SEASONALITY OF MOOD AND BEHAVIOR IN THE OLD ORDER AMISH

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CONTRIBUTORS

All authors contributed to the intellectual content of the final draft of the manuscript. Uttam K. Raheja contributed to data management, literature search, and wrote the first draft of the manuscript. Sarah H. Stephens contributed to statistical analysis, tables, and results section. Braxton D. Mitchell contributed to statistical analysis, heritability analysis, and writing results and discussion. Kelly J. Rohan contributed to editing the manuscript, and writing introduction and discussion. Dipika Vaswani contributed to data collection, data management, and writing methods. Theodora G. Balis contributed to writing the discussion. Gagan V. Nijjar contributed to data collectoin, data management, result interpretation and writing methods. Aamar Sleemi contributed to mailing of questionnaires, data management, and writing methods. Toni I. Pollin contributed to results interpretation and writing discussion. Kathleen Ryan contributed to IRB approvals, data management, data storage and protection, and writing methods. Gloria M. Reeves contributed to results interpretation and writing the discussion. Nancy Weitzel contributed as liaison with the Amish participants and with the writing methods and discussion. Mary Morrissey contributed as liaison with the Amish participants and with writing methods and discussion. Hassaan Yousufi contributed to data collection data management, and methods. Patricia Langenberg contributed to statistical analysis, results, and tables, and writing results. Alan R. Shuldiner contributed to design, implementation and writing the discussion section. Teodor T. Postolache (principal investigator) designed the study, obtained funding, wrote the protocol, managed all phases of the study, and contributed to all sections of the manuscript.

Abstract

Background/Objective—We examined seasonality and winter seasonal affective disorder (SAD) in the Old Order Amish of Lancaster County, Pennsylvania, a unique population that prohibits use of network electric light in their homes.

Methods—We estimated SAD using the Seasonal Pattern Assessment Questionnaire (SPAQ) in 1,306 Amish adults and compared the frequencies of SAD and total SAD (i.e., presence of either SAD or subsyndromal-SAD) between men and women, young and old, and awareness of (ever vs. never heard about) SAD. Heritability of global seasonality score (GSS) was estimated using the maximum likelihood method, including a household effect to capture shared environmental effects.

Results—The mean ($\pm$ SD) GSS was 4.36 ($\pm$ 3.38). Prevalence was 0.84% (95% CI: 0.36 – 1.58) for SAD and 2.59% (95% CI: 1.69 – 3.73) for total SAD. Heritability of GSS was 0.14 ± 0.06 (SE) (p = 0.002) after adjusting for age, gender, and household effects.

Limitations—Limitations include likely overestimation of the rates of SAD by SPAQ, possible selection bias and recall bias, and limited generalizability of the study.

Conclusions—In the Amish, GSS and SAD prevalence were lower than observed in earlier SPAQ-based studies in other predominantly Caucasian populations. Low heritability of SAD suggests dominant environmental effects. The effects of awareness, age and gender on SAD risk were similar as in previous studies. Identifying factors of resilience to SAD in the face of seasonal changes in the Amish could suggest novel preventative and therapeutic approaches to reduce the impact of SAD in the general population.

Keywords

Introduction

Changes in mood and behavior with changes in season, referred to as seasonality, have been recognized since ancient times [Wehr and Rosenthal, 1989]. Winter seasonal affective disorder (SAD) was first defined in 1984 by Rosenthal and colleagues as a syndrome characterized by recurrent episodes of depression in the autumn and winter with remission in the spring and summer [Rosenthal et al, 1984]. While patients with SAD must have at least one episode of Major Depression according to the Rosenthal criteria [Ibid.] or two episodes of Major Depression in two consecutive years according to DSM-IV criteria [American Psychiatric Association, 2000], a form with shorter or milder forms of depression, often with predominant neurovegetative symptoms (sleep and appetite changes), has been described as subsyndromal SAD (s-SAD) [Kasper et al, 1989a].

