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Ambient temperature and solar insolation are associated with decreased prevalence of SSRI-treated psychiatric disorders

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ABSTRACT

Serotonergic function is known to fluctuate in association with light and temperature. Serotonin-related behaviors and disorders similarly vary with climatic exposure, but the associations are complex. This complexity may reflect the importance of dose and timing of exposure, as well as acclimation. This cross-sectional study tests how average climate exposures (ambient temperature and solar insolation) vary with the prevalence of a group of SSRI-treated disorders. For comparison, we similarly studied a group of disorders not treated by SSRIs (i.e substance use disorders). Psychiatric prevalence data were obtained from the Collaborative Psychiatric Epidemiology Surveys (CPES). Average yearly solar insolation was obtained from NASA's NLDAS-2 Forcing Dataset Information. Average yearly temperature was obtained from NOAA's US Climate Normals. Logistic regression models were generated to assess the relationship between these two climatic factors and the prevalence of SSRI-treated and substance use disorders. Age, gender, race, income, and education were included in the models to control for possible confounding. Temperature and insolation were significantly associated with the SSRI-responsive group. For an average 1 GJ/m^2/year increase, OR was 0.90 (95% CI 0.85–0.96, p = 0.001), and for an average 10 °F increase, OR was 0.93 (95% CI 0.88–0.97, p = 0.001). This relationship was not seen with substance use disorders (insolation OR: 0.97, p = 0.682; temperature OR: 0.96, p = 0.481). These results warrant further investigation, but they support the hypothesis that chronic exposure to increased temperature and light positively impact serotonin function, and are associated with reduced prevalence of some psychiatric disorders. They also support further investigation of light and hyperthermia treatments.

1. Introduction

A number of psychiatric disorders, as well as suicide and violence, have pronounced seasonal rhythms (Coimbra et al., 2016; Rosenthal and Wehr, 1992). These seasonal fluctuations are thought to be related to serotonin, as the availability of the serotonin in the brain fluctuates across seasons (Praschak-Rieder et al., 2008). While difficult to parse, the effects of climatic change on serotonin seem to be primarily driven by changes in ambient light and temperature (Lambert et al., 2002; Matheson et al., 2015; Raison et al., 2015). The major serotonin metabolite in cerebrospinal fluid (5-HIAA) varies inversely with daily temperature (Brewerton et al., 2018), and serotonin 1A receptor binding in limbic regions correlates with global light exposure (Spindelegger et al., 2012). However, the effects of ambient light and temperature on serotonin-related behaviors and disorders are difficult to interpret, as different studies report seemingly antithetical results.

A sizable literature reports that acute increases in ambient light and temperature are associated with worsening of SSRI-treated psychiatric illness. For example, acute increases in ambient temperature are linked to increased emergency room mental health visits for depression, bulimia, and posttraumatic stress disorder (PTSD) (Amr and Volpe, 2012; Huibers et al., 2010; Lam et al., 1996; Solt et al., 1996; Stordal et al., 2008; Vida et al., 2012; Wang et al., 2014). Serotonin abnormalities are also strongly linked with impulsive violence (Virkkunen et al., 1996), and multiple studies show that hotter climates and hotter days in a given location are correlated with higher rates of violence (Gamble and

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Hess, 2012; Sorg and Taylor, 2011). Similarly, several studies have identified violent suicide to be specifically correlated with acute increases in temperature and sunlight (Dixon et al., 2014; Hee-Jung et al., 2017; Linkowski et al., 1992).

There are multiple reasons to think that patients with presumed serotonergic disturbances might struggle with acute changes in climate. Physiologically, serotonin has been shown to play a significant role in maintaining temperature homeostasis (Schneider and Nadeau, 2015). Heat loss during exercise is in part controlled by serotonin activity in the preoptic area (Rodrigues et al., 2009), and peripheral serotonin controls thermogenesis in adipose tissue by modulating b-adrenergic stimulation of UCP-1 (Crane et al., 2015). Clinically, serotonin abnormalities appear to be associated with wide-ranging difficulties in tolerating heat stress (Norden, 1995). Depressed patients have elevated baseline temperatures and reduced amplitude of circadian temperature rhythms, which suggests these patients have problems regulating heat-loss (Avery et al., 1982). Patients with seasonal affective disorder also have reduced rates of cooling down post-exercise compared to controls and compared to after recovery (Arbisi et al., 1994).

However, in contrast to this literature, there is also a growing body of work that has studied the effects of chronic climatic factors on psychiatric illness, which actually suggests a salutary effect of warmer, sunnier climates. One study finds a strongly positive correlation between suicide deaths and a nation's distance from the equator (Davis and Lowell, 2002). A survey by the World Health Organization notes that some of the lowest reported prevalences of psychiatric illness occur in areas of the world with the highest mean solar insolations and temperatures (Kessler et al., 2007). Concordant findings appear in another cross-national prevalence study (Rotgé et al., 2014). These studies have not controlled for socioeconomic and demographic factors that may confound the observed effect, but differences in average light and temperature among regions seems to be a plausible explanation.

Clinical trials using supplemental light and heat therapy support the observation that repeated episodic exposure to increased heat and light improves outcomes in SSRI-treated psychiatric illness. While this may seem contradictory to the heat wave literature discussed above, the experience of daily temperature and light fluctuations may mirror what individuals living in warm, bright climates experience when they move to and from climate-controlled indoor environments. Extensive evidence supports the effectiveness of bright light treatment for seasonal affective disorder (Pail et al., 2011), and preliminary data suggest supplemental light therapy has efficacy in treating non-seasonal depression, panic disorder, and bulimia (Crowley and Youngstedt, 2012; Even et al., 2008; Wirz-Justice et al., 2011). There have also been several clinical trials that show whole-body hyperthermia therapy effectively treats major depressive disorder (Janssen et al., 2016; Kay-U Hanusch et al., 2013). These results are in keeping with recent studies and reviews that report beneficial effects of increased ambient temperature on mood and the serotonergic system (Lowry et al., 2009; Raison et al., 2015).

