Photoperiod is associated with hippocampal volume in a large community sample

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Abstract

Although animal research has demonstrated seasonal changes in hippocampal volume, reflecting seasonal neuroplasticity, seasonal differences in human hippocampal volume have yet to be documented. Hippocampal volume has also been linked to depressed mood, a seasonally varying phenotype. Therefore, we hypothesized that seasonal differences in day-length (i.e., photoperiod) would predict differences in hippocampal volume, and that this association would be linked to low mood. Healthy participants aged 30–54 ($M = 43$; $SD = 7.32$) from the University of Pittsburgh Adult Health and Behavior II project ($n = 404$; 53% female) were scanned in a 3T MRI scanner. Hippocampal volumes were determined using an automated segmentation algorithm using FreeSurfer. A mediation model tested whether hippocampal volume mediated the relationship between photoperiod and mood. Secondary analyses included seasonally fluctuating variables (i.e., sleep and physical activity) which have been shown to influence hippocampal volume. Shorter photoperiods were significantly associated with higher BDI scores ($R^2 = 0.01$, $\beta = -0.12$, $p = 0.02$) and smaller hippocampal volumes ($R^2 = 0.40$, $\beta = 0.08$, $p = 0.04$). However, due to the lack of an association between hippocampal volume and Beck Depression Inventory scores in the current sample, the mediation hypothesis was not supported. This study is the first to demonstrate an association between season and hippocampal volume. These data offer preliminary evidence that human hippocampal plasticity could be associated with photoperiod and indicates a need for longitudinal studies.

Keywords

photoperiod; depression; neuroplasticity

Introduction

The value of investigating seasonal differences in brain morphology is twofold. It may improve our understanding of (1) the neural mechanisms of seasonally recurrent psychopathology, as well as (2) the temporal factors that shape naturally occurring neuroplasticity. The time frame over which naturally occurring structural changes may occur

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is pooly understood (e.g., Lövdén et al., 2013). Within the experience-dependent literature, brain volume changes have been observed in as little as 3 days after color word learning (Kwok et al., 2011) and as long as 12 months following an aerobic exercise intervention (Erickson et al., 2011). Although volume changes associated with learning and exercise provide insight into the timing of neuroplasticity, the time frames of studies in this area are constructed around interventions and leave natural environmental effects unexplored. Investigation into brain volume differences between seasons with different durations of day length, or photoperiod, may thus improve our understanding of naturally occurring neuroplasticity.

Seasonal grey matter volume changes, reflecting seasonal neuroplasticity, have been observed in birds and non-human mammals, especially in the hippocampus (Smulders et al., 1995; Clayton et al., 1997; Tramontin and Brenowitz, 2000; Hoshooley et al, 2006; Sherry and Hoshooley, 2010; Yaskin, 2011). Specifically, smaller hippocampal size has been associated with shorter winter-like photoperiods. Photoperiodic whited-footed mice (*Peromyscus leucopus*) in short photoperiods, restricted to 8 hours of light exposure, exhibit smaller hippocampal volumes (Pyter et al., 2005) relative to mice exposed to long 16-hour summer-like photoperiods. This volume change may be the result of reduction in dendritic spine density in the CA1 (Pyter et al., 2005) and CA3 regions (Workman et al., 2009) measured during short photoperiods. Further, hamsters exposed to 8-hour short photoperiods exhibit significantly reduced cell body area in pyramidal cells in the CA1 region relative to those exposed to 16 hour long photoperiods (Workman et al., 2011). In contrast, larger hippocampal volumes measured during long photoperiods have been associated with increased dendritic branching complexity in the CA1 region (Pyter et al., 2005), suggesting that seasonal variation in dendritic complexity in hippocampal regions may result in global hippocampal volume changes. Overall, the animal literature points to a consistent photoperiodic change in hippocampal volume and morphology that has yet to be explored in humans.

Photoperiod associated changes in the hippocampus may contribute to seasonally occurring phenotypes, including mood. Morphological hippocampal changes in hamsters exposed to short photoperiods have been associated with increased immobility during the forced swim test, representing depressive-like behavior (Workman et al., 2011). Further, spatial learning performance, which is decreased in humans who are non-seasonally depressed (Veiel, 1997) and seasonally depressed (O'Brien et al., 1993), is also impaired in animals exposed to short photoperiod lengths (Pyter et al., 2005; Workman et al., 2009). Together, evidence suggests that seasonal changes in hippocampal volume are linked to depressive like behaviors.