The dual vulnerability hypothesis of SAD [Lam et al, 2001] proposes that SAD is a result of chronobiological vulnerability and vulnerability to affective dysregulation. A tendency toward an extension of nocturnal duration of melatonin secretion in response to shortened day length (photoperiod) [Wehr et al, 2001] and delays of circadian rhythms in response to limited (or reduced) exposure to morning light in fall and winter [Lewy et al, 2006] represent the major chronobiological mechanisms proposed for SAD. Symptoms of SAD resemble seasonal changes in photoperiodic mammals in response to shortening of photoperiod, including hyperphagia and weight gain, hypersomnia, anergia, and decreased libido [Wehr, 2001; Workman and Nelson, 2011]. These symptoms of SAD respond favorably to treatment with bright light [Eastman et al, 1998; Lewy et al, 1998; Terman et al, 1998; Golden et al, 2005]. Like photoperiodic mammals, patients with SAD, but not healthy

controls, have a longer duration of melatonin secretion in winter than in summer [Wehr et al, 2001].

Lewy et al have reported that light can suppress secretion of melatonin in humans, provided it is of sufficiently high intensity (about 2500 lux) [Lewy et al, 1980]. More recent studies have demonstrated that exposure to even low levels of light corresponding to ordinary room light (about 180 lux) can affect the circadian pacemaker and suppress melatonin secretion [Boivin et al, 1996; Zeitzer et al, 2000; Gooley et al, 2011]. It is therefore likely that, in modern societies, exposure to electric light may mask the exposure to longer nights in winter and thereby possibly reduce the observed prevalence of SAD. In fact, to our knowledge, all epidemiological studies of SAD to date have been conducted on populations that use network electric lighting (lighting powered by the electric grid) [Magnússon, 2000]. By corollary, one could postulate that a population with limited use of electric light would be more susceptible to the seasonal effects of long nights and would potentially have a higher prevalence of SAD.

The Old Order Amish of Lancaster, Pennsylvania (40 °N), are such a population. There are approximately 30,000 Old Order Amish in Lancaster County, about half of whom are over the age of 18 years, constituting a rural, primarily agrarian community [Kraybill, 2008]. The Old Order Amish religion prohibits technologies – such as the use of telephones in the home, driving cars, and wrist watches – that are perceived as colliding with their beliefs and practices [Ibid.]. This community has not linked to the electric power grid and does not use electric light in the home; rather they use relatively low-intensity propane-powered gas lighting and candles [Scott and Pellman, 1999]. The Amish, thus, represent a convenient population to conduct a study on SAD in which the masking effects of artificial light on natural photoperiod are minimized.

The role of genetic factors in SAD was initially suggested by an increased prevalence of affective disorders and SAD in first degree relatives of SAD patients. Since then, a number of studies have suggested a genetic contribution for seasonality [Rosenthal et al, 1998; Willeit et al, 2003; Thierry et al, 2004; Roecklein et al, 2009]. For instance, a study of 4,639 adult twins in an Australian registry reported a 29% heritability of seasonality [Madden et al, 1996]. To our knowledge, there is no study of heritability of seasonality in a population with limited exposure to modern artificial lighting, such as the Amish.

We thus conducted a cross-sectional study of seasonality of mood and prevalence of SAD based on the Seasonal Pattern Assessment Questionnaire (SPAQ) [Rosenthal et al, 1987] in the Old Order Amish. We hypothesized that the global seasonality score (GSS), a measure of magnitude of seasonal behavioral changes, and the prevalence of SAD would be higher in the Amish than in other populations previously studied at similar latitudes [Kasper et al, 1989b; Rosen et al, 1990]. As reported in previous epidemiological studies [Magnússon, 2000], we further hypothesized that women would have a higher prevalence of SAD than men, and that awareness (whether or not the subject had ever heard about SAD) and younger age would be associated with higher GSS and frequency of SAD. Since all Lancaster Amish are related through a well-documented 14-generation genealogy, we also estimated the heritability of GSS in the Amish.

Methods

Procedures and Sample Selection

We mailed the Seasonal Pattern Assessment Questionnaire (SPAQ) [Rosenthal et al, 1987] to 2,260 Amish individuals, aged 18 and older, who had previously participated in studies of cardiovascular, metabolic, and bone health conducted at the University of Maryland

[Streeten et al, 2006; Hseuh et al, 2007; Mitchell et al, 2008; Rampersaud et al, 2009]. A letter was included with directions to complete the questionnaire and return it in a pre-stamped, addressed envelope. A $1 bill was included as a token of appreciation. The letter sent to the participants explicitly stated that their completing the questionnaire would document their consent to participate in this study. This study and all previous studies were approved by the Institutional Review Board of the University of Maryland School of Medicine. The Seasonal Pattern Assessment Questionnaires were mailed in May, 2010 with a second mailing to non-responders to the first in September, 2010. A total of 1,306 questionnaire responses, representing a response rate of 57.8%, were received back before December 31, 2011 and are included in the dataset.