The resolution of what appears to be a paradox in ecological studies may lie in part with the importance of dose, duration, and timing of heat and light exposures, and in part with the difference between acute and chronic exposures. Peak incidence of depression and suicide generally occur not at times of highest sunshine levels and temperature (i.e. mid-summer), but rather at times of rapidly rising sunshine and temperature (i.e. spring) (Brewerton, 1991; Souêtre et al., 1990). These late-spring peaks may be analogous to what is seen with heat wave mortality, where the temperature during the heat wave is less important than whether the heat wave occurs early or late in the year (Allen and Sheridan, 2018). Once people acclimate to the change in temperature, it appears that the dangers of heat are greatly reduced. With this in mind, and given the growing evidence of the benefit of light and hyperthermia therapy, it seems reasonable to hypothesize that living in a warmer, sunnier climate has a salutary effect on SSRI-treated conditions.

This study strove to relate the effects of average light and temperature levels (i.e chronic exposure) with SSRI-treated psychiatric disorder prevalence. To do this, we paired prevalence data from the Collaborative Psychiatric Epidemiology Studies (CPES) with average annual solar insolation and temperature data from NASA's North American Land Data Assimilation System Phase 2 (NLDAS-2) Forcing Dataset and NOAA's US Climate Normals, respectively. We hypothesized that climates with higher average sunlight and temperature are associated with reduced prevalence of SSRI-treated disorders. We hypothesized that this relationship would not exist for psychiatric conditions that are not treated with SSRIs.

2. Methods

2.1. Datasets

For this study, we assembled a dataset comprising information from three sources: the Collaborative Psychiatric Epidemiology Studies (CPES), NASA's NLDAS-2 Forcing Dataset Information, and the NOAA's US Climate Normals. The CPES dataset encompasses three national surveys of mental health in the US population: the National Comorbidity Survey Replication (NCS-R) (Kessler et al., 2004), the National Study of American Life (NSAL) (Jackson et al., 2004) and the National Latino and Asian American Study of Mental Health (NLAAS) (Alegria et al., 2004). These data were collected and collated by the Survey Research Center in the Institute for Social Research at the University of Michigan. The NASA NLDAS-2 Forcing Dataset Information is assembled by mathematically modeling data from satellites and ground-based observations to generate 12-km gridded estimates of meteorological variables for the United States from 1979-Present (Al-Hamdan et al., 2014; Cosgrove et al., 2003). A yearly integral of solar radiation was calculated by Al-Hamdan et al. (2014), and this is referred to as “solar insolation,” which has units of gigajoules per meters squared per year (GJ/m^2/year) (Kent et al., 2014). The NOAA's US Climate Normals 1971–2000 dataset, assembled by averaging meteorological data collected over a 30-year period, is considered to be the most comprehensive daily climate data for the USA (Arguez et al., 2012; Menne et al., 2012). The CPES, NASA's NLDAS-2 Forcing, and NOAA's US Climate Normals datasets were paired using the FIPS county codes recorded for each participant in the CPES dataset.

2.2. Measures

The outcome of interest in this study was meeting 12-month criteria (i.e. the occurrence of symptoms within 12 months of the CPES interview) for any of nine DSM-IV disorders assessed in the CPES survey that have FDA approval for treatment with selective serotonin reuptake inhibitors (SSRIs) (Widiger, 1994), and they are described as “SSRI-treated disorders” below. These include posttraumatic stress disorder, agoraphobia without panic disorder, agoraphobia with panic disorder, general anxiety disorder, major depression disorder, dysthymia disorder, social phobia disorder, bulimia eating disorder, and panic disorder. Because over 30% of CPES subjects had missing data for explosive disorder, this SSRI-responsive condition was excluded from our analysis. All other nine disorders had less than 5% missing data, which were imputed using a Monte Carlo random forest multiple imputation algorithm as implemented in the ‘mice’ package in R (van Buuren and Groothuis-Oudshoorn, 2011). Using these data, a new variable “SSRI-treated disorders” was generated for individuals with one or more of these nine diagnoses (n = 3030). As a control, this analysis also studied DSM-IV diagnoses surveyed in CPES that do not have FDA approval for treatment with SSRIs. These include bipolar disorder, mania, hypomania, nicotine dependence disorder, alcohol abuse disorder, alcohol dependence disorder, drug abuse disorder, and drug dependence disorder. Over 20% of subjects were missing data for bipolar disorder, mania, and hypomania, and over 50% of subjects were missing data for

nicotine dependence disorder. Consequently, these diagnoses were excluded from our analysis, and a new variable "substance use disorders" was generated for individuals with one or more of the remaining diagnoses (n = 505). All 20,013 CPES subjects were included in the final analysis.

2.3. SES

Prior papers analyzing the CPES data have controlled for socioeconomic factors using education and household income (Gavin et al., 2010; Lorant et al., 2003). All subjects reported education levels, and this was treated as a categorical variable based on self-reported number of years of education (i.e. < 12 years, 12 years, 13–15 years, ≥16 years). As has been previously reported, these categories were created based on significant markers of educational attainment and the distribution of years of education in the study population (Gavin et al., 2010). Household income was obtained from self-reported income for the year preceding the survey, and these were grouped into approximate quartiles and analyzed as categorical variables (< US$17,000, US $17,000–49,999, US$45,000–79,999, and ≥US$80,000). Of note, over 20% of subjects had missing income data. X^2 tests showed that these missing subjects were not randomly distributed, and, thus, they could not be excluded from the analysis without the risk of biasing the results. As income was considered to be an important potential confounder to include in the model, we ran models in which missing income was replaced with the mean income of the dataset (i.e. US$50,182), as well as models in which income was imputed using the random forest procedure described above. Both models showed comparable results with little change in estimated ORs or their significance, so the imputed data were used. We also considered including geographical region as a covariate to control for possible unaccounted for region-specific influences, but we found that region was highly collinear with climate, so this was not pursued.

2.4. Demographic measures

Age, gender, and race were included as demographic measures. Age was reported for all subjects (measured in years) and it was treated as a continuous variable. Gender was reported for all subjects and was treated as a categorical variable (i.e. 'is male'). Race was reported for all subjects, though the CPES dataset originally categorized participants into 12 racial groups. In accordance with other analyses of this dataset, these racial categories were regrouped into five broader racial categories (i.e. Asian, Latino, Black, White, and Other) (Asnaani et al., 2009; Gavin et al., 2010).

