

Exploring Seasonality in Catatonia Diagnosis: Evidence from a Large-Scale Population Study

1. Introduction

Catatonia is a severe psychomotor syndrome that includes motor, behavioral, affective and neurovegetative symptoms and signs. According to the 11th Revision of the International Classification of Diseases (ICD-11), catatonia can be diagnosed as associated to a mental disorder, as induced by substances or medication, or as secondary to medical conditions. In 80% of cases, catatonia is thought to be associated with psychiatric disorders, such as mood disorders or schizophrenia (Oldham, 2018). In 20% of cases, non-psychiatric conditions are found as the principal cause of catatonia, including inflammatory, autoimmune, infectious and neurodegenerative disorders, as well as traumatic or drug-related conditions (Oldham, 2018; Rogers et al., 2019; Solmi et al., 2018). In spite of the diverse etiologies of catatonia, this syndrome usually responds well to treatment. Lorazepam is used as first-line medication, and in cases of treatment-resistance, electroconvulsive therapy (ECT) is recommended (Bush et al., 1996; Solmi et al., 2018). If not recognized or rapidly treated, catatonia can lead to death via numerous complications, including infections, rhabdomyolysis, and thromboembolic phenomena (Funayama et al., 2018). The pathophysiology of catatonia is still unknown, and brain mechanisms underlying this syndrome are being studied using various neuroimaging techniques (Cattarinussi et al., 2022; Magnat et al., 2022; Walther et al., 2019). Similarly, epidemiological and clinical approaches have proven to be useful in elucidating the links between environmental factors and the development of catatonia (Mastellari et al., 2023; Rogers et al., 2021; Yeoh et al., 2022).

The analysis of seasonality has been used for the study of the different risk factors involved in psychiatric disorders (Zhang et al., 2021). Seasonality studies have largely been conducted in mood disorders and schizophrenia, allowing interesting insights into pathophysiological mechanisms and etiopathogenesis (Castrogiovanni et al., 1998; Geoffroy et al., 2014; Hinterbuchinger et al., 2020; Maruani et al., 2018; McCutcheon et al., 2020). Regarding mood disorders, for example, studies of seasonality have resulted in pathophysiological theories involving the role of circadian rhythms, core clock genes, temperature and daylight hours (Ambar Akkaoui et al., 2022; Geoffroy et al., 2015, 2014). As for schizophrenia, the role of infections during the perinatal period was suggested in the light of studies of seasonality (Watson et al., 1984). Interestingly, the role of seasonality in psychiatric disorders can also be assessed clinically, at the individual level, using psychometric instruments, such as the Seasonal Pattern Assessment Questionnaire (SPAQ) (Reynaud et al., 2021).

Although still scarce, research on seasonality of catatonia might be helpful to identify the underlying mechanisms and causes of this clinical syndrome. Moreover, for many of the disorders that can cause catatonia, a seasonal pattern has been described. In terms of psychiatric causes, studies on the seasonality of mood disorders and psychosis have been replicated several times worldwide, and have shown that seasonal patterns are associated with more severe manifestations (Bauer et al., 2021; Geoffroy et al., 2013). Considering mood disorders, depressive phases have been described as more common during early winter, while manic phases have been found to be more frequent in early summer (Geoffroy et al., 2014, 2013; Partonen and Lönqvist, 1998). Similarly, studies of schizophrenia have shown a seasonal presentation of psychotic symptoms during the year (Hinterbuchinger et al., 2020; Owens and McGorry, 2003; Zhang and Volkow, 2023). Seasonality studies of other psychiatric disorders exist, but results have been far less replicated (Ambar Akkaoui et al., 2022; Geoffroy and Amad, 2016; Liang et al., 2018; Pires et al., 2022). Regarding non-psychiatric conditions, seasonal patterns are known for certain infections, as well as for the activity of the human immune system (Dopico et al., 2015; Fisman, 2007; Wyse et al., 2021), which both seem to play a role in some forms of non-psychiatric catatonia (Rogers et al., 2019).

Regarding the seasonality of catatonia, a seasonal pattern was recently described for the first time in a cohort of 955 patients, throughout ten years in South London (Mastellari et al., 2023). An initial peak of cases was found at the end of winter, and a second peak at the end of summer. It was suggested that this seasonal pattern of catatonia reflected the impact of the underlying psychiatric disorders, e.g., mood disorders, which show a similar seasonal pattern. However, no stratified analyses by the underlying disorder could be performed to confirm that hypothesis, due to insufficient statistical power and limited sample size. Moreover, the external validity was limited, as cases were limited to one geographic area.