Seasonal Pattern Assessment Questionnaire (SPAQ)

The SPAQ [Rosenthal et al, 1987] is a research and screening tool that is widely used in studies of seasonality and SAD. The SPAQ evaluates severity of global seasonal changes, degree of functional impairment with those changes ("problem"), and seasonal pattern (summer vs. winter) if the other two criteria are met. The GSS was calculated based on responses to the six parameters of seasonality (sleep duration, social activity, mood, weight, appetite, and energy level) as rated on a 0 ("no change") to 4 ("extremely marked change") scale reflecting degree of change across the seasons [Kasper et al, 1989b]. In a few cases where responses to one or more of the six items were left blank, the GSS was estimated using a proportion based calculation. A convenience sample analysis of test-retest reliability of the GSS and problem rating score (PRS) on the SPAQ in 68 study subjects yielded satisfactory results (GSS, $\alpha = 0.87$, $p < 0.001$; PRS, $\alpha = 0.79$, $p < 0.001$) [Kuehner et al, 2013 (in press)].

SAD was defined according to three criteria: a) GSS score, b) "problem" and c) seasonal pattern [Magnússon, 2000]. Subjects were classified as having SAD if they had a GSS of 11 or higher, if they experienced seasonal changes as a problem to at least a moderate degree, and if they reported a fall-winter pattern of mood disturbance, i.e., if they felt worst during one or more months from September to February. Subjects were classified as having s-SAD if they had a GSS of at least 11 but the problem score was less then moderate (i.e., mild or none) or if they had a GSS of 9 or 10 and considered seasonal changes as at least a mild problem. For subjects who met GSS and problem criteria for either SAD or s-SAD, and had a predominantly fall/winter pattern with one or more months falling outside the fall/winter range, we used the following criterion to classify the pattern: If subjects felt worst during months in both fall-winter (September - February) and spring-summer (March – August), then they were classified as having SAD or s-SAD only if the number of months in which they felt worst during the fall- winter period (September – February) exceeded the number of months in which they felt worst during the spring-summer period (March – August) by at least two. If subjects met GSS and problem criteria for SAD or s-SAD but felt worst for several consecutive months that overlapped the cut-off between summer and fall (i.e., August/September) or winter and spring (i.e., February/March), then they were classified as having a winter pattern when at least two of these consecutive months were in the fall or winter and only one of these months was in the spring or summer. For example, if a participant indicated that he or she felt worst in January, February, and March *or* in August, September, and October, he or she was considered to have a winter pattern.

Awareness was assessed by a single question on the SPAQ ("Have you ever heard about Seasonal Affective Disorder (S.A.D.)?") to which the subject responded by checking either "Yes" or "No."

Statistical Analysis

We compared the distribution of variables (e.g., age, BMI) between groups (e.g., men vs. women, aware vs. not aware) using linear models that accounted for family structure because many of the study subjects were related. This was accomplished using a variance components model that included the relationship matrix as a random effect. The heritability of GSS was estimated by quantitative genetic procedures [Falconer and Mackay, 1996; Hseuh et al, 2000] with adjustments made for age, gender, and household, the latter included to allow for an environmental effect shared among household members. Heritability was defined as the proportion of the total trait variance attributable to the additive effect of genes and was estimated by modeling the phenotypic covariance (conditional upon covariate effects) between any two individuals in the pedigree as a function of their degree of biological association. All parameter effects, including heritability, were estimated using the maximum likelihood method with the SOLAR software package (Texas Biomedical Research Institute, San Antonio, Texas) [Almasy and Blangero, 2010].

Results

Demographic characteristics of sample (Table 1)

The sample included 736 women (56.3%) and 570 men (43.6%). The mean age (± SD) was 55.6 (± 14.8) years and mean body mass index (BMI) was 27.1 (± 5.0) kg/m^2. Out of all respondents, 271 (20.8%) had heard of SAD before. There was no significant difference in GSS in respondents who completed two SPAQ mailings.