2.5. Climate measures

Average ambient temperature and annual solar insolation were obtained for each subject's county from NOAA's US Climate Normals and NASA's NLDAS-2 Forcing Dataset, respectively. Average annual temperatures ranged from 40 to 78 °F. Temperature was reported in units of degrees Fahrenheit, and it was treated as a continuous variable. Average annual solar insolation ranged from 4.77 GJ/m^2/year – 7.67 GJ/m^2/year. Insolation was reported in units of KJ/m^2/year, and it was treated as a continuous variable. Maps of county annual averages of temperature and insolation can be visualized in Fig. 1.

2.6. Statistical analysis

All statistical analyses were performed using the R statistical programming language version 3.5.0 (RCoreTeam, 2014). Prior to performing logistic regression modeling, we assessed for collinearity of light and temperature, and, as expected, these variables are correlated (R^2 = 0.52). We next modeled disorder prevalence (both "SSRI-treated disorders" and "substance use disorders") with insolation, temperature, and an interaction term of insolation and temperature. We found significant interaction (p = 0.0005) between light and temperature, and we proceeded by using insolation and temperature as independent variables in separate models. Finally, multivariate logistic regression was performed for "SSRI-treated disorders" and "substance use disorders" as dependent variables using age, gender, race, education, and income with either temperature or insolation as independent variables. Of note, we considered stratifying the data into quintiles of temperature and light to better parse the effects of light and temperature, respectively; however, stratification reduced statistical power significantly, and this analysis did not prove to be edifying.

3. Results

The descriptive statistics for the climatic, socioeconomic, and psychiatric variables among the participants of the CPES survey are summarized in Table 1. The results of the multivariate logistic regression models are summarized in Table 2. As hypothesized, average annual insolation and temperature are significantly, inversely related to the prevalence of SSRI-treated disorders. For an average 1 GJ/m^2/year increase in annual insolation, there was a 10% decrease in a respondent's adjusted odds of having an SSRI-treated disorder (OR 0.90, 95% CI 0.85–0.96, p = 0.001). For an average 10 °F increase in annual temperature, there was a 7% reduction in a respondent's adjusted odds of having an SSRI-treated disorder (OR 0.93, 95% CI 0.88–0.97, p = 0.001). These relationships were not seen with substance use disorders (insolation OR 0.97, p = 0.682; temperature OR 0.96, p = 0.481). Fig. 2 graphically depicts the unadjusted relationship between prevalence of SSRI-treated disorders and temperature or insolation by grouping data from multiple subjects at the county level.

The relationships of psychiatric disorder prevalence with the other covariates in the model were largely similar between the SSRI-treated disorders and substance use disorder groups. Increasing age was inversely related to disorder prevalence. Self-identifying as Asian was associated with decreased illness prevalence compared with the other four racial categories, with self-identifying as White or Other being the largest of the racial risk factors. Household incomes above $17,000 were all associated with decreased disorder prevalence. There were no significant differences in illness prevalence above this household income level.

Two of the demographic covariates differed between the models for SSRI-treated disorders and substance use disorders. Whereas being male was associated with a decreased prevalence of SSRI-treated disorders (OR 0.57, p«0.001), being male was associated with an increased prevalence of substance use disorders (OR 2.31, p«0.001). In general, higher educational attainment was associated with decreased illness prevalence for both SSRI-treated Disorders and substance use disorders; however, for SSRI-treated disorders, prevalence was not significantly different between those that did not complete high school and those that did not complete college.

4. Discussion

We find that warmer and sunnier places have a lower prevalence of a group of nine SSRI-treated, non-psychotic, psychiatric disorders. This relationship was significant even with correcting for age, sex, race, income, and education as potential confounders. Our control group of substance use disorders showed no significant association with either average yearly solar insolation or ambient temperature. These findings are consistent with our hypothesis that chronic exposure to a climate with increased heat and light has a beneficial effect on SSRI-treated disorders.

It is impressive that the relationship between climate and SSRI-treated disorders is observed even after accounting for a number of possible demographic and socioeconomic confounders. The average age of the US population is geographically heterogeneous. The North East

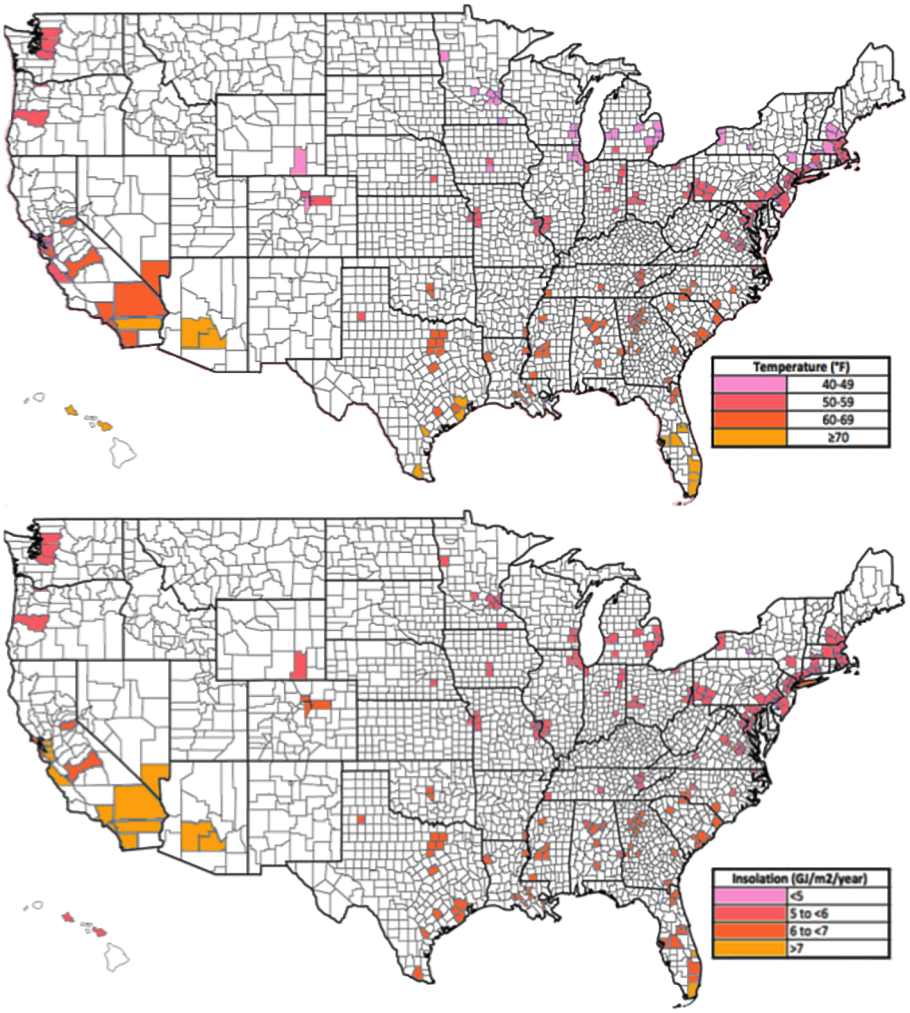

Fig. 1. Maps of average annual temperature and insolation by county in the CPES dataset.

