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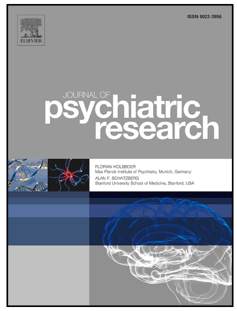

Association between solar insolation and a history of suicide attempts in bipolar I disorder

Michael Bauer, Tasha Glenn, Martin Alda, Ole A. Andreassen, Elias Angelopoulos, Raffaella Ardau, Yavuz Ayhan, Christopher Baethge, Rita Bauer, Bernhard T. Baune, Claudia Becerra-Palars, Frank Bellivier, Robert H. Belmaker, Michael Berk, Yuly Bersudsky, Şule Bicakci, Harriet Birabwa-Oketcho, Thomas D. Bjella, Jorge Cabrera, Eric Y. Wo Cheung, Maria Del Zompo, Seetal Dodd, Markus Donix, Bruno Etain, Andrea Fagiolini, Kostas N. Fountoulakis, Mark A. Frye, Ana Gonzalez-Pinto, John F. Gottlieb, Paul Grof, Hirohiko Harima, Chantal Henry, Erkki T. Isometsä, Sven Janno, Flávio Kapczinski, Mathias Kardell, Slim Khaldi, Sebastian Kliwicki, Barbara König, Timur L. Kot, Rikke Krogh, Mauricio Kunz, Beny Lafer, Mikael Landén, Erik R. Larsen, Ute Lewitzka, Rasmus W. Licht, Carlos Lopez-Jaramillo, Glenda MacQueen, Mirko Manchia, Wendy Marsh, Mónica Martinez-Cengotitabengoa, Ingrid Melle, Fátima Meza-Urzúa, Mok Yee Ming, Scott Monteith, Gunnar Morken, Enrica Mosca, Anton A. Mozzhegorov, Rodrigo Munoz, Starlin V. Mythri, Fethi Nacef, Ravi K. Nadella, Fabiano G. Nery, René E. Nielsen, Claire O'Donovan, Adel Omrani, Yamima Osher, Helle Østermark Sørensen, Uta Ouali, Yolanda Pica Ruiz, Maximilian Pilhatsch, Marco Pinna, Francisco D.R. da Ponte, Danilo Quiroz, Raj Ramesar, Natalie Rasgon, M.S. Reddy, Andreas Reif, Philipp Ritter, Janusz K. Rybakowski, Kemal Sagduyu, Bharathram Sathur Raghuraman, Ângela M. Scippa, Emanuel Severus, Christian Simhandl, Paul W. Stackhouse, Jr., Dan J. Stein, Sergio Strejilevich, Mythily Subramaniam, Ahmad Hatim Sulaiman, Kirsi Suominen, Hiromi Tagata, Yoshitaka Tatebayashi, Leonardo Tondo, Carla Torrent, Arne E. Vaaler, Edgar Vares, Julia Veeh, Eduard Vieta, Biju Viswanath, Maria Yoldi-Negrete, Mark Zetin, Yosra Zgueb, Peter C. Whybrow

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Abstract

In many international studies, rates of completed suicide and suicide attempts have a seasonal pattern that peaks in spring or summer. This **exploratory** study investigated the association between solar insolation and a history of suicide attempt in patients with bipolar I disorder. **Solar insolation is the amount of electromagnetic energy from the sun striking a surface area on earth.** Data were collected previously from 5536 patients with bipolar I disorder at 50 collection sites in 32 countries at a wide range of latitudes in both hemispheres. Suicide related data were available for 3365 patients from 310 **onset** locations in 51 countries. 1047 (31.1%) had a history of suicide attempt. There was a significant inverse association between a history of suicide attempt and the ratio of mean winter solar insolation/mean summer solar insolation. This ratio is smallest near the poles where the winter insolation is very small compared to the summer insolation. This ratio is largest near the equator where there is relatively little variation in the insolation over the year. Other variables in the model that were positively associated with suicide attempt were being female, a history of alcohol or substance abuse, and being in a younger birth cohort. Living in a country with a state-sponsored religion decreased the association. (All estimated coefficients **$p<0.01$**). In summary, living in locations with large changes in solar insolation between winter and summer may be associated with increased suicide attempts in patients with bipolar disorder. Further investigation of the impacts of solar insolation on the course of bipolar disorder is needed.