Characteristics of SAD and total SAD in the Amish

Table 1 shows mean characteristics of the study sample by gender. The mean GSS (± SD) was 4.36 (± 3.38) and was slightly higher, although not significantly so, in women (4.5 ± 3.5) compared to men (4.2 ± 3.1). There were 11 cases of SAD in the sample (0.84%; 95% CI 0.36 – 1.58). The number of total SAD (defined as subjects with either SAD or s-SAD) cases was 34 (2.59%; 95% CI 1.69 – 3.73) with a higher prevalence in women than in men (3.4% vs. 1.6%, p < 0.05). There was little difference in age between those with (n = 11) and without (n = 1295) SAD (56.8 vs. 55.6 yrs., p = 0.91), although subjects with total SAD (n = 34) were significantly younger than those without total SAD (n = 1272) (49.1 vs 55.8 yrs, p = 0.006).

Awareness of SAD was similar between men and women (Table 2). Subjects aware of SAD tended to be younger, albeit not significantly (54.2 vs 55.6 yrs, sex-adjusted p = 0.13), and were more likely to have SAD (2.2% vs 0.4%, p = 0.03) and total SAD (5.9% vs 1.6%, p = 0.0003) compared to subjects not aware of SAD.

Heritability

Heritability of GSS was estimated to be 13.6% (n = 1286; p = 0.002; 95% CI = 2.5%-24.7%) after controlling for age and gender. The heritability estimate was unaltered when adding household effect as a random effect to the model (h^2=13.6%; p=0.002; 95% CI = 2.5%-24.8%).

Discussion

To our knowledge, this is the first study on seasonality and its heritability in the Amish population and also the first SAD study in a population with limited exposure to bright electric light. Global seasonality scores and prevalence of SAD in the Amish were found to be lower than expected based on earlier studies in other populations [Magnússon, 2000]. Studies performed in different countries, continents, and hemispheres show SAD prevalence

estimates from 0 in the Philippines, a tropical country, to over 10% in Denmark [Dam et al, 1998], with a significant correlation between prevalence and latitude in North America, but only a non-significant trend in European studies [Mersch et al, 1999]. Certain populations appear to be less vulnerable to SAD. For instance, SAD is less common in Icelanders (3.8%) [Magnússon and Stefánsson, 1993] than in residents of Maryland (4.3% and 7.3% [Kasper et al, 1989b; Rosen et al, 1990]), New York (4.7%), and New Hampshire (9.7%) in the US [Rosen et al, 1990], even though Iceland is at a higher latitude. Interestingly, SAD prevalence is also low in individuals of Icelandic descent in Canada (1.2%) [Magnússon and Axelsson, 1993] (again at higher latitude than in US studies, suggesting that there may be resilience to SAD in Icelanders). In Finland, one study found that SAD is more common in Finns than in Lapps [Saarijärvi et al, 1999], possibly suggesting resilience in the latter group. In Switzerland, the country of origin of the Amish founders [Cross, 1976], the prevalence of SAD is relatively low (2.2%) [Wirz-Justice et al, 2003]. Contrary to our primary hypothesis, the frequencies of SAD (0.84%) and s-SAD (1.75%) were found to be lower in the Amish than in other populations at similar latitudes [Kasper et al, 1989b; Rosen et al, 1990], and were even lower than in populations living in temperate climates with previously documented low frequencies of SAD such as Icelanders, Swiss, and Lapps [Magnússon and Stefánsson, 1993; Magnússon and Axelsson, 1993; Saarijärvi et al, 1999; Wirz-Justice et al, 2003]. In fact, the observed prevalence of SAD in this Amish sample is the lowest in all SPAQ-based studies of SAD prevalence conducted in predominantly Caucasian populations [Magnússon, 2000].