Accordingly, it is plausible that seasonal differences in hippocampal volume may contribute to the high prevalence of seasonal variation in mood among humans. Seasonal changes in mood are common, with up to 92% of community residents reporting some degree of lower mood in the winter months during shorter photoperiods and an increase in mood during the spring and summer months (Kasper et al., 1989). Clinically significant levels of seasonal changes in mood are found in winter seasonal affective disorder (SAD), in which people experience depressive episodes during the winter months and a change to euthymic, manic, or hypomanic states in summer (Rosenthal et al., 1984). SAD winter episode occurrence has

been thought to result from lower light levels and shorter photoperiods (Roecklein et al. 2013a), which is supported by the efficacy of light therapy to increase morning exposure to light (Terman et al., 2001). Although one study points to the importance of the hypothalamus (Vandewalle et al., 2011), a paucity of research has explored neurobiological factors linking light exposure and mood. Importantly, meta-analyses have shown depression is associated with reduced hippocampal volume with a moderate-to-large effect size (Campbell et al., 2004; Videbech and Ravnkilde, 2004; McKinnon et al., 2009). Therefore, seasonal changes in mood may be partly due to seasonal changes in hippocampal volume. In addition to mood disorders, other phenotypes may be similarly affected by photoperiod, as suggested by the efficacy of bright light therapy in the treatment of eating and neurocognitive disorders (Braun et al., 1999; Willis and Turner, 2007; Dowling et al., 2008).

In light of research linking photoperiod to variation in mood and in hippocampal volume, the aim of the current cross-sectional study was to explore whether photoperiod associated with hippocampal volume, as well as depressive symptomatology, and if so, whether the effect of photoperiod on mood might be mediated by seasonal variation in hippocampal morphology. To this end, the current study explored associations between photoperiod, hippocampal volume, and mood in a sample of healthy adults. Additionally, we statistically adjusted for the impact of variables that vary seasonally, including sleep duration and physical activity, which are also associated with hippocampal volume. We predicted that individuals scanned on short photoperiod days would report higher depression scores, and this relationship would be mediated by hippocampal volume.

Methods

Participants

Participants were drawn from the Adult Health and Behavior Project – Phase 2 (AHAB-II), a study of psychosocial factors, behavioral and biological risk factors, and subclinical cardiovascular disease. Individuals were excluded if they (a) had a history of cardiovascular disease, schizophrenia or bipolar disorder, chronic hepatitis, renal failure, major neurological disorder, chronic lung disease, or stage 2 hypertension (BP ≥ 160/100 mm Hg); (b) reported drinking ≥ 35 portions of alcohol per week; (c) took fish-oil supplements (because of the requirements for another substudy); (d) were prescribed insulin or glucocorticoid, anti-arrhythmic, antihypertensive, lipid-lowering, psychotropic, or prescription weight-loss medications; (e) were pregnant; (f) had less than 8th grade reading skills; or (g) were shift workers. Informed consent was obtained in accordance to the guidelines of the University of Pittsburgh Institutional Review Board. Demographic information, including height, weight, race, and years of education, and questionnaire data were collected over multiple laboratory visits. In an effort to limit differences in photoperiod between scan day and on the days that other variables thought to vary seasonally (sleep, physical activity and depression: Rosenthal et al., 1984; Wehr, 1991; Tucker and Gilliland, 2007) were collected, the sample was restricted to those who completed the Pittsburgh Sleep Quality Index (PSQI: Buysse et al., 1989), the Paffenbarger Physical Activity Questionnaire (Paffenbarger et al., 1993), the Beck Depression Inventory (BDI: Beck et al., 1961), and the Center of Epidemiological Studies Depression Scale (CES-D: Radloff, 1977) within 30 days

of scan date. Therefore, individuals were included in the current study if they 1) had successful acquisition of MRI structural images and 2) if they completed sleep, exercise, and depression measures within 30 days of their MRI scan. Of the 459 individuals with successful MRI acquisition, 55 individuals were excluded because additional study assessments were not collected within 30 days of the scan date. The 55 individuals excluded due to assessment timing were not significantly different from the final sample ($n = 404$) in age ($F_{458} = 1.17$, $p = 0.28$), sex ($\chi^2_1 = 1.17$, $p = 0.28$), race ($\chi^2_2 = 1.70$, $p = 0.43$), years of education ($F_{458} = 0.87$, $p = 0.35$), BDI ($F_{458} = 1.01$, $p = 0.32$) and CES-D ($F_{452} = 0.70$, $p = 0.40$) score, or hippocampal volume ($F_{458} = 2.55$, $p = 0.11$).