Keywords: Bipolar disorder, suicide, sunlight, solar insolation, seasonal variation

Association between solar insolation and a history of suicide attempts in bipolar I disorder

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1. Introduction

Patients with bipolar disorder have a very high risk of suicidal behavior with about 1/3 of patients attempting suicide at least once (Novick et al., 2010; Tondo et al., 2016). A complex interplay of diverse factors contribute to suicidal behavior, including cultural, socioeconomic, genetic, stressful life experiences, the course of bipolar disorder and physical health (Schaffer et al., 2015; Tondo et al., 2016). Research has also found a relation between environmental factors and suicide rates. Many international studies of the general population have reported a seasonal variation in completed suicide and suicide attempts with peak rates in spring or summer (**Barker et al., 1994;** Christodoulou et al., 2012; Coimbra et al., 2016; Dixon and Kalkstein, 2018; Woo et al., 2012; Galvão et al., 2018; Odagiri et al., 2011; Petridou et al., 2002**)**. Seasonality in suicide may be associated with a prior psychiatric diagnosis (Postolache et al., 2010; Reutfors et al., 2009; Rocchi et al., 2007).

This association of suicide rates with environmental factors is of considerable concern since circadian rhythm disturbances are found in many psychiatric illnesses, including bipolar disorder (Carr et al., 2018; Jagannath et al., 2013; Jones and Benca, 2015; Logan and McClung, 2019). Although strongly linked, the relationship between circadian disruption and the development and course of bipolar disorder is complex, bidirectional and not understood (Bechtel 2015; Harvey, 2008; Ketchesin et al., 2018; Logan and McClung, 2019; McCarthy, 2018; McCarthy and Welsh, 2012; Oliveira et al., 2018**). Circadian disturbances that occur frequently in bipolar disorder include** alterations to the sleep/wake cycle and daily hormonal secretion, and misalignments between external time and social activities (Abreu and Bragança, 2015; Bellivier et al., 2015; Talih et al., 2018; Wirz-Justice, 2006). **While symptoms of circadian disruption are most prominent during episodes of mania or depression**, **many occur** when patients are euthymic including **sleep disturbances, irregular social rhythms, preference for evening activities, and abnormalities in melatonin secretion** (**Alloy et al., 2017; Melo et al., 2017; Ng et. al., 2015;** Soreca, 2014; Takaesu, 2018). About one-fourth of patients with bipolar disorder experience a seasonal pattern in episode type, with manic episodes peaking in spring/summer and depression in winter (Geoffroy et al., 2014; 2015). Hospitalizations for mania are more numerous in spring/summer than in winter (Aguglia et al., 2017; Geoffroy et al., 2014). Some treatments for bipolar disorder may directly or indirectly target the circadian system (Bellivier et al., 2015; McClung, 2007).

Analyzing a large global sample, we previously found a strong, inverse relation between the maximum monthly increase in solar insolation in springtime and the age of onset of bipolar I disorder (Bauer et al., 2012; 2014; 2017), where solar insolation is defined as the amount of electromagnetic energy from the Sun striking a surface area of the Earth, expressed in kilowatt hours/square meter/day (kWh/m^2/day) (Stackhouse et al., 2018). **This replicated finding suggests that some patients with bipolar disorder may have difficulty adjusting to an environmental challenge to the circadian system.** The purpose of this **exploratory** post-hoc analysis was to investigate if solar insolation was associated with a history of suicide attempts in patients with bipolar I disorder, using the data previously collected.

2. Methods

2.1 Data collection

Data were collected between 2010 and 2016 by researchers at 50 sites in 32 countries to study the effects of solar insolation on the age of onset of bipolar disorder (Bauer et al., 2017). The database contains information on **7392 patients** of which 5536 patients **have** a diagnosis of bipolar I disorder based on DSM-IV criteria. Data were obtained by patient questioning, record review or both. Study approval, **including for data collection,** was obtained according to local requirements, using local institutional review boards. To maximize global participation, the database only includes minimal clinical data. Three locations were collected for every patient: birth location, onset location of bipolar disorder, and current location. Details about the project methodology were published previously (Bauer et al., 2012; 2014; 2017).