While it is possible that the use of a mailed pen and paper questionnaire lowered response rates in the Amish, this is an unlikely scenario because the response rate of our study is quite similar to the response rates in other studies using mailed questionnaires (approximately 50% for mailed SPAQs [Magnússon, 2000]), and the prevalence of SAD was higher in those previous studies. The response rates in our study match well with the response rates for general physician questionnaires [Cummings et al, 2001]. However, Amish-specific cultural factors may have played a role in answering the SPAQ. The Amish may be more stoical than other populations and may be less inclined to report emotional or behavioral problems, especially in an impersonal context inherent to pen and paper questionnaire completion. This may affect the way in which they respond to questions regarding whether seasonal issues are a "problem" for them and the months in which they "feel worst." To take these factors into consideration, we considered individuals who had GSS values and problem ratings that met the criteria for SAD or s-SAD but who did not indicate the months during which they felt worst. By considering the months in which these participants indicated they felt "best" and assuming the inverse of these months as the months in which they felt worst, we were able to identify 3 new "cases" of SAD, bringing the number of cases from 11 (0.8%) to 14 (1.1%). The number of cases of total SAD increased from 34 (2.6%) to 47 (3.6%). These prevalence rates are still notably lower than most other predominantly Caucasian populations studied.

One could hypothesize that a lower awareness of SAD and its treatment in the Amish could not only be the result of lower rates of SAD, but could also contribute to underreporting of problems and thus contribute to a lower rate of SAD. Indeed, only 21% of the surveyed Amish were aware of SAD, in contrast to approximately half of the non-Amish respondents in Montgomery County, MD more than 20 years earlier [Kasper et al, 1989b].

If not a response bias, perhaps routine patterns of exposure to sunlight play a role in contributing to this low prevalence of SAD. While light intensity during early morning and late evening in winter is likely to be reduced in the Amish (although there are no direct measurements reported to date), it is likely that light exposure during daytime is greater in the Amish because they spend more time working outdoors in general, although fewer than

half are now farmers [Kraybill, 2008]. It is conceivable that people who spend more time working outdoors, such as the Amish, might have a lower likelihood of developing SAD. In addition, actigraphic studies of physical activity in the Amish of Lancaster County have found much higher levels of physical activity in this population [Rampersaud et al, 2009; Evans et al, 2011]. Exercise has potential beneficial effects in patients with non-seasonal depression [Rimer et al, 2012] and possibly also in seasonal depression [Partonen et al, 1998] and thus, physical work may contribute to the low prevalence of SAD in the Amish.

Our primary hypothesis that the Amish would have higher seasonality and more cases of SAD was based on the photoperiod hypothesis of SAD, which states that SAD is a result of shortened photoperiod in the winter. In animals, the effects of photoperiod are mediated by changes in duration of nocturnal melatonin secretion which converts the calendar signal (duration of external night) [Wehr, 2001]. In humans, the duration of nocturnal melatonin secretion is longer in winter than in summer in patients with SAD but not in healthy individuals in their regular habitat [Wehr et al, 2001]. Extension of the photoperiod with light therapy is efficacious for treating SAD [Rosenthal et al, 1984], further providing evidence for the photoperiodic hypothesis.

Another dominant theory, i.e. the phase shift hypothesis of SAD, posits that SAD is a result of phase delay of endogenous circadian rhythms in relation to the external clock, the sleep-wake cycle, or other rhythms [Lewy et al, 2006] due to insufficient exposure to morning light in winter. According to the well replicated phase response curve to light exposure, exposure to bright light in the morning results in a phase advance whereas exposure to bright light in the evening induces a phase delay, with mid-day exposure having no effect [Van Cauter et al, 1994; Khalsa et al, 2003]. There is evidence for [Lewy et al, 1987; Terman et al, 1988; Lewy et al, 1998; Lewy et al, 2006] and against [Wirz-Justice et al, 1993] the phase shift hypothesis. In particular, studies attempting to unmask sleep and environment from circadian factors in SAD resulted in conflicting results. For instance, a "constant routine" protocol (which unmasks endogenous circadian rhythms by studying subjects in a controlled setting for 36 hours to minimize the influence of masking effects) confirmed phase delays of temperature and cortisol in hypersomnic seasonal depression [Avery et al, 1997]. In contrast, going against the phase- delay hypothesis, a study utilizing a forced desynchrony routine (a gold-standard protocol to unmask endogenous circadian rhythms while minimizing effects of sleep deprivation) found no difference in the temperature and variations of mood with circadian phase or sleep-wake cycles between subjects with and without SAD [Koorengevel et al, 2002], failing to provide support for the phase delay hypothesis. The strongest evidence supporting the phase shift hypothesis is the consistently reported superiority of morning light as compared to evening light for treatment of SAD [Golden et al, 2005].