The aim of the present study is to examine for a seasonal pattern in the onset of catatonia, extending previous findings in a larger independent sample and to perform subgroup analyses, stratifying by main associated psychiatric disorder (focusing on mood disorders and psychosis).

2. Methods

2.1. Database and study population

Catatonic cases were included using the French national hospitals database, *Programme de Médicalisation des Systèmes d'Information* (PMSI). This database includes all hospital admissions in the French territory, with details on the date of admission, length of stay, and hospital code number. In the PMSI dataset, diagnoses can be registered as main diagnosis or as associated diagnosis. Principal diagnosis is usually the main reason for admission (one code only is allowed), while associated diagnoses are often related to comorbidities, and more than one associated diagnosis is possible. Diagnoses are classified using the 10th edition of the International Statistical Classification of Diseases and Related Health Problems (ICD-10). Each patient receives a national identification number, that remains constant and unique across hospitalisations.

PMSI allows access to anonymous data, under the regulation of the national French Public Health Agency. Therefore, ethical approvals are not required when accessing this specific database (Arrêté du 19 juillet 2013; Boudemaghe and Belhadj, 2017). All procedures used in this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and follow the Declaration of Helsinki, 1975 and revised in 2008.

Hospital admissions for a diagnosis of catatonia were identified searching ICD-10 codes F061 (Catatonic disorder due to a known physiological condition) and F202 (Catatonic schizophrenia), as a principal or associated diagnostic code. Cases of catatonia were included between 2015 and 2022.

When catatonia was identified as a principal diagnosis in the PMSI dataset, other ICD-10 codes were searched for in the associated diagnoses, as follows: F20-F29 (Schizophrenia and related disorders), F30-F39 (Mood disorders), F70-F90 & F95 (Neurodevelopmental disorders), F40-F49 (Neurotic disorders), F50-F69 & F91-F94 & F98 (Personality and behavioral disorders), F10-F19 (Substance use disorders), F00-F09 & non-F codes (Other medical conditions).

When catatonia was identified as an associated diagnosis in the PMSI dataset, the other ICD-10 codes (as above) were searched for in the principal diagnosis, or in the associated diagnoses.

For this study, hospitalisations in metropolitan France only were included. Hospitalisations in the overseas departments and territories were excluded, to avoid the inclusion of hospitals where seasons are extremely different over the course of the year.

2.2. Statistical analyses

Descriptive analyses were performed using absolute numbers and percentages for qualitative variables and median and interquartile range (IQR) for quantitative variables.

Analyses were performed using *R* Studio version 4.4.2., and the *season* package version 0.3.15., which examines seasonal trends using a cosinor model (Hughes, 2022).. After identifying a seasonal pattern, a linear regression model was performed to detect peaks (with β as the coefficient). Analyses of seasonal patterns were repeated in two main diagnostic subgroups: schizophrenia and related disorders, and mood disorders, as they are more frequently associated with catatonia (Solmi et al., 2018). For these subgroup analyses, patients suffering with both schizophrenia and mood disorders were excluded. Analyses of seasonality were also performed considering hospital admissions for any psychiatric disorder in metropolitan France, to look for a global seasonal pattern that might explain a seasonal pattern for catatonia. Data extraction was performed using SAS Enterprise Guide.

3. Results

A total of 17,996 hospitalisations for catatonia were found between 2015 and 2022, in metropolitan France, corresponding to 6,225 unique patients. A number of 3,215 patients (51.6%) were included with a diagnostic code F061, while 2,664 patients (42.8%) were included as F202, and 346 patients (5.6%) were identified having both F061 and F202.

The evolution of the number of diagnoses of catatonia is presented in Figure 1. The number of diagnoses in metropolitan France increased from 2015 to 2018 (+8.09% in 2016, +6.80% in 2017 and +3.42% in 2018), then decreased from 2019 to 2021 (-0.55% in 2019, -5.74% in 2020 and -4.85% in 2021), and finally increased again in 2022 (+1.39%).

Figure 1. Number of patients diagnosed with catatonia in metropolitan France by month, from 2015 to 2022. The number of diagnoses increased from 2015 to 2018 (+8.09% in 2016, +6.80% in 2017 and +3.42% in 2018), then decreased from 2019 to 2021 (-0.55% in 2019, -5.74% in 2020 and -4.85% in 2021), and finally increased again in 2022 (+1.39%).

