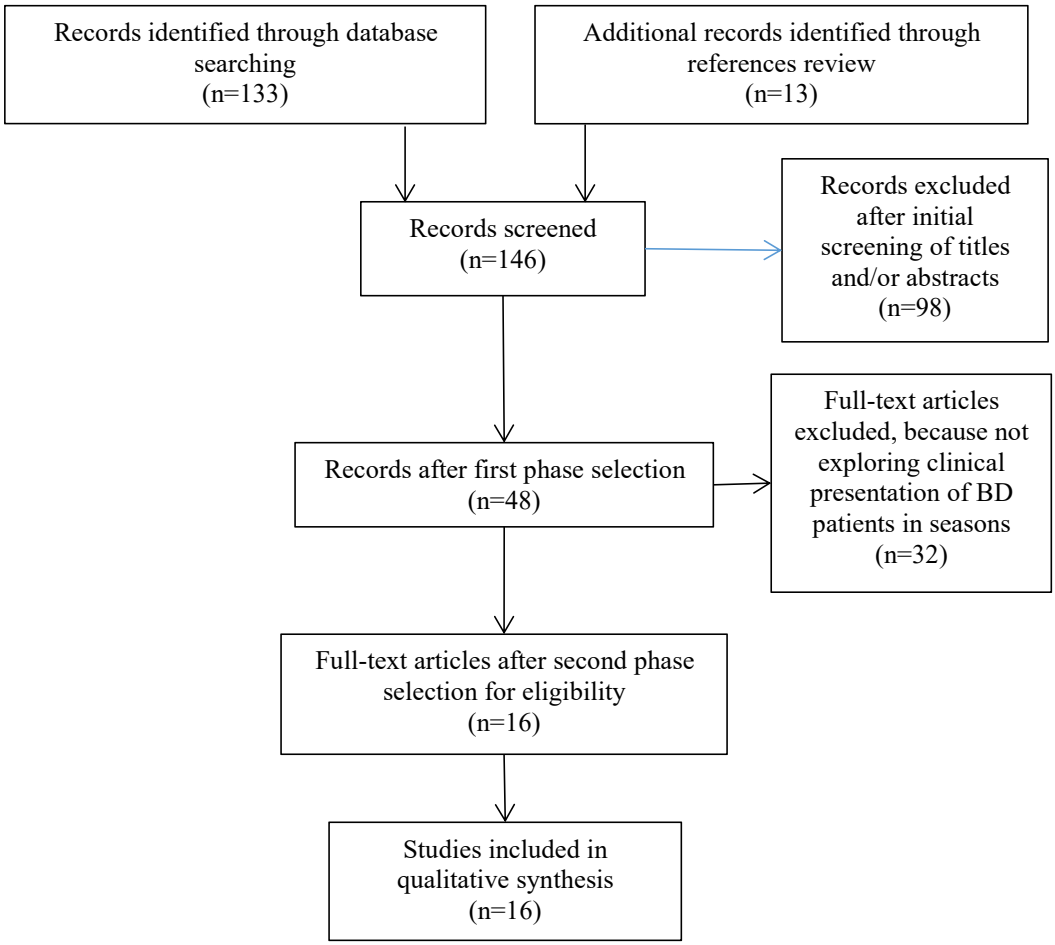

Table 1. Studies included in the systematic review by year.

Authors, year of publication	Location	Study design	Participants	Mood Status	Other characteristics	BD criteria	Seasonality criteria	Key findings
Rajajärvi et al, 2010	Finland	Case-control study	32 BD-I, 40 relatives and 50 controls	23 in full remission and 9 in partial remission	F/M= 1,29 Mean age 50,7 y.	DSM-IV	SPAQ	BD patients with seasonal variation of mood and behaviour and their relatives performed worse in the measures of visuoconstructional functions and visuospatial reasoning, auditory attention and working memory and verbal memory compared to those with no seasonal variation. Individuals tested during winter performed worse than those tested in spring, summer and autumn, in the measures of visual and verbal attention and working memory, verbal ability, verbal fluency and executive functioning.
Choi et al., 2011	South Korea	Case-control study	61 female BP and 122 female controls	Euthymic	BD-II/BD-I =1,03 Mean age 33,2 y.	DSM-IV	SPAQ	Significant association between seasonality and PMS was found in

								the patient group.
Brambilla et al., 2012	Italy	Cross-sectional study	67 BP and 46 MDD	Euthymic	Mean age 51,3 y.	DSM-IV-TR	SPAQ+	BP patients with positive family history of BP have significantly higher seasonality
Geoffroy et al., 2013	France	Case-control study	102 BP with SP+ and 350 with SP-	Euthymic	F/M = 1,76 Mean age 44,7 y.	DSM-IV	DSM-IV	SP+ was significantly more frequent among patients with BD II. Patients with SP+ were also more likely to meet criteria for rapid cycling, have a lifetime history of eating disorders and report significantly more mood episodes; especially more major depressive episodes. Patients with SP+ also had a significantly earlier age of onset of BD than patients without SP. In males, there was a significant association between SP+ and BD II subtype and total number of depressive episodes. In females, there was a significant association between SP+ and presence