The 50 collection sites are in both the northern and southern hemispheres: Aalborg, Denmark; Aarhus, Denmark; Adelaide, Australia; Ankara, Turkey; Athens, Greece; Bangalore, India; Barcelona, Spain; Beer Sheva, Israel; Buenos Aires, Argentina; Cagliari, Sardinia, Italy (2 sites); Calgary, Canada; Cape Town, South Africa; Dresden, Germany; Halifax, Canada; Helsinki, Finland; Hong Kong; Hyderabad, India; Kampala, Uganda; Kansas City, KS, USA; Khanti-Mansiysk, Russia; Kuala Lumpur, Malaysia; Los Angeles, CA, USA; Medellín, Colombia; Melbourne/Geelong, Australia; Mexico City, Mexico; Oslo, Norway; Ottawa, Canada; Palo Alto, CA, USA; Paris, France; Porto Alegre, Brazil; Poznan, Poland; Rochester, MN, USA; San Diego, CA, USA; Santiago, Chile (2 sites); Salvador, Brazil; São Paulo, Brazil; Siena, Italy; Singapore;

Stockholm/Gothenburg, Sweden; Tartu, Estonia; Thessaloniki, Greece; Tokyo, Japan; Trondheim, Norway; Tunis, Tunisia; Vitoria, Spain; Wiener Neustadt, Austria; Worcester, MA, USA, and Würzburg, Germany.

2.2 Solar Insolation

The NASA POWER database provides global 35+ year average monthly solar insolation data based on satellite observations collected between 1983 and the present (Stackhouse et al., 2018). This study uses a 22-year climatology of solar insolation spanning 1983 to 2005 at a spatial resolution of 1º x 1º latitude/longitude. The pattern of monthly solar insolation varies by latitude during the course of a year, with little change at the equator and the greatest change near the north and south poles. Local conditions including cloud cover, aerosols (including dust and pollution), water vapor amounts, and altitude result in very different solar insolation for locations at the same latitude. **For example, Nice, France at latitude 43.70 N, and Toronto, Canada at latitude 43.67 N have the same hours of daylight but receive different solar insolation due to local conditions.**

For every location, monthly and seasonal variables were created using the monthly solar insolation averages. The ratio of the mean northern hemisphere winter (December, January, February) to mean summer (June, July, August) insolation was calculated as mean winter insolation/mean summer insolation. The insolation data from the southern hemisphere were shifted by 6 months for comparison to data from the northern hemisphere to account for the seasonal cycle.

2.3 Country data

A variety of socioeconomic variables were investigated including the physician density of any specialty per 1000 population, psychiatrists per 100,000, GDP per capita, total healthcare spending as a percent of GDP, the Gini index of income inequality, and the country median age (CIA World Factbook, 2016; WHO, 2005). Data were also obtained on whether the country has a state-sponsored or officially favored religion (Pew Research, 2017).

2.4 Statistics

The generalized estimating equations (GEE) statistical technique was selected to account for both the correlated data and unbalanced number of patients at the international collection sites. The GEE uses a population averaged or marginal approach, estimating the dependent variable as a function of the covariates across the entire population rather than within a cluster (Zeger and Liang, 1986). The GEE models were estimated using a binomial distribution, exchangeable working correlation matrix and a logit link function. In all models, a history of suicide attempts was the dependent variable. **Several approaches were used to select the variables and the best model.** The potential variables from univariate analyses that were significant at a level of 0.05, **and variables found in prior suicide research** were entered into multivariate models. The corrected quasi-likelihood independence model criterion was used to assist with multivariate model fitting (Pan, 2001). The odds ratios and confidence intervals generated by the GEE are reported. A significance level of 0.01 was used for multivariate model evaluation **to reduce the chance of type I errors.** Demographic variables were reported using descriptive statistics. SPSS version 24.0 was used for all analyses.

3. Results

3.1 Patient demographics and locations

There were 5536 patients with **a diagnosis of** bipolar I disorder in the database, **of which a history of suicide was available for 3897 patients.** However, only 3365 patients were included in the analysis after eliminating those who did not have all five variables in the final model. **All 532 patients eliminated for not having the five variables were missing only one variable. Of the 532 patients, all but 2 were missing a history of alcohol or substance abuse data.** Of the 3365 patients **in the final model,** 1908 (56.7%) were female**,** 1457 (43.3%) were male, and 1047 (31.1%) had a history of suicide attempt. The demographic characteristics of the 3365 patients are shown in Table 1. The birth cohort groups from our prior analyses were used, with 4.8% born before 1940, 29.1% born between 1940-1959, and 66.1% born 1960 or later (Bauer et al., 2012; 2014; 2015; 2017).