population is older than that in the West and South West where temperature and insolation are on average higher (Bureau, 2016; Johnson, 2017). Even so, sunlight and temperature are significant after accounting for age in the model. The prevalence of psychiatric illnesses differs by race (Alegría et al., 2007; Breslau et al., 2005, 2006; Williams et al., 2007), which is significant to this study given pronounced differences in the geographical distribution of races in America. Specifically, a greater proportion of Latinos and Blacks live in western and southern states, respectively, compared to the White and Asian populations (Brittingham and de la Cruz, 2004). Even so, temperature and insolation are significant when race is included in the model, and no interactions are found between the climate variables and race. It is possible that warmer, sunnier climates, particularly on the West Coast, are more desirable, expensive places to live, which could have confounded our analysis. Household income and education are related to the prevalence of psychiatric disorders (Muntaner et al., 2004, 2007). However, controlling for household income did not alter the significance of temperature and insolation in the model. The same was true of education status.

Because this is a cross-sectional study, it is not possible to make conclusions about a causal relationship between chronic climate conditions and psychiatric disorder prevalence, as it is possible that unknown confounders may account for the association. For example, living in a warmer, sunnier climate may simply encourage people to get outside and exercise more, which has been shown to improve outcomes in depression (Cooney et al., 2014). Nevertheless, it is biologically plausible that there is a causal link underlying this relationship. As discussed, randomized clinical trials show that light and heat therapies improve symptoms in depressed patients. Climate studies of insolation and temperature are natural-experiments of these therapies, and, as discussed, they could exert effects through serotonergic mechanisms.

We propose that the apparent paradoxical effects of climate on psychiatric illness noted in the literature may in part be due to a distinction between acute versus chronic exposure. As discussed, many mood-disordered patients have thermoregulatory deficits centered around heat loss. However, we know from studies of acclimation that chronic exposure to heat predictably results in improved ability to thermoregulate and lose heat (Lorenzo and Minson, 2010). Thus, whereas someone exposed to a sudden rise of temperature in the spring may become “over-heated” and impulsively violent, the same person later in the summer may tolerate the heat challenge easily after acclimating. It is also possible that hotter climates only become aversive for some individuals above a certain temperature. We observed that some of the lowest prevalence rates recorded in this study for SSRI-treated disorders were recorded in areas with an average temperature of 60–65 °F. It is possible that a U-shaped curve may ultimately best

Table 1
Descriptive statistics for all variables in the analysis (Subjects in CPES, n = 20,013).

Descriptive Statistics (Subjects in CPES, n = 20,013)			
Insolation (GJ/m^2/year)	%	**Education (Category)**	%
< 5.44	19.9	< 12 years	20.3
5.44–5.80	19.9	12 years	29.7
5.81–6.20	19.5	13–15 years	26.4
6.21–6.84	19.5	≥16 years	23.6
6.85–7.67	21.1	**Income (Category)**	%
Temperature (°F)	%	< $17,000	22.9
< 50	14.4	$17,000–44,999	34.4
50-53	18	$45,000–79,999	22.6
54-60	24.9	≥$80,000	20.0
61-64	14.2	**SSRI-Treated Disorders**	n
≥65	28.4	PTSD	602
Age (year)	%	Agoraphobia w/o Panic	313
< 30	21.8	Agoraphobia w/Panic	191
30-39	22.4	General Anxiety	646
40-49	20.9	Major Depression Disorder	1293
50-65	20.7	Dysthymia	286
> 65	14.2	Social Phobia	1153
Sex	%	Bulimia	80
Male	42.7	Panic Disorder	504
Female	57.3	Subjects with ≥1 disorder	3030
Race (Category)	%	**Substance Use Disorders**	n
Asian	11.4	Alcohol Abuse	361
Latino	18.1	Alcohol Dependence	182
Black	31.2	Drug Abuse	188
White	37.9	Drug Dependence	77
Other	1.4	Subjects with ≥1 disorder	505

describe the relationships of heat and psychiatric illness prevalence, though this study did not have sufficient statistical power to identify such a subtlety in the relationship. This is an important question to be addressed in further study.

While we had hoped to assemble a more diverse control group of non-SSRI treated disorders that would highlight whether SSRI-response was a critical distinction, missing data for some disorders in the CPES dataset limited our control group to substance use disorders. Therefore, we can only say that the relationship between chronic climatic factors and psychiatric illness does not extend to substance use disorders. It is worth noting that, while we used "SSRI-treated disorders" as a way of grouping illnesses that are thought to be driven by serotonin dysfunction, the serotonin system is implicated in the pathophysiology of many other psychiatric disorders (Carrard et al., 2011; Kishi et al., 2011; Selvaraj et al., 2014). It is possible that a relationship with climatic light and heat may exist for some of these other conditions not treated with SSRIs. For example, there is preliminary evidence that light therapy benefits those with bipolar disorder (Tseng et al., 2016). It is also possible, though less likely, that one of the other several neurotransmitters shared in the pathophysiology of these disorders may be driving the relationship between psychiatric disorders and climate;