Photoperiod

Day of scan sunrise and sunset times in Pittsburgh, PA were extracted from the United States Naval Observatory online data repository (http://aa.usno.navy.mil/data/docs/RS_OneYear.php). Photoperiod was calculated by subtracting sunset from sunrise, yielding duration in hours of daylight (decimal fraction of hours instead of minutes) specific to the study location of Pittsburgh, PA on the participant scan date.

Volume Extraction

MRI Acquisition—MRI scans were collected on a 3T Trio TIM whole-body scanner (Siemens, Erlangen, Germany) using a 12 –channel head coil. High resolution T1-weighted 3D magnetization-prepared rapid gradient echo (MPRAGE) neuroanatomical images were acquired over 7 min 17 sec by these parameters: FOV = 256×208 mm, matrix = 256×208, TR = 2100 ms, inversion time (TI) = 1100 ms, TE = 3.31 ms, and FA = 8° (192 slices, 1mm thick, no gap).

Volumetric Segmentation and Analyses—Volumetric segmentation was completed using the FreeSurfer 5.1 software package (http://surfer.nmr.mgh.harvard.edu). Volumetric data by subcortical region as well as intracranial vault was calculated for each subject using the software's automatic Bayesian segmentation technique. Automatic segmentation was accomplished through use of the FreeSurfer atlas of structure location probabilities (Fischl et al., 2002), identifying 40 subcortical structures on a voxel by voxel basis. Once labeled, the number of voxels per region, per subject, was calculated and used as the volumetric measure (Fischl et al., 2004). FreeSurfer also computed intracranial volume (ICV) for each subject using the determinant of the Talairach transformation matrix (resulted from registration to MNI atlas and normalization) and a scaling factor (the slope of a fitted line of estimated vs. manual ICV data from T2-weighted scans of 22 subjects; Buckner et al., 2004). All segmentations of subcortical brain regions were visually checked for errors and corrected by methods established by FreeSurfer guidelines.

Depression Measures

To explore associations between depression, photoperiod, and hippocampal volume, the BDI was used as the primary measure of depression, as it was created to measure self-reported symptoms and severity of clinical depression (Beck et al., 1961). In an effort to allow for comparisons across studies, the CES-D, a measure meant to capture depression symptomology in a healthy population (Radloff, 1977), was included as an additional

measure of depression in study analyses. Importantly, six individuals did not complete the CES-D and therefore all analyses including this measure were completed in a sample of 398.

Seasonal Variables

In an effort to determine whether the association between photoperiod and hippocampal volume could be accounted for by seasonally fluctuating variables previously associated with hippocampal volume, sleep, and physical activity were included in analyses. Self-reported average hours of sleep per night over the past month were calculated from the PSQI. Physical activity was measured as average weekly kilocalories expended based on the Paffenbarger Physical Activity Questionnaire. Two participants were missing this questionnaire and therefore analyses including physical activity were reduced to 402 participants.

Additional Covariates

Due to the stability of body mass index (BMI; Herman et al., 2009) over time, BMI measurements were not restricted to within 30 days of scan date. Blood pressure was included to be consistent with previous analyses (Marsland et al., 2008). Although blood pressure exhibits a seasonal pattern (Brennan et al., 1989), the majority of participants were not tested within 30 days of their scan date and therefore the date could not be restricted for the blood pressure measure. Nursing staff recorded BMI and blood pressure. Participants' height and weight were measured, and used to calculate BMI ((weight[lbs]/height[in^2]) x 703). Further, both systolic and diastolic blood pressure were measured twice over two visits and averaged. Two individuals did not have blood pressure data and were excluded from secondary analyses exploring the impact of blood pressure on seasonal hippocampal volume differences.