The onset location was used in all analyses. Of the 3365 patients, the onset location country and current country was the same for 3286 (97.7%), and the onset location city and current city was the same for 2746 (81.6%). For the 3365 patients, the onset of bipolar disorder occurred in 310 locations in 51 countries. **The larger number of onset locations than collection sites is consistent with worldwide migration into urban**

areas (WHO 2018). The onset locations represent a wide range of latitudes in the northern and southern hemispheres as shown in Table 2. Each location contained a mean of 11 patients, with 5.3% of the 3365 patients in a location of one.

3.2 Ratio of mean winter solar insolation/mean summer solar insolation

In locations that are near the poles, the mean solar insolation in winter is very small when compared to the summer solar insolation, resulting in a very small ratio. For example, the ratio was 0.067 for Trondheim, Norway and 0.095 for Khanti-Mansiysk, Russia. In contrast, locations near the equator have little change in winter and summer insolation and a ratio near 1, such as 1.140 for Kampala, Uganda and 1.056 for Singapore. See Table 2. Log transformation of the ratio was not required.

3.3 Model results

The best fitting model for a history of suicide attempts is shown in Table 3. This model includes the ratio of mean winter solar insolation/mean summer solar insolation, gender, history of alcohol or substance abuse, living in a country with a state-sponsored or favored religion, and birth cohort. The estimated coefficients suggested that a 0.1 percent increase in the ratio of mean winter to summer insolation will decrease the odds of a suicide attempt by about 4.9%. Comparing the largest ratio (near the equator) to the smallest ratio (near the north pole), there was a 49% decrease in the odds of a suicide attempt. Being male will decrease the odds of a suicide attempt by 47%, and living in a country with a state-sponsored or favored religion will decrease the odds by 32%. Having a history of alcohol or substance abuse will increase the odds of a suicide attempt by 66%. Being in the youngest birth cohort will increase the odds of a suicide attempt by 116%, and being in the middle birth cohort will increase the odds by 97%.

The other solar insolation and socioeconomic values were not significant or the model results not as meaningful.

4. Discussion

In this global sample, 31% of the patients with bipolar I disorder have a history of suicide attempt, similar to prior research (Tondo et al., 2016; Vieta et al., 2018). The ratio of the mean winter solar insolation/mean summer solar insolation was inversely associated with an increased risk of suicide attempts. Patients from locations with smaller differences between mean winter and summer insolation such as near the equator (high ratio) had fewer suicide attempts, while those from locations with larger differences between mean winter and summer insolation (small ratio) had more suicide attempts. In the general population, suicide is a major public health challenge in polar regions with very high rates in places such as Greenland, arctic areas of Canada and Russia, and Alaska (Alaska Epidemiology, 2013; Bjerregaard and Larsen, 2015; Lehti et al., 2009; Young et al., 2015), and higher than national suicide rates in southernmost Argentina and Chile (Bustamante et al., 2016; Lawrynowicz and Baker, 2005).

There are few studies of solar radiation and suicide rates in the general population, with all studies occurring within a single country. Increased solar radiation in spring and summer was associated with an increased suicide rate in South Korea (Jee et al., 2017), and increased solar radiation may precede suicidal acts in Germany and Greece (Müller et al., 2011; Papadopoulos et al., 2005). The cumulative low solar radiation during the long northern winter was associated with an increased risk of suicide in Finland (Ruuhela et al., 2009). Several additional lines of evidence suggest that solar insolation may be associated with suicide attempts.