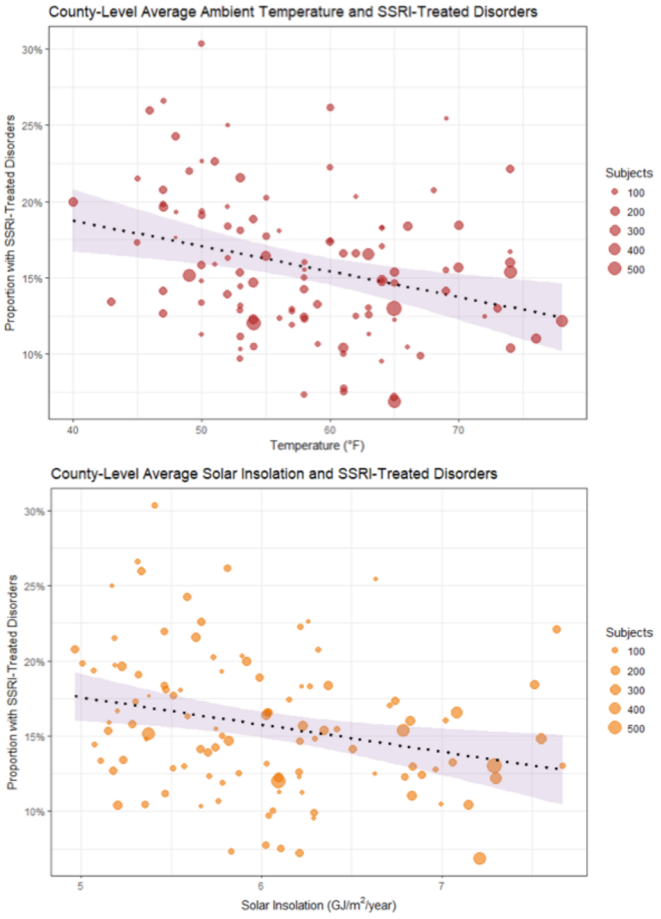

Fig. 2. Scatterplots of SSRI-treated Disorder prevalence by county with average annual insolation and temperature. (Caption: Only counties with ≥50 subjects were included. The error bounds mark the 95% CI for the trend lines.).

Table 2
Odds ratios from multivariate logistic regression for all independent variables.

Odds Ratios	SSRI-Treated Disorders		Substance Use Disorders	
Temperature (10 °F)	0.93 (0.88–0.97)**		0.96 (0.88–1.08)	
Insolation (GJ/m^2/year)		0.90 (0.85–0.96)**		0.97 (0.87–1.14)
Age (1 year)	0.98 (0.98–0.99)***	0.98 (0.98–0.99)***	0.95 (0.94–0.96)***	0.95 (0.94–0.96)***
Sex (Male)	0.57 (0.52–0.62)***	0.57 (0.52–0.62)***	2.31 (1.90–2.73)***	2.31 (1.89–2.72)***
Latino v Asian	1.81 (1.52–2.16)***	1.8 (1.51–2.14)***	1.74 (1.14–2.63)*	1.73 (1.14–2.63)*
Black v Asian	1.52 (1.28–1.79)***	1.48 (1.24–1.74)***	1.66 (1.10–2.49)*	1.65 (1.10–2.52)*
White v Asian	2.23 (1.89–2.61)***	2.19 (1.85–2.57)***	2.59 (1.79–3.95)***	2.60 (1.81–4.05)***
Other v Asian	3.33 (2.42–4.49)***	3.27 (2.38–4.42)***	3.95 (2.09–7.50)***	3.96 (2.11–7.61)***
12yrs education vs < 12yrs	0.84 (0.76–0.95)***	0.84 (0.75–0.95)***	0.65 (0.50–0.79)***	0.65 (0.50–0.79)***
13–15yrs education vs < 12yrs	0.89 (0.79–1.01)	0.89 (0.80–1.01)	0.60 (0.46–0.76)***	0.60 (0.47–0.76)***
≥16yrs education vs < 12yrs	0.85 (0.76–0.99)*	0.86 (0.77–0.996)*	0.43 (0.31–0.57)***	0.43 (0.31–0.57)***
$17,000-$44,999 income vs < $17,000	0.75 (0.66–0.81)***	0.75 (0.66–0.80)***	0.75 (0.60–0.93)*	0.75 (0.60–0.93)*
$45,000-$79,999 income vs < $17,000	0.65 (0.56–0.71)***	0.65 (0.56–0.71)***	0.61 (0.45–0.76)***	0.61 (0.45–0.76)***
≥ $80,000 income vs < $17,000	0.64 (0.54–0.70)***	0.64 (0.56–0.71)***	0.67 (0.50–0.89)***	0.67 (0.50–0.89)***

*p ≤ 0.05, **p ~ 0.001, ***p«0.001.

however, the literature is most robust in suggesting a relationship with serotonin and climate. These are areas of research that we could not address in this study that would benefit from further investigation.

Our study also had limited resolution of CPES subjects' individual light and temperature exposures. County level averages were used to approximate annual solar insolation and temperature for each subject. However, if subjects spent significant amounts of time in climate-controlled buildings, these estimates might not reflect their true experiences. Similarly, the CPES survey did not note how long subjects lived in their counties of residence at the time of being surveyed. It is possible that some participants moved shortly before being assessed. If so, these subjects' chronic climatic exposures would not be accurately represented by their documented county averages. In an ideal analysis, one would have monitored each subject's individual light and temperature exposure with a wearable device. However, the effects of climate-controlled lifestyles and subject relocation would likely only have weakened the relationship observed in our analysis by making subjects' actual temperature and light exposures more homogenous.

Lastly, we hoped to parse whether climatic light or temperature individually drive the relationship between climate and SSRI-treated disorders. Climatic light and temperature are significantly collinear, which made this determination difficult. We attempted to address this issue through stratified analysis of the data, but given that the effect sizes of temperature and insolation on SSRI-treated disorder prevalence are small, they lost statistical significance when the dataset was broken into quintiles. Less formally, we attempted to address this issue by individually examining SSRI-treated disorder prevalence in counties with either relatively high average temperature/low insolation and in counties with relatively low average temperature/high insolation. Examples of the former are Honolulu, HI (74 °F, 5.20 GJ/m^2/year) and Harris County, TX (70 °F, 6.23 GJ/m^2/year), and examples of the latter are San Diego County, CA (63 °F, 7.67 GJ/m^2/year) and Denver County, CO (50 °F, 6.22 GJ/m^2/year). Yet in all four of these regions, SSRI-treated disorder prevalences were low. It may be that climatic temperature and light have independent, inverse relationships with SSRI-treated disorder prevalence. This would be consistent with the independent therapeutic benefits observed with heat and light therapys. Future investigations will hopefully be able to better parse the effects of both.