Because exposure to artificial lights in the evening can result in phase delays, one possible speculative, and somewhat paradoxical, explanation of our results is that in modern humans electric light exposure in the evening is contributing to, rather than alleviating, seasonal changes in mood. Boivin and colleagues have shown that even light of low intensity equivalent to room light (likely above the light intensities generated in the Amish homes) can result in phase shifting effects [Boivin and Czeisler, 1998]. It could be that a greater number of individuals in modern populations, but not in the Amish, would tend to be phase-delayed in the winter in part because of extended exposure to evening bright light, and, according to the phase shift hypothesis, to be more likely to develop seasonal depression. This novel hypothesis could be formally tested in future studies.

The heritability of seasonality was found to be 13.6% after adjustment of age, sex, and household. It is possible that environmental factors play a larger role in seasonality in the

Amish than genetic factors. The limitations of heritability should also be kept in mind. For example heritability is not constant and may change over the course of time due to changes in environmental factors or gene-environment interactions [Visscher et al, 2008].

The limitations of the study include the likely overestimation of the rates of SAD by SPAQ in comparison to clinical diagnostic criteria [Levitt and Boyle, 2002; Steinhausen et al, 2009]. Thus, it is possible that the actual rate of SAD in the Amish population is even lower than that found in our study. It should be emphasized that the SPAQ is a screening and research tool, not a diagnostic tool. The diagnosis would need to be verified by clinical interview or questionnaires, which was not done in our study. Also, there is the potential for selection bias and recall bias with mailed questionnaires. Obviously, the results of this study, which was done in a very specific population, have limited generalizability. Further studies examining the level of exposure of the Amish to light and, possibly, of genes potentially involved in SAD would help elucidate the reasons for the low prevalence of SAD in the Amish.

Conclusion

This was, to our knowledge, the first study in a population without regular exposure to network electric lighting. Our hypothesis that the prevalence of SAD in the Amish would be higher than in other populations due to their limited exposure to electric lighting was not supported. In fact, contrary to expectation, the Amish had the lowest prevalence of SAD in all SPAQ-based population studies in Caucasians [Mersch et al, 1999; Magnússon, 2000]. Similarly, heritability of GSS in the Amish was found to be relatively low. Further studies involving clinical interviews and non-Amish controls would be required to confirm this first report and potentially to identify the mechanisms responsible for the lower seasonality score, heritability of seasonality scores, and prevalence of SAD in the Old Order Amish. This may lead to identifying new factors of resilience to SAD, which may better inform future preventative and curative approaches

Acknowledgments

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Table 1

Mean GSS and frequencies of seasonal affective measures in Amish men and women.

	Men (n = 570)	Women (n = 736)	Total (n = 1306)	p-value[*]
Mean age	54.7 ± 15.2	56.4 ± 14.4	55.6 ± 14.8	0.05
Mean BMI	26.2 ± 3.9	27.8 ± 5.6	27.1 ± 5.0	<0.0001
Mean GSS	4.2 ± 3.1	4.5 ± 3.5	4.4 ± 3.4	0.23
% Reporting Awareness	18.4 (n = 105)	22.6 (n = 166)	20.8 (n = 271)	0.17
% With SAD	0.35 (n = 2)	1.2 (n = 9)	0.85 (n = 11)	0.07
% With total SAD	1.6 (n = 9)	3.4 (n = 25)	2.6 (n=34)	0.03

Total SAD = SAD + subsyndromal-SAD

[*] All p-values adjusted for age (except age)

Table 2

Frequency of SAD and Total SAD in those aware and not aware of SAD.

	Aware of SAD (n = 271)	Not aware of SAD (n = 968)	Adjusted p-value, conditional on family structure
Mean age (yrs)	54.2±12.3	55.6±15.4	0.13
Men, %	38.7 (n=105)	35.5 (n=436)	0.09
Mean GSS	4.8±3.5 (n=270)	4.2±3.2 (958)	0.04
SAD, %	2.2 (n=6)	0.4 (n=4)	0.03
Total SAD, %	5.9 (n=16)	1.6 (n=15)	0.0003

[*] Age adjusted for sex, sex adjusted for age, and GSS and SAD adjusted for age and sex