								of rapid cycling and lifetime history of eating disorders.
Yang et al., 2013	Taiwanl	Cross-sectional	9619 BD	Not specified	M/F = 1,05	ICD-9-CM	EMD method	Female patients experienced a higher seasonal influence for depressive than manic episodes. Male patients experienced a higher seasonality for manic than depressive. Patients with index admission at young adulthood experienced higher seasonality than those with index admissions at middle age. Acute admissions for predominantly depressive episodes showed higher seasonality than predominantly manic episodes .
Bae et al., 2014	South Korea	Cross-sectional study	313 individuals	Not specified	F/M = 1,57 Mean age 33,5 y.	HCL-32	SPAQ	'Irritable/risk taking' symptoms (irritable, impulsive, and careless) were shown to have a more significant association with seasonality

								than ‘active/elated’ symptoms (active, elated, self-confident, and cognitively enhanced), in patients with hypomanic episodes
Baek et al., 2014	South Korea	Case-control study	103 BD-I, 97 BD-II, 270 controls	Euthymic	Age 18-45 y.	DSM-IV	SPAQ	Seasonality in BP patients was significantly associated with evening preference and irregularity of weekday bed-rise time.
Ezquiaga et al., 2014	Spain	Prospective cohort study	285 BD	Any	F/M = 1,42 Mean age = 47,8 y.	DSM-IV-TR	Not specified	SP in BD patients is strong predictor of dropout/irregular follow-up.
Kim et al., 2015	South Korea	Cross-sectional	204 BD-I and 308 BD-II	Any		DSM-IV	SPAQ	The global seasonality score on the SPAQ was significantly higher in the BD II group than in the BD I group. In the BD I group, seasonality was associated with suicide attempt history. In the BD II group, on the other hand, seasonality was associated with female gender, depressive predominance, and PMDD.

Geoffroy et al., 2015	France	Cross-sectional study	269 BD	Euthymic	SP-/SP+ = 2,84	DSM-IV	DSM-IV-TR	Patients with BD and SP demonstrated more mood recurrences, an earlier age at onset and were more associated with a BD II subtype. In contrast, no differences were observed between groups regarding gender, age, duration of BD and education levels
Ozdemiroglu et al., 2015	Turkey	Case-control study	48 BD, 32 BD-OCD, 61 OCD	Euthymic	Age 18-65 y.	DSM-IV	Not specified	Patients with BD-OCD presented higher seasonality than BD patients.
Hochman et al., 2016	Israel	Retrospectiv cohort	148 BD-I	Any		DSM-IV-TR	Not specified	SP+ of manic episode admissions was found to be associated with increased rates of male gender, psychotic features during the manic episodes and comorbid substance use disorder. The presence of psychotic features during manic episodes and male gender were predictors of a SP of manic episode admissions.

Geoffroy et al., 2017	France	Retrospective cohort study	1471 BD	Any		DSM-IV	DSM-IV-TR	SP+ patients, compared to SP– patients, were older, were BD type II diagnosis and had longer illness duration, as well as more depressive and hypomanic episodes. SP+ patients, compared to SP– patients, had higher systolic blood pressure, higher fasting glucose and increased risk of obesity.
Keskin et al., 2017	Turkey	Cross-sectional study	122 BD	Euthymic	F/M = 1,77 Mean age 38,7 y.	DSM-IV-TR	Not specified	BP patients with SP+ are over three times more likely to have poor sleep quality than those with SP-.
Altınbaş et al., 2019	Turkey	Cross-sectional study	66 BD-I	Euthymic	F/M = 1,75 Mean age 34,7 y.	DSM-IV	SPAQ	There was no statistically significant difference between patients with and without seasonality in terms of gender, age, education level, age at onset, index episode, illness duration and rapid cycling course. Depressive and anxious temperament scores were significantly

								higher in SP+ patients.
Fellinger et al., 2019	Austria	Cross-sectional study	60,607 hospital admissions of BD	Any	Mean age 47, 6 y.	ICD-10	Not specified	The influence of sex on SP, if existing at all, is relatively small. Young women (15-35 y.) seem to be more vulnerable to SP.

BD: bipolar disorder; DSM:Diagnostic and Statistical Manual of Mental Disorders; SPAQ: Seasonal Pattern Assessment Questionnaire; PMS: premenstrual syndrome; MDD: Major Depressive Disorder; SP: Seasonal Pattern; ICD: International Classification of Diseases; EMD method: empirical mode decomposition; HCL-32: Hypomania Checklist; PMDD: Premenstrual Dysphoric Disorder; OCD: Obsessive-Compulsive Disorder.

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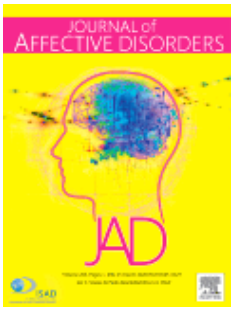

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