The limitations and caveats noted for this study call attention to the importance of replicating these results in other populations; however, the strengths of this study are considerable. First, this is a large, well-characterized community sample of people carefully diagnosed according to DSM criteria. Second, the climate data used in this analysis are derived from the most reliable climate sources available. Third, significant potential confounders identified from previous studies of the CPES dataset are incorporated into our analysis. This study indicates that both light and heat deserve to be the focus of more research directed at understanding the mechanisms by which these climate variables interact with the body in both health and disease. Hopefully, light and heat treatments can be harnessed to improve treatment outcomes, which are currently far from satisfactory for most psychiatric disorders.

Conflicts of interest

The authors have no conflicts of interests to declare.

Declarations of interest

None.

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CRediT authorship contribution statement

J.R. Wortzel: Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Validation, Visualization, Writing – original draft, Writing – review & editing. **J.G. Norden:** Data curation, Formal analysis, Investigation, Methodology. **B.E. Turner:** Formal analysis, Investigation, Methodology, Visualization. **D.R. Haynor:** Conceptualization, Data curation, Methodology, Supervision. **S.T. Kent:** Conceptualization, Data curation. **M.Z. Al-Hamdan:** Data curation. **D.H. Avery:** Conceptualization, Resources, Supervision. **M.J. Norden:** Conceptualization, Data curation, Investigation, Project administration, Resources, Supervision, Writing – original draft, Writing – review & editing.

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References

Al-Hamdan, M.Z., Crosson, W.L., Economou, S.A., Estes Jr., M.G., Estes, S.M., Hemmings, S.N., Kent, S.T., Puckett, M., Quattrochi, D.A., Rickman, D.L., Wade, G.M., McClure, L.A., 2014. Environmental public health applications using remotely sensed data. Geocarto Int. 29 (1), 85–98.

Alegria, M., Takeuchi, D., Canino, G., Duan, N., Shrout, P., Meng, X.L., William, V., Nolan, Z., Doryliz, V., Meghan, W., Mildred, V., Peter, G., Sergio, A.g., Stanley, S., Javier, E., Keh-ming, L., Fong, G., 2004. Considering context, place and culture: the national Latino and Asian American study. Int. J. Methods Psychiatr. Res. 13 (4), 208–220.

Alegría, M., Mulvaney-Day, N., Torres, M., Polo, A., Cao, Z., Canino, G., 2007. Prevalence of psychiatric disorders across Latino subgroups in the United States. Am. J. Public Health 97 (1), 68–75.

Allen, M.J., Sheridan, S.C., 2018. Mortality risks during extreme temperature events (ETEs) using a distributed lag non-linear model. Int. J. Biometeorol. 62 (1), 57–67.

Amr, M., Volpe, F.M., 2012. Seasonal influences on admissions for mood disorders and schizophrenia in a teaching psychiatric hospital in Egypt. J. Affect. Disord. 137 (1), 56–60.

Arbisi, P.A., Depue, R.A., Krauss, S., Spoont, M.R., Leon, A., Ainsworth, B., Muir, R., 1994. Heat-loss response to a thermal challenge in seasonal affective disorder. Psychiatr. Res. 52 (2), 199–214.

Arguez, A., Durre, I., Applequist, S., Vose, R.S., Squires, M.F., Yin Jr., X., H, R.R., Owen, T.W., 2012. NOAA's 1981–2010 U.S. Climate Normals: an overview. Bull. Am. Meteorol. Soc. 93 (11), 1687–1697.

Asnaani, A., Gutner, C.A., Hinton, D.E., Hofmann, S.G., 2009. Panic disorder, panic attacks and panic attack symptoms across race-ethnic groups: results of the collaborative psychiatric Epidemiology studies. CNS Neurosci. Ther. 15 (3), 249–254.

Avery, D.H., Wildschiødtz, G., Rafaelsen, O.J., 1982. Nocturnal temperature in affective disorder. J. Affect. Disord. 4 (1), 61–71.

Breslau, J., Kendler, K.S., Su, M., Gaxiola-Aguilar, S., Kessler, R.C., 2005. Lifetime risk and persistence of psychiatric disorders across ethnic groups in the United States. Psychol. Med. 35 (3), 317–327.

Breslau, J., Aguilar-Gaxiola, S., Kendler, K.S., Su, M., Williams, D., Kessler, R.C., 2006. Specifying race-ethnic differences in risk for psychiatric disorder in a USA national sample. Psychol. Med. 36 (1), 57–68.

Brewerton, T.D., 1991. Fluotexine-induced suicidality, serotonin, and seasonality. Biol. Psychiatry 30 (2), 190–196.

Brewerton, T.D., Putnam, K.T., Lewine, R.R.J., Risch, S.C., 2018. Seasonality of cerebrospinal fluid monoamine metabolite concentrations and their associations with meteorological variables in humans. J. Psychiatr. Res. 99, 76–82.

Brittingham, A., de la Cruz, G., 2004. Ancestry: 2000. US Census Bureau.

Bureau, U.C., 2016. 2016 American Community Survey 1-Year Estimates.

Carrard, A., Salzmann, A., Malafosse, A., Karege, F., 2011. Increased DNA methylation status of the serotonin receptor < em > 5HTR1A < /em > gene promoter in schizophrenia and bipolar disorder. J. Affect. Disord. 132 (3), 450–453.

Coimbra, D.G., Pereira e Silva, A.C., de Sousa-Rodrigues, C.F., Barbosa, F.T., de Siqueira Figueredo, D., Araújo Santos, J.L., Barbosa, M.R., de Medeiros Alves, V., Nardi, A.E., de Andrade, T.G., 2016. Do suicide attempts occur more frequently in the spring too? A systematic review and rhythmic analysis. J. Affect. Disord. 196, 125–137.

Cooney, G., Dwan, K., Mead, G., 2014. Exercise for depression. J. Am. Med. Assoc. 311 (23), 2432–2433.

Cosgrove, B.A., Lohmann, D., Mitchell, K.E., Houser, P.R., Wood, E.F., Schaake, J.C., Robock, A., Marshall, C., Justin, S., Qingyun, D., Lifeng, L., Wayne, H.R., T, P.R., Dan, T.J., Jesse, M., 2003. Real-time and retrospective forcing in the North American Land data assimilation system (NLDAS) project. J. Geophys. Res.: Atmosphere 108 (D22).