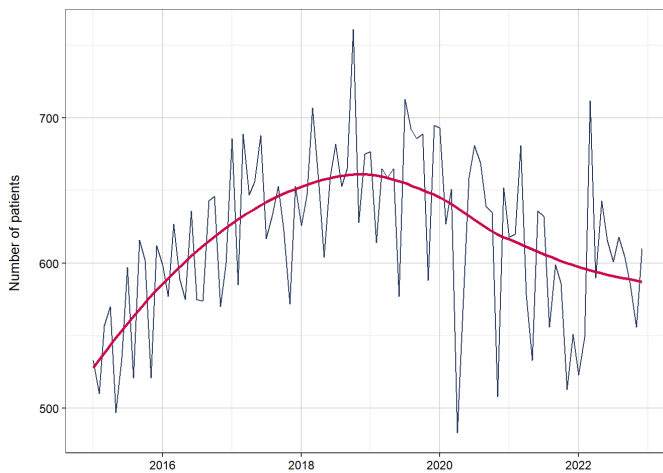


Table 1 shows the number of patients with an associated diagnosis to catatonia, with their socio-demographic characteristics, and according to the diagnostic subgroup. It is to be noted that each patient could be registered with more than one associated diagnosis, explaining the total percentage above one hundred.

Table 1. Socio-demographic and clinical characteristics of patients with a catatonia diagnosis

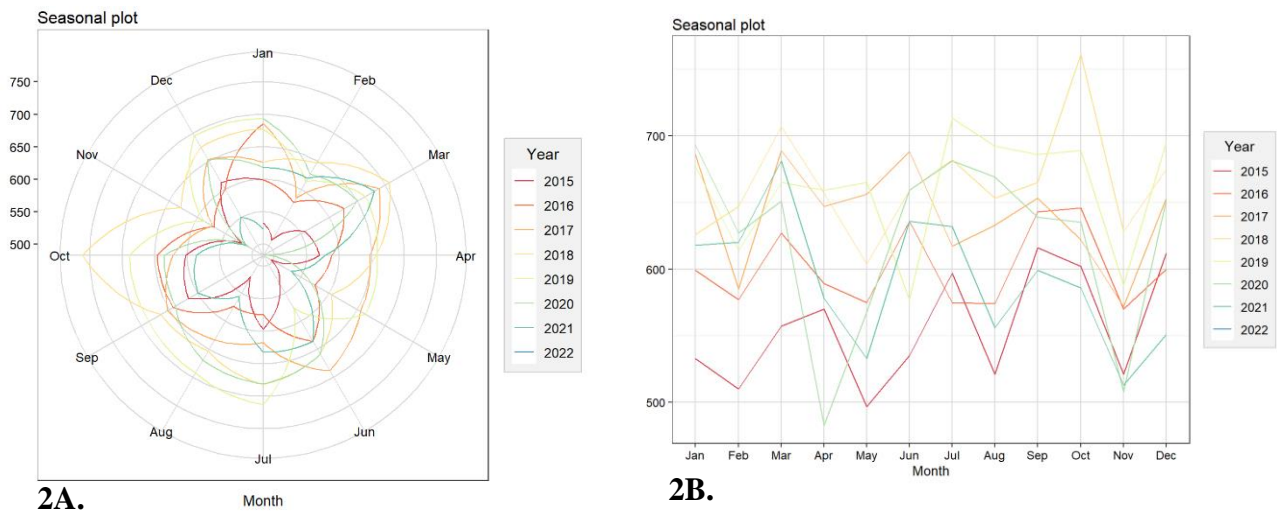
	Number (%)*	Age, Median (IQR)	Sex (Female), <i>n</i> (%)
Catatonia	6,225 (100)	55 (37-69)	3,348 (53.8)
Diagnosis associated to Catatonia			
Mood disorders (F30-F39)	1,621 (26.0)	64 (53-74)	1,074 (66.3)
Schizophrenia and related disorders (F20-F29)	830 (13.3)	53 (36-64)	445 (53.6)
Neurotic disorders (F40-F49)	792 (12.7)	59 (41.5-73)	506 (63.9)
Substance use disorders (F10-F19)	518 (8.2)	51.5 (38-61)	177 (34.2)
Personality and behavioral disorders (F50-F69 & F91-F94, F98)	584 (9.4)	52 (32.5-66.5)	345 (59.1)
Neurodevelopmental disorders (F70-F90 & F95)	237 (3.8)	34 (17-53)	121 (51.1)
Other medical conditions (F00-F09 & non-F codes)	4,722 (75.9)	57 (40-69)	2,521 (53.4)

*As more than one associated diagnosis is possible, the total percentage for this column is > 100%.