4.1 Fundamental importance of sunlight

Sunlight has broad impacts on human physiology and behavior (Munch et al., 2017; Wirz-Justice, 2006). Humans have adapted to the 24 hour light-dark cycles on Earth by developing a complex, hierarchical endogenous circadian system that is involved in virtually all physiological processes, tissue homeostasis and cellular functions (AMA, 2012; Richards and Gumz, 2013; Rosenwasser and Turek, 2015). The circadian system includes a central pacemaker in the suprachiasmatic nucleus (SCN) of the hypothalamus, and extends to circadian clock genes throughout the brain and all peripheral tissues (Rosenwasser and Turek, 2015). Although the periodicity of the endogenous circadian system is near 24 hours, daily entrainment is required to maintain alignment with the natural environment (AMA, 2012). Light is the primary signal that entrains the human circadian system to the environment, allowing for anticipation and adaptation to environmental and seasonal changes (AMA, 2012; Roenneberg and Merrow, 2016; Silver and Lesauter, 2008). Entrainment involves a small subset of melanopsin-expressing inner retinal ganglion cells, not involved in image formation, that detect fluctuations in the intensity of environmental light and project to the brain including the SCN (Berson et al., 2002; Hatori and Panda, 2010). The melanopsin system is involved in many other non-image forming responses to light, including melatonin suppression, sleep regulation, the pupillary light response, and enhancing alertness (Benarroch, 2011; Berman et al., 2018; Ksendzovsky et al., 2017; Warthen and Provencio, 2012). Circadian health requires both external synchronization with the environment and internal synchronization of central and peripheral clocks (Roenneberg and Merrow, 2016; Rosenwasser and Turek, 2015)

4.2 Seasonal variations in neurotransmitters

There are seasonal variations in the neurotransmitters involved in mood regulation, and these changes may be triggered by sunlight (Christodoulou et al., 2012; Petridou et al., 2002). It is postulated that complex interactions involving genetic vulnerabilities, circadian signaling pathways and altered neurotransmitter homeostasis may modify the seasonal response in bipolar disorder, and that seasonal variations in neurotransmitter expression may trigger switches between mood states (Maruani et al., 2018; Young and Dulcis, 2015).

Many studies focus on serotonin. In studies primarily of healthy humans, serotonin turnover by the brain is lowest in winter (Lambert et al., 2002), serotonin metabolite levels in cerebrospinal fluid peak in spring (Brewerton et al., 2018; Luykx et al., 2012), and brain serotonin transporter binding density, which increases with lower synaptic levels, is higher in fall and winter (Praschak-Rieder et al., 2008). There is also diurnal variation in brain serotonin receptors and transporters levels associated with the hours of daylight (Matheson et al., 2015). Serotonin is the neurotransmitter most frequently linked with aggressive and suicidal behavior (Coccaro et al., 2015; Manchia et al., 2017; van Heeringen and Mann, 2014). One hypothesis is that serotonergic medications may enhance the association between sunlight and suicide in the short term (Makris et al., 2016). Studies of dopamine synthesis and turnover report inconsistent seasonal changes with some finding higher dopamine in summer (Aumann et al., 2016; Tsai et al., 2011) and others in winter (Brewerton et al., 2018; Eisenberg et al., 2010). There are also seasonal changes in the neurotransmitter modulator BDNF with serum levels increasing in spring and decreasing in winter (Molendijk et al., 2012).

Vitamin D is a neurosteroid that modulates multiple functions in the developing and adult brain (Cui et al., 2017; Groves et al., 2014). Seasonality is also found in vitamin D levels globally, with lowest levels in winter in most age groups in most areas (Mithal et al., 2009). Vitamin D deficiency may be associated with mental disturbances including bipolar disorder and depression (Boerman et al., 2016; Lerner et al., 2018; Parker et al., 2017; Spedding, 2014), and an increased risk of suicide (Grudet et al., 2014; Umhau et al., 2013).

4.3 Consistency of other variables with prior research

The other variables associated with a history of suicide attempts in this analysis are consistent with prior research. A strong association between alcohol and substance abuse and a history of suicide attempts was found in patients with bipolar disorder (Carrà et al., 2014; Østergaard et al., 2017; Tidemalm et al., 2007), and in international studies of the general population (Borges and Loera 2010; Norström and Rossow, 2016; Pompili et al., 2010) including in low- and middle-income countries (Breet et al., 2018). This strong association is of considerable concern given the high prevalence of alcohol and substance abuse in patients with bipolar disorder (Hunt et al., 2016). More frequent suicide attempts by females than males were also noted in studies of bipolar disorder and of the general population (Borges et al. 2010; Schaffer et al., 2015; Tondo et al., 2016).