Crane, J.D., Palanivel, R., Mottillo, E.P., Bujak, A.L., Wang, H., Ford, R.J., Collins, A., Blümer, R.M., Fullerton, M.D., Yabut, J.M., Kim, J.J., Ghia, J.-E., Hamza, S.M., Morrison, K.M., Schertzer, J.D., Dyck, J.R.B., Khan, W.I., Steinberg, G.R., 2015. Inhibiting peripheral serotonin synthesis reduces obesity and metabolic dysfunction

by promoting brown adipose tissue thermogenesis. Nat. Med. 21 (2), 166–172.
Crowley, S.K., Youngstedt, S.D., 2012. Efficacy of light therapy for perinatal depression: a review. J. Physiol. Anthropol. 31 (1), 15.
Davis, G.E., Lowell, W.E., 2002. Evidence that latitude is directly related to variation in suicide rates. Can. J. Psychiatr. 47 (6), 572–574.
Dixon, P., Sinyor, M., Schaffer, A., Levitt, A., Haney, C., Ellis, K., Sheridan, S., 2014. Association of weekly suicide rates with temperature anomalies in two different climate types. Int. J. Environ. Res. Publ. Health 11 (11), 11627.
Even, C., Schröder, C.M., Friedman, S., Rouillon, F., 2008. Efficacy of light therapy in nonseasonal depression: a systematic review. J. Affect. Disord. 108 (1), 11–23.
Gamble, J.L., Hess, J.J., 2012. Temperature and violent crime in dallas, Texas: relationships and implications of climate change. West. J. Emerg. Med. 13 (3), 239–246.
Gavin, A.R., Walton, E., Chae, D.H., Alegria, M., Jackson, J.S., Takeuchi, D., 2010. The associations between socio-economic status and major depressive disorder among Blacks, Latinos, Asians and non-Hispanic Whites: findings from the Collaborative Psychiatric Epidemiology Studies. Psychol. Med. 40 (1), 51–61.
Hanusch, Kay-U., Janssen, Clemens H., Billheimer, Dean, Jenkins, Isaac, Spurgeon, Erin, Lowry, Christopher A., Raison, Charles L., 2013. Whole-body hyperthermia for the treatment of major depression: associations with thermoregulatory cooling. Am. J. Psychiatry 170 (7), 802–804.
Hee-Jung, J., Chul-Hyun, C., Jin, L.Y., Nari, C., Hyonggin, A., Heon-Jeong, L., 2017. Solar radiation increases suicide rate after adjusting for other climate factors in South Korea. Acta Psychiatr. Scand. 135 (3), 219–227.
Huibers, M.J.H., de Graaf, L.E., Peeters, F.P.M.L., Arntz, A., 2010. Does the weather make us sad? Meteorological determinants of mood and depression in the general population. Psychiatr. Res. 180 (2), 143–146.
Jackson, J.C., Torres, M., H, C.C., W, N.H., M, N.R., Joseph, T.R., J, T.S., R, W.D., 2004. The National Survey of American Life: a study of racial, ethnic and cultural influences on mental disorders and mental health. Int. J. Methods Psychiatr. Res. 13 (4), 196–207.
Janssen, C.W., Lowry, C.A., Mehl, M.R., et al., 2016. Whole-body hyperthermia for the treatment of major depressive disorder: a randomized clinical trial. JAMA Psychiatry 73 (8), 789–795.
Johnson, D., 2017. These Are the Youngest States in America, TIME.
Kent, S.T., Kabagambe, E.K., Wadley, V.G., Howard, V.J., Crosson, W.L., Al-Hamdan, M.Z., Judd, S.E., Peace, F., McClure, L.A., 2014. The relationship between long-term sunlight radiation and cognitive decline in the REGARDS cohort study. Int. J. Biometeorol. 58 (3), 361–370.
Kessler, R.C., Berglund, P., Tat, C.W., Olga, D., Steven, H., Eva, H., Robert, J., Beth-Ellen, P., E, W.E., Alan, Z., Hui, Z., 2004. The US national comorbidity survey replication (NCS-R): design and field procedures. Int. J. Methods Psychiatr. Res. 13 (2), 69–92.
Kessler, R.C., Angermeyer, M., Anthony, J.C., De Graaf, R.O.N., Demyttenaere, K., Gasquet, I., De Girolamo, G., Gluzman, S., Gureje, O.Y.E., Haro, J.M., Kawakami, N., Karam, A., Levinson, D., Medina Mora, M.E., Oakley Browne, M.A., Posada-Villa, J., Stein, D.J., Adley Tsang, C.H., Aguilar-Gaxiola, S., Alonso, J., Lee, S., Heeringa, S., Pennell, B.-E., Berglund, P., Gruber, M.J., Petukhova, M., Chatterji, S., ÜStÜN, T.B., For The Who World Mental Health Survey, C., 2007. Lifetime prevalence and age-of-onset distributions of mental disorders in the world health organization's world mental health survey initiative. World Psychiatr. 6 (3), 168–176.
Kishi, T., Okochi, T., Tsunoka, T., Okumura, T., Kitajima, T., Kawashima, K., Yamanouchi, Y., Kinoshita, Y., Naitoh, H., Inada, T., Kunugi, H., Kato, T., Yoshikawa, T., Ujike, H., Ozaki, N., Iwata, N., 2011. Serotonin 1A receptor gene, schizophrenia and bipolar disorder: an association study and meta-analysis. Psychiatr. Res. 185 (1), 20–26.
Lam, R., Goldner, E., Arvinder, G., 1996. Seasonality of symptoms in anorexia and bulimia nervosa. Int. J. Eat. Disord. 19 (1), 35–44.
Lambert, G.W., Reid, C., Kaye, D.M., Jennings, G.L., Esler, M.D., 2002. Effect of sunlight and season on serotonin turnover in the brain. Lancet 360 (9348), 1840–1842.
Linkowski, P., Martin, F., De Maertelaer, V., 1992. Effect of some climatic factors on violent and non-violent suicides in Belgium. J. Affect. Disord. 25 (3), 161–166.
Lorant, V., Deliège, D., Eaton, W., Robert, A., Philippot, P., Ansseau, M., 2003. Socioeconomic inequalities in depression: a meta-analysis. Am. J. Epidemiol. 157 (2), 98–112.
Lorenzo, S., Minson, C.T., 2010. Heat acclimation improves cutaneous vascular function and sweating in trained cyclists. J. Appl. Physiol. 109 (6), 1736–1743.
Lowry, C., Lightman, S., Nutt, D., 2009. That warm fuzzy feeling: brain serotonergic neurons and the regulation of emotion. J. Psychopharmacol. 23 (4), 392–400.