Statistical Approach

Primary Analyses—As the result of previous associations of age, gender, race, education, BMI and blood pressure with hippocampal volume, bivariate correlations with hippocampal volumes were calculated. Significant correlations were found between hippocampal volume and age, gender, race, and intracranial volume (ICV) and these were therefore included as covariates. Regression models representing each leg of the mediation model (photoperiod$\rightarrow$ hippocampal volume, hippocampal volume$\rightarrow$ BDI, and photoperiod$\rightarrow$ BDI) were created including study covariates in order to statistically test for mediation using the Sobel method (Sobel, 1982). As noted above, models including the BDI were replicated using the CES-D (hippocampal volume$\rightarrow$ CES-D, and photoperiod$\rightarrow$ CES-D). Laterality effects were explored by creating separate models using left and right hippocampal volume.

Due to the novelty of the photoperiod and hippocampal volume analyses, the relationship was further explored to understand how much variance in hippocampal volume was explained by photoperiod using a hierarchical regression model. The first step of the model included study covariates and photoperiod on the day of scan was added in a second step of the model. Further, because sleep and physical activity are associated with hippocampal volume (Taki et al., 2008; Noble et al., 2011) and vary seasonally (Wehr, 1991; Tucker and Gilliland, 2007), these variables were added in a separate step before photoperiod, to

determine whether the effect of photoperiod on hippocampal volume persisted after removing variability associated with these measures of lifestyle.

Secondary Analyses—To test whether covariates influenced the significance of the association between photoperiod and hippocampal volume, separate stepwise hierarchical regressions were created for each covariate. Step one included age, gender, race, and ICV, step two included a given covariate (education, BMI, systolic or diastolic blood pressure) and step three included photoperiod.

Results

Participants

The total study sample ($n = 404$) was 53% female with an average age of 43.0 years ($SD = 7.32$). The sample had an average of 16.9 years of education ($SD = 2.85$). Most of the sample self-identified as Caucasian (82.2%) and African American (15.6%), with the remainder (2.2%) identifying themselves as Asian, of Mixed Ethnicity or Other. The range of observed photoperiods in Pittsburgh, PA is from 9.28 hours in winter to 15.07 hours in summer. See Supplemental Figure 1 for frequency of scan by month. Overall, the sample reported low depression scores, with an average BDI score of 4.4 ($SD = 4.42$). Bivariate correlations can be found in Table 1.

Primary Analyses

Associations between Photoperiod and Hippocampal Volume—The photoperiod→ hippocampal volume path was significant, with longer photoperiods associated with higher total ($R^2 = 0.40$, $\beta = 0.08$, $p = 0.04$) and left ($R^2 = 0.35$, $\beta = 0.09$, $p = 0.02$) hippocampal volume, but not right hippocampal volume ($R^2 = 0.36$, $\beta = 0.06$, $p = 0.15$). In order to further explore the observed association between photoperiod and hippocampal volume, a stepwise regression model was performed to better understand the variance in hippocampal volume explained by photoperiod. Step one of the model revealed that age, gender, race, and ICV were significantly associated with total hippocampal volume, predicting 38.5% ($p < 0.001$) of the variance. In step two, photoperiod was a significant predictor of total hippocampal volume, with decreasing volumes associated with decreasing photoperiods. The effect size of photoperiod ($\beta = 0.08$, $p = 0.04$) represents a statistically significant proportion of additional variance in hippocampal volume (0.6%) above and beyond the effect of the demographic and ICV covariates (Table 2). When exploring laterality of the effect, photoperiod was not a significant predictor of right hippocampal volume ($\beta = 0.06$, $R^2 = 0.003$, $p = 0.15$). However, photoperiod was a significant predictor of left hippocampal volume ($\beta = 0.09$, $R^2 = 0.009$, $p = 0.02$) suggesting that left hippocampal volume is driving the association between photoperiod and total hippocampal volume.