A number of 4,722 patients (75.9%) had at least a diagnosis of a medical condition (F00-F09 and non-F codes) (Table 1). However, 2,711 of these patients (43.6% of the total sample) had a diagnosis of a medical condition alone, associated to catatonia (Figure S1, in Supplementary Materials). Similarly, 2,011 out of the 4,722 patients (32.3% of the total sample) had both a diagnosis of a medical condition, and a diagnosis of a psychiatric disorder (F30-F39, F20-F29, F40-F49, F10-F19, F50-F69, F91-F94, F98, F70-F90, F95) (Figure S1). Finally, 1,503 patients out of 6,225 (24.1%) had received only one or more diagnoses of a psychiatric disorder (Figure S1). The full list of codes for “Other medical conditions” is showed in Supplementary materials, Table S1.

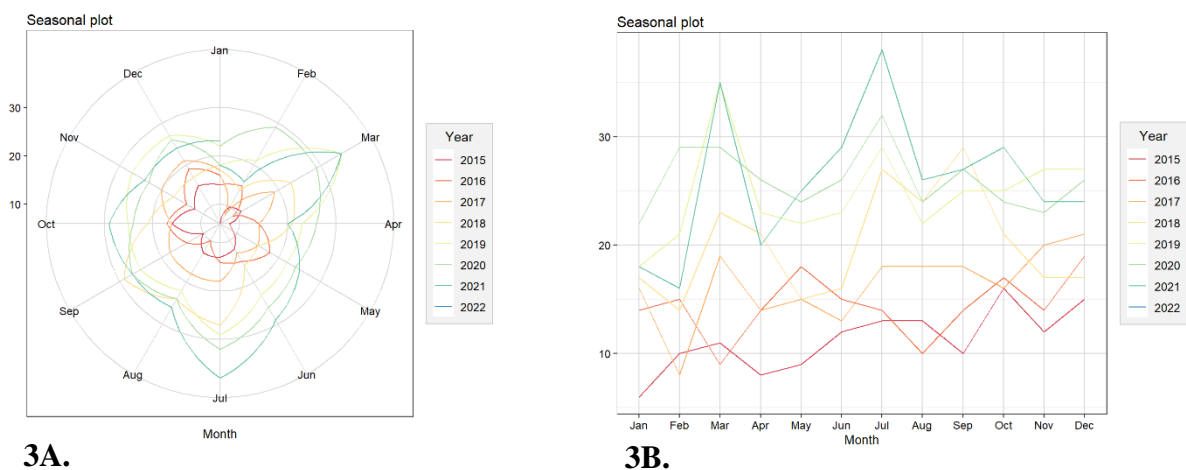
Regarding seasonality, a significant seasonal pattern by month for catatonia was found ($p < 0.001$). A first peak of cases is showed in March ($\beta = 661.12$, $p < 0.01$). Then, cases increase during summer with a second peak in September-October ($\beta = 638.12$, $p < 0.01$, $\beta = 640.75$, $p < 0.01$) (see Figure 2).

Figure 2. Number of hospitalisations for catatonia in metropolitan France by month, from 2015 to 2022, using a polar plot (2A) and a line chart (2B).