The finding that living in a country with a state-sponsored or preferred religion decreases the risk of suicide attempts also concurs with international research. Review articles including all major world religions have reported that the prevalent religion has a strong cultural impact, that suicide rates are lower in religious countries, and that religion may be protective against suicide and suicide attempts (Bertolote and Fleischmann, 2002; Lawrence et al., 2016; Norko et al., 2017; Stack and Kposowa, 2011; Wu et al., 2015). The finding of increasing risk of suicide attempts in younger birth cohorts is consistent with well established birth cohort effects of increasing suicide rates in younger cohorts in many countries (Granizo et al., 1996; Gunnell et al., 2003; Kwon et al., 2009; Murphy and Wetzel, 1980; Odagiri et al., 2011; Phillips, 2014). Broad societal changes are thought to contribute increasing vulnerability to suicide in younger birth cohorts including a loss of social integration and assimilation, and rapid shifts in the norms and customs that regulate behavior (Griffith and Bryan, 2016; Phillips, 2014; Stockard and O'Brien, 2002).

4.4 Limitations

There are limitations **to this post-hoc exploratory study. The data analysis plan was not pre-specified, and the analyses cannot demonstrate causality or predict individual behavior.** The database was not designed to collect data about suicide. There was no information on individual parameters associated with suicide attempts including marital status, education, income, employment, childhood trauma, family history of suicide, psychiatric and medical comorbidities, temperament, and individual religiosity (Borges et al. 2010; Hansson et al., 2018; Isometsä, 2014; Schaffer et al., 2015; Tondo et al., 2018). **There was no data on patients receiving long-term lithium treatment, which may lower suicide risk (Baldessarini et al., 2006), or other therapies that target or modify the circadian system (Bellivier et al., 2015).** There was no data on the timing of the suicide attempts, the patient age when attempts were made, relation of attempts to the phase of illness (Pallaskorpi et al., 2016). There was no individual data on sun or lighting exposure (Bauer et al., 2018). Although based on DSM-IV criteria, data gathering was not standardized across the collection sites including both the definition of suicide attempt and assessment method. **Additionally, both the increase in diagnosis (Blader and Carlson, 2007) and excess mortality of bipolar disorder (Osby 2001), may bias findings relating to birth cohort effects.**

Shifting data from the southern hemisphere by 6 months may discount cultural impacts of seasonality. Social variables may also be seasonal, such as the start of school sessions, but were not available (Matsubayashi et al., 2016). This analysis also did not investigate life habits, now common in the 21st century, which may enable or directly cause circadian disruption including working shifts and irregular hours (Lunn et al., 2017; McMenamin, 2007) and exposure to light-emitting diodes (LED). White LEDs, used for lighting and to backlight digital devices, have a dominant spectral wavelength in the blue light range near the peak sensitivity for the melanopsin system (Bauer et al., 2018). Other environmental factors were not considered (Bakian et al., 2014; Berk et al., 2006; Fountoulakis et al., 2016).

4.5 Solar insolation limitations

Two important issues related to solar insolation cannot be analyzed with this database. First, with winters lasting longer than 3 months near the poles, the association of continuous low solar insolation with suicidal behaviors needs investigation. Second, the 22-year average solar insolation values capture the dramatic variation in solar insolation experienced at locations around the globe but do not highlight the regional variance in insolation that has occurred over decadal timeframes (Wild et al., 2005). In many parts of the world, there was declining insolation or solar dimming between the 1950s and 1980s, followed by increasing insolation or solar brightening since the 1980s (Wild, 2012). Solar dimming and brightening are caused by changes in the transparency of the atmosphere, not directly by the Sun. Increasing clouds, aerosols and gases in the atmosphere often from air pollution are associated with solar dimming, while the opposite environmental controls are associated with brightening (Tollenaar et al., 2017; Wild, 2012). For example, in the post-2000 decade, strong solar brightening was noted in some areas of the US and Japan, with dimming in some areas of India and China (Hatzianastassiou et al., 2012; Tollenaar et al., 2017; Wild 2009; 2012). Areas within a country may have opposite tendencies or may not be impacted, and the direction of future changes is unclear (Hatzianastassiou et al., 2012; Tollenaar et al., 2017; Wild 2009; 2012). The potential relation between local insolation variability and suicidal behaviors should be investigated.