Seasonal Covariates: Sleep and Physical Activity—To investigate whether the association between photoperiod and hippocampal volume could be explained by sleep duration and physical activity, a three-step regression model was performed, with sleep duration as calculated from bed and wake times reported on the PSQI and physical activity

as measured by average weekly kilocalories expended based on the Paffenbarger Physical Activity Questionnaire. Step one included demographic characteristics and ICV, step two included sleep duration (β_s) and physical activity (β_p), and step three included photoperiod. The addition of sleep duration and physical activity did not significantly contribute to total hippocampal volume ($\beta_s = 0.06$, $\beta_p = 0.01$, $R^2 = 0.004$, $p = 0.27$), left ($\beta_s = 0.06$, $\beta_p = 0.02$, $R^2 = 0.004$, $p = 0.27$), or right ($\beta_s = 0.05$, $\beta_p = 0.002$, $R^2 = 0.003$, $p = 0.42$) hippocampal volume. Adding photoperiod predicted an additional amount of variance in total hippocampal volume ($\beta = 0.08$, $R^2 = 0.006$, $p = 0.048$) and left hippocampal volume ($\beta = 0.09$, $R^2 = 0.008$, $p = 0.03$) but not right hippocampal volume ($\beta = 0.06$, $R^2 = 0.003$, $p = 0.18$), indicating that photoperiod-based differences in hippocampal volume are not explained by sleep duration and physical activity in the left hippocampus.

Associations between Photoperiod and Depression Scores—Although both the BDI ($r = -0.12$, $p = 0.02$) and CES-D ($r = -0.12$, $p = 0.02$) were significantly correlated with photoperiod, regression models examining the photoperiod → depressive symptoms pathway were not significant (BDI: $R^2 = 0.02$, $p = 0.23$; CES-D: $R^2 = 0.02$, $p = 0.23$). Although there were no significant associations between study covariates (age, gender, race, and ICV) and depression scores in the current sample, covariates explained enough of the variance in depression scores that removing them reveals significant models (BDI: $R^2 = 0.01$, $\beta = -0.12$, $p = 0.02$; CES-D: $R^2 = 0.02$, $\beta = -0.12$, $p = 0.02$).

Associations between Depression Scores and Hippocampal Volume—The total hippocampal volume ($R^2 = 0.009$, $\beta = -0.08$, $p = 0.64$), left ($R^2 = 0.008$, $\beta = -0.07$, $p = 0.68$), and right volume ($R^2 = 0.008$, $\beta = -0.07$, $p = 0.68$) to BDI pathways were not significant. Similarly, the total hippocampal volume ($R^2 = 0.009$, $\beta = -0.10$, $p = 0.64$), left ($R^2 = 0.004$, $\beta = -0.06$, $p = 0.89$), and right volume ($R^2 = 0.01$, $\beta = -0.13$, $p = 0.44$) to CES-D pathways were not significant. Due to the lack of significance of the depression symptoms → hippocampal volume pathway, mediation was not further investigated.

Secondary Analyses

Additional Covariates in the Association between Photoperiod and Hippocampal Volume

—Although education, BMI and the blood pressure variables were not significantly correlated with hippocampal volume, the impact of these covariates on the association between photoperiod and hippocampal volume were explored. Step one of all models was significant (i.e., age, gender, race, and ICV). Step two of each model revealed that education, BMI, diastolic and systolic blood pressure variables did not independently add a statistically significant amount of variance explained above and beyond step one. Further, each model revealed that the effect of photoperiod remained significant with similar effect sizes, indicating these variables did not significantly impact the association between photoperiod and hippocampal volume.

Discussion

Results revealed a novel association between photoperiod and hippocampal volume in a cross-sectional study of human participants. This significant association survived statistical

adjustment for several covariates known to be associated with hippocampal volume (i.e., age, gender, race, education, BMI, blood pressure, sleep and physical activity). Although sleep duration has been previously associated with hippocampal volume in a sample of individuals with Posttraumatic Stress Disorder (Neylan et al., 2010), self-reported sleep duration did not significantly predict hippocampal volume in the current sample. Nor was sleep time associated with photoperiod. Consistent with previous research (e.g. Erickson et al., 2011), physical activity was significantly correlated with hippocampal volume; however, physical activity did not significantly contribute to the variance explained in hippocampal volume when included with study covariates. Importantly, the relationship between photoperiod and hippocampal volume survived correction for both sleep and physical activity, with the amount of variance in hippocampal volume explained by photoperiod being similar across models. Interestingly, the current findings were lateralized to the left hippocampus, a result contrary to a previous study demonstrating seasonal volume difference in the right hippocampus of black-capped chickadees (Smulders et al., 1995). However, lateralized results are difficult to interpret, as many literatures show inconsistent laterality findings in volumetric analyses of the hippocampus (e.g. Woon et al., 2010; Steffens et al., 2011, Zannas et al., 2013). Taken together, these results support an association between photoperiod and hippocampal volume above-and-beyond seasonal differences in sleep, physical activity, and other potential confounders.