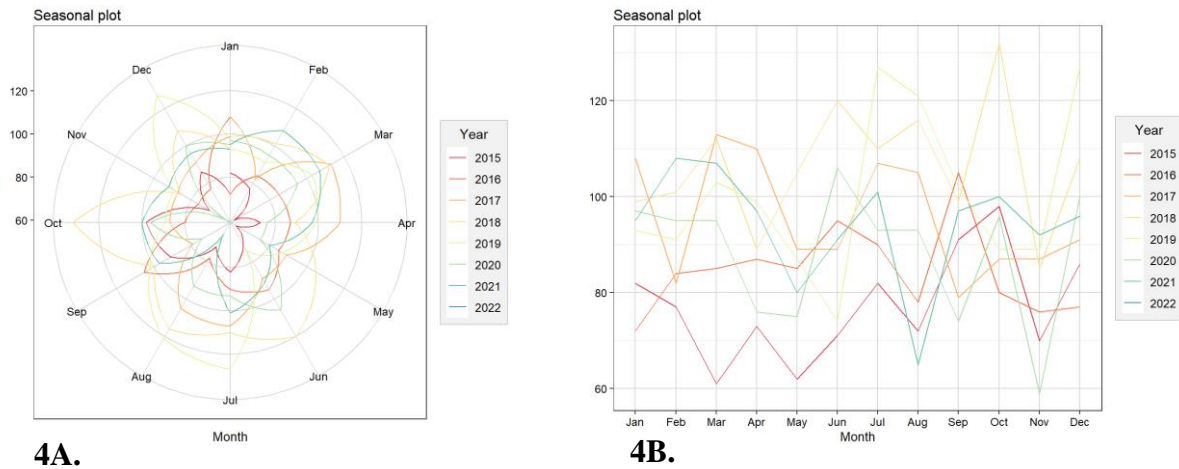
A significant seasonal pattern by month was found for patients with a diagnosis of catatonia and suffering with mood disorders ($p = 0.03$). A first peak of cases is showed in March ($\beta = 24.50$, $p < 0.001$). Then, cases increase during summer with a second peak in July ($\beta = 25.87$, $p < 0.001$) (see Figure 3).

Figure 3. Number of hospitalisations for catatonia in metropolitan France by month, from 2015 to 2022, for patients suffering with mood disorders, using a polar plot (3A) and a line chart (3B).



No significant seasonal pattern by month was found for patients with a diagnosis of catatonia and suffering with schizophrenia and related disorders ($p = 0.07$) (Figure 4).

Figure 4. Number of hospitalisations for catatonia in metropolitan France by month, from 2015 to 2022, for patients suffering with schizophrenia and related disorders, using a polar plot (4A) and a line chart (4B).



Analyses of seasonality were repeated for all psychiatric admissions to French hospitals, from 2015 to 2022 (Figure S2, in Supplementary Materials). No seasonal patterns were found ($p = 0.30$).

4. Discussion

To our knowledge, this study in metropolitan France from 2015 and 2022 ($n = 6,225$) is the first to examine the seasonality of catatonia on a national scale and the first to stratify by the main associated psychiatric disorder.

We showed a general increase in the number of diagnosis of catatonia, from 2015 to 2022, as described by other recent studies performed in South London (Mastellari et al., 2023; Rogers et al., 2021). The slight decrease observed during the COVID-19 pandemic might be explained by the underuse of healthcare systems and the diminished hospital admissions for all psychiatric and non-psychiatric reasons at that time (Tuppin et al., 2022). The main hypothesis regarding the increase of admissions for catatonia from 2015 to 2022 includes better recognition and increased research interest around this syndrome (Hirjak and Northoff, 2023; Weleff et al., 2023).

We identified two main peaks of diagnosis of catatonia in March and around September-October. Interestingly, two peaks were also found in a recent seasonality study, performed in South London, in which a first peak of cases was described at the end of winter (February), and a second peak at the end of the summer (August) (Mastellari et al., 2023). Although various hypotheses might explain why catatonia diagnosis presents a seasonal pattern (Mastellari et al., 2023), one of the main factors explaining this seasonality might include the role of the underlying psychiatric disorder, as catatonia

is a common clinical end-point for several mental illnesses, explaining about 80% of the causes of this syndrome.

When stratifying for patients diagnosed with catatonia suffering with mood disorders (unipolar depression or bipolar disorder), a first peak of cases is found after the end of winter (peak in March), and a second peak in mid-summer (peak in July). This is consistent with previous studies on mood disorders where depressive episodes were found to be more common in winter, and manic phases in summer (Geoffroy et al., 2014).

When analysing seasonal patterns for patients diagnosed with catatonia and schizophrenia, no significant seasonal effect is found. Previous studies on the seasonality of schizophrenia exist, but results are less homogeneous compared to mood disorders. Kazuhiko Abe, 1963 (Abe, 1963) found that peaks of admissions for affective disorders occurred about a month earlier than for schizophrenia, but this was not confirmed by further studies (Takei et al., 1992). Peaks in both winter and summer were described for schizophrenia in a few studies, and various hypotheses developed, including the role of temperature and weather, photoperiod, neurobiological changes and social factors (Hinterbuchinger et al., 2020; Owens and McGorry, 2003; Zhang and Volkow, 2023). However, it is noteworthy that we excluded patients with both schizophrenia and mood disorders, and we could not identify any affective symptoms that might be associated with schizophrenia, thus influencing the seasonal pattern.