Matheson, G.J., Schain, M., Almeida, R., Lundberg, J., Cselényi, Z., Borg, J., Varrone, A., Farde, L., Cervenka, S., 2015. Diurnal and seasonal variation of the brain serotonin system in healthy male subjects. Neuroimage 112, 225–231.
Menne, M.J., Durre, I., Vose, R.S., Gleason, B.E., Houston, T.G., 2012. An overview of the global historical climatology network-daily database. J. Atmos. Ocean. Technol. 29 (7), 897–910.
Muntaner, C., Eaton, W.W., Miech, R., O'Campo, P., 2004. Socioeconomic position and major mental disorders. Epidemiol. Rev. 26, 53–62.
Muntaner, C., Borrell, C., Chung, H., 2007. Class relations, economic inequality and mental health: why social class matters to the sociology of mental health. In: Avison, W.R., McLeod, J.D., Pescosolido, B.A. (Eds.), Mental Health, Social Mirror. Springer US, Boston, MA, pp. 127–141.
Norden, M.J., 1995. Beyond Prozac: Brain-toxic Lifestyles, Natural Antidotes, & New Generation Antidepressants. HarperCollings Publishers, New York.
Pail, G., Huf, W., Pjrek, E., Winkler, D., Willeit, M., Praschak-Rieder, N., Kasper, S., 2011. Bright-light therapy in the treatment of mood disorders. Neuropsychobiology 64 (3), 152–162.
Praschak-Rieder, N., Willeit, M., Wilson, A.A., Houle, S., Meyer, J.H., 2008. Seasonal variation in human brain serotonin transporter binding. Arch. Gen. Psychiatr. 65 (9), 1072–1078.
Raison, C., Hale, M., Williams, L., Wager, T., Lowry, C., 2015. Somatic influences on subjective well-being and affective disorders: the convergence of thermosensory and central serotonergic systems. Front. Psychol. 5 (1580).
RCoreTeam, 2014. R: a Language and Environment for Statistical Computing. R Foundation for Statistical Computing, Vienna, Austria.
Rodrigues, A.G., Soares, D.D., Marubayashi, U., Coimbra, C.C., 2009. Heat loss during exercise is related to serotonin activity in the preoptic area. Neuroreport 20 (8), 804–808.
Rosenthal, N.E., Wehr, T.A., 1992. Towards understanding the mechanism of action of light in seasonal affective disorder. Pharmacopsychiatry 25 (1), 56–60.
Rotgé, J.-Y., Fossati, P., Lemogne, C., 2014. Climate and prevalence of mood disorders: a cross-national correlation study. J. Clin. Psychiatr. 75 (4), 408.
Schneider, Jochen G., Nadeau, Joseph H., 2015. Turn up the heat: circulating serotonin tunes our internal heating system. Cell Metabol. 21 (2), 156–158.
Selvaraj, S., Arnone, D., Cappai, A., Howes, O., 2014. Alterations in the serotonin system in schizophrenia: a systematic review and meta-analysis of postmortem and molecular imaging studies. Neurosci. Biobehav. Rev. 45, 233–245.
Solt, V., Chen, C.-J., Roy, A., 1996. Seasonal pattern of posttraumatic stress disorder admissions. Compr. Psychiatr. 37 (1), 40–42.
Sorg, E.T., Taylor, R.B., 2011. Community-level impacts of temperature on urban street robbery. J. Crim. Justice 39 (6), 463–470.
Souêtre, E., Wehr, T.A., Douillet, P., Darcourt, G., 1990. Influence of environmental factors on suicidal behavior. Psychiatr. Res. 32 (3), 253–263.
Spindelegger, C., Stein, P., Wadsak, W., Fink, M., Mitterhauser, M., Moser, U., Savli, M., Mien, L.-K., Akimova, E., Hahn, A., Willeit, M., Kletter, K., Kasper, S., Lanzenberger, R., 2012. Light-dependent alteration of serotonin-1A receptor binding in cortical and subcortical limbic regions in the human brain. World J. Biol. Psychiatr. 13 (6), 413–422.
Stordal, E., Morken, G., Mykletun, A., Neckelmann, D., Dahl, A.A., 2008. Monthly variation in prevalence rates of comorbid depression and anxiety in the general population at 63–65° North: the HUNT study. J. Affect. Disord. 106 (3), 273–278.
Tseng, P.-T., Chen, Y.-W., Tu, K.-Y., Chung, W., Wang, H.-Y., Wu, C.-K., Lin, P.-Y., 2016. Light therapy in the treatment of patients with bipolar depression: a meta-analytic study. Eur. Neuropsychopharmacol. 26 (6), 1037–1047.
van Buuren, S., Groothuis-Oudshoorn, K., 2011. Mice: multivariate imputation by chained equations. R. J. Stat. Software 45 (3), 1–67.
Vida, S., Durocher, M., Ouarda, T.B.M.J., Gosselin, P., 2012. Relationship between ambient temperature and humidity and visits to mental health emergency departments in québec. Psychiatr. Serv. 63 (11), 1150–1153.
Virkkunen, M., Goldman, D., Linnoila, M., 1996. Serotonin in Alcoholic Violent Offenders. Ciba Foundation symposium, pp. 194.
Wang, X., Lavigne, E., Ouellette-kuntz, H., Chen, B.E., 2014. Acute impacts of extreme temperature exposure on emergency room admissions related to mental and behavior disorders in Toronto, Canada. J. Affect. Disord. 155, 154–161.
Widiger, T.A., 1994. In: Widiger, Thomas A. (Ed.), DSM-IV Sourcebook, first ed. American Psychiatric Association, Washington, D.C..
Williams, D.R., González, H.M., Neighbors, H., et al., 2007. Prevalence and distribution of major depressive disorder in african americans, caribbean blacks, and non-hispanic whites: results from the national survey of american life. Arch. Gen. Psychiatr. 64 (3), 305–315.
Wirz-Justice, A., Bader, A., Frisch, U., Stieglitz, R.-D., Alder, J., Bitzer, J., Hösli, I., Jazbec, S., Benedetti, F., Terman, M., Wisner, K.L., Riecher-Rössler, A., 2011. A randomized, double-blind, placebo-controlled study of light therapy for antepartum depression. J. Clin. Psychiatr. 72 (7), 986–993.