5. Conclusion

In conclusion, t**his exploratory analysis suggests** that living in locations with large changes in solar insolation between winter and summer may be associated with increased suicide attempts in patients with bipolar disorder. Given the increased recognition of the importance of sunlight on human behavior and the frequent presence of circadian rhythm dysfunction in bipolar disorder, more knowledge of the relation of solar insolation to suicide attempts is needed.

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Table 1. Demographics of Bipolar I Patients (N=3365)

Parameter	Value	N	%
Gender			
	Female	1908	56.7
	Male	1457	43.3
First Episode[a]			
	Manic/Hypomanic	1575	49.1
	Depressed	1634	50.9
Family History of Mood Disorder[a]			
	No	1374	44.0
	Yes	1748	56.0
Alcohol or Substance Abuse			
	No	2208	65.6
	Yes	1157	34.4
State-Sponsored Religion in Country of Onset			
	No	1796	53.4
	Yes	1569	46.6
History of Suicide Attempts			
	No	2318	68.9
	Yes	1047	31.1
Cohort Group			
	DOB < 1940	162	4.8
	DOB >= 1940 and < 1960	978	29.1
	DOB >= 1960	2225	66.1
Parameter		**Mean**	**SD**
Age		50.5	15.01
Age of Onset		25.7	10.71

[a] Missing values excluded

Table 2. Distribution of latitudes for patient onset locations (N=3365)

Degrees Latitude North + South	N	%	Ratio Mean Winter Insolation/Mean Summer Insolation	Example Locations
0-9	219	6.5	1.0283	Kampala,Uganda Medellín, Columbia Singapore
10-19	212	6.3	1.0686	Bangalore, India Hyderabad, India Mexico City, Mexico
20-29	215	6.4	0.7238	Cancun, Mexico Hong Kong, China São Paulo, Brazil
30-39	965	28.7	0.3843	Adelaide, Australia Athens, Greece Beersheva, Isreal Cagliari, Italy Cape Town, South Africa Los Angeles, CA, USA Santiago, Chile Tokyo, Japan Tunis, Tunisia
40-49	1153	34.3	0.2939	Barcelona, Spain Boston, MA, USA Nova Scotia, Canada Paris, France Siena, Italy Vienna, Austria Würzburg, Germany
50-59	365	10.8	0.1453	Aarhus, Denmark Poznan, Poland Stockholm, Sweden Tartu, Estonia
60-69	235	7.0	0.0853	Helsinki, Finland Khanti-Mansiysk, Russia Trondheim, Norway
70-79	1	0.0	0.0195	Hammerfest, Norway
Hemisphere	N	%		
Northern Hemisphere	2834	84.2	0.3917	
Southern Hemisphere	531	15.8	0.5278	

Table 3. Estimated parameters explaining a history of suicide attempts for patients with bipolar I disorder (N=3365)[a]

Parameters	Coefficient estimate	Standard error	99% Confidence interval		Coefficient significance	
			Lower	Upper	Wald Chi-square	P
Ratio mean winter insolation/mean summer insolation at onset location	-0.679	0.2061	-1.210	-0.149	10.869	0.001
State sponsored religion in onset country	-0.380	0.1409	-0.743	-0.018	7.291	0.007
Male	-0.635	0.0934	-0.875	-0.394	46.140	<0.001
History of alcohol or substance abuse	0.506	0.0682	0.331	0.682	55.152	<0.001
DOB ≥ 1960	0.770	0.2324	0.171	1.369	10.980[b]	0.001[b]
DOB ≥ 1940 and DOB < 1960	0.679	0.2103	0.138	1.221	10.440[b]	0.001[b]

[a] Dependent variable: History of suicide attempts (yes/no). Model: intercept, ratio of mean winter insolation/mean summer insolation at onset location, state sponsored religion in onset country (yes/no), gender (male/female), alcohol or substance abuse (yes/no) and birth cohort group (DOB <1940, DOB >= 1940 and DOB < 1960, DOB >= 1960).
[b] Individual parameters Wald chi-square statistic and significance. The model effects Wald chi-square and significance for the cohort parameter was 11.266 and 0.004 respectively with 2 degrees of freedom.

Declarations

Conflict of interest:

All authors declare that they have no conflict of interest.

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Contributors:

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