One of the hypotheses to explain more diagnosis of catatonia during summer is the increased number of admissions for all psychiatric reasons during the warmest months (Nori-Sarma et al., 2022). However, in our study we explored the seasonality of admissions to hospital for all psychiatric disorders, and no significant pattern was found. To our knowledge, there are no studies having evaluated if countries with warmer weathers register higher prevalence of catatonia, compared to other countries.

Several limitations of the present study should be acknowledged. There is a possible delay of several days or even weeks in some cases between the date of admission and the date of registration of the diagnosis, which would generate a measurement bias. However, in our study we did not consider dates of registration, and we included dates of admission only. Underestimation of catatonic cases is also highly probable, due to under-reporting, under-coding or misdiagnosis during clinical practice (Jaimes-Albornoz and Serra-Mestres, 2013; Mustafa and Nayar, 2020; van der Heijden et al., 2005). However, this underdiagnosis issue is not expected to differ between seasons and therefore impact our analyses. Similarly, outpatients with a diagnosis of catatonia were not included in this study. However, catatonia usually requires rapid inpatient treatment, and cases of catatonia diagnosed in

outpatient settings are likely to be transferred shortly to hospital. Moreover, we did not include in our model meteorological variables such as temperature, hours of sunshine, percentage of humidity or pollution data, which could be interesting factors to adjust for in future studies. Further research should try to extend these findings to other countries and continents, to test the impact of different latitudes. Similarly, considering the seasonal pattern for catatonia diagnosis in patients suffering with mood disorders, it would be interesting to explore if seasonal affective disorder is particularly linked to this syndrome. Finally, the seasonality of catatonia might also be assessed on the individual clinical level, allowing correlation with concomitant psychiatric symptoms and catatonic subtypes (e.g., periodic catatonia or catatonia resistant to benzodiazepine treatment).

In terms of external validity, it is important to note that in our sample a psychiatric diagnosis was associated with catatonia in 24.1% of cases, a medical condition diagnosis was associated with catatonia in 43.6% of cases, and both diagnoses were associated with catatonia in 32.3% of cases. These proportions are quite different compared to what is described in the literature (Oldham, 2018), and generalisation of our findings should be considered with caution. However, ICD-10 codes for “Other medical conditions” represent not only medical causes of catatonia, but also comorbidities and complications of catatonia (e.g., venous thromboembolism, dehydration, pressure ulcers, acute renal failure), that cannot be differentiated with the PMSI dataset. Therefore, if the internal validity for seasonality analyses remain solid, external validity might be considered carefully, and further seasonality studies in different countries and settings are needed.

Finally, in our study we did not include catatonic cases due to drugs or medication, as ICD-10 codes Y49.3, Y49.4 and Y49.5 (Medical complications of phenothiazine antipsychotics, butyrophenone and thioxanthene neuroleptics, and other antipsychotics), are not specific enough to detect catatonia. Further studies using ICD-11 codes might further develop this aspect.

In terms of perspectives, studies on seasonality represent an epidemiological approach to better understand the link between the environment and the development of catatonia. Secondly, health care services might consider adapting their resources to the peaks of catatonic cases, in particular where access to electroconvulsive therapy is limited.

5. Conclusion

In this study on the seasonality of catatonia performed in metropolitan France, we showed that a seasonal pattern exists in the diagnosis of this syndrome during the year. Two main peaks were described, in March and around September-October, for all causes of catatonia. However, seasonal patterns differ according to the main associated psychiatric disorder. In patients with mood disorders, peaks of diagnosis of catatonia were identified after the end of winter (March) and in summer (July), as hypothesised based on previous literature. In patients suffering with schizophrenia, no seasonal pattern was found.

Declaration of interests

This study was not funded. We declare no competing interests.

CRediT authorship contribution statement

Tomas Mastellari: Conceptualization, Methodology, Writing – original draft, Writing – review and editing. **Chloé Saint-Dizier:** Data curation, Formal analysis, Methodology, Writing – review and editing. **Thomas Fovet:** Methodology, Writing – review and editing. **Pierre-Alexis Geoffroy:** Writing – review and editing. **Jonathan Rogers:** Writing – review and editing. **Antoine Lamer:** Data curation, Formal analysis, Methodology, Writing – review and editing. **Ali Amad:** Conceptualization, Methodology, Writing – review and editing.

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