Current study results found photoperiod to be significantly associated with hippocampal volume and mood, as measured by the BDI and CES-D. However, the association between hippocampal volume and mood failed to reach significance. This lack of association is consistent with some results (e.g. Rusch et al., 2001; Posener et al., 2003) but contradicts the majority of the literature which has found hippocampal volume sizes to be smaller in those who are depressed (Videbech and Ravnkilde, 2004; McKinnon et al., 2009) associated with length of depressive episode (Saylam et al., 2006) and with clinical severity (Vakili et al., 2000; Saylam et al., 2006). This may be explained by a floor effect, in which the current healthy sample reported low depression symptomology. This lack of variability created a skew towards zero in the CES-D and BDI measures, therefore making it difficult to find an association between mood and hippocampal volume. Future research including a sample with larger variance in depression may be more fruitful in investigating relationships between photoperiod, hippocampal volume and depressed mood. If further research supports the association between hippocampal volume and mood, along with the currently supported photoperiod-hippocampal link and photoperiod-mood link, findings would support the hypothesis that reductions in hippocampal volume during shortened photoperiods increases vulnerability for low mood in winter.

Potential Biological Mechanisms

If future longitudinal studies including a depressed sample support the association between shorter photoperiod and smaller hippocampal volumes in those with low mood, it may then be important to understand why some individuals may be more sensitive than others to photoperiodic changes leading to vulnerability to low mood. One potential explanation for this individual variation in the impact of photoperiod is photoreceptor abnormalities in the retina, resulting in individual differences in light sensitivity. The retinal sub-sensitivity

hypothesis, a theory in SAD development, suggests that individual differences in photoreceptor sensitivity may decrease retinal transduction of light to the brain, creating vulnerability to depression during the winter when light levels are lower (Hébert et al., 2002). Research supporting this hypothesis has found that genetic variation in a gene which encodes the circadian and non-visual photopigment melanopsin in the retina increases vulnerability to SAD (Roecklein et al., 2013b). In the context of the current study, individuals with higher depression scores may experience more extreme seasonal variation in hippocampal volume due to individual differences in retinal photoreceptor sensitivity, a hypothesis that warrants further study.

Although the present study demonstrated that hippocampal volume correlated with photoperiod length cross-sectionally, the biological mechanism linking seasonal photoperiodic differences in hippocampal volume is unknown. One potential candidate is brain derived neurotrophic factor (BDNF), a member of the nerve growth factor gene family that has been associated with neuronal survival and proliferation (for review see Binder and Scharfman, 2004). In the hippocampus, BDNF has been specifically associated with increased dendritic spine density in the CA1 region (Tyler and Miller, 2001), a morphological change similar to that reported above in rodents during long photoperiods (Pyter et al., 2005), and would result in increased structure volume. Further, a genetic polymorphism, which has been found to impact BDNF trafficking, has been associated with variation in hippocampal volume (Val166Met; Bueller et al., 2006). Human serum BDNF levels are reported to vary according to photoperiod, with the highest levels in the late summer and early fall months (Molendijk et al., 2012). Additionally, light induced photoperiod advances are associated with increased BDNF protein levels in the rat hippocampus (Sei et al., 2003), suggesting that light may have a direct influence on BDNF levels in the hippocampus. Therefore, seasonal changes in light exposure may directly increase the amount of BDNF available in the hippocampus, thereby influencing hippocampal volume through increased dendritic arborization. Interestingly, BDNF has also been implicated in the development of depression (Duman and Monteggia, 2006). Within the context of the current study, it may be that decreased BDNF may mediate the relationship between shorter photoperiods and smaller hippocampal volumes.

Potential Evolutionary Advantage

Decreased hippocampal neurogenesis in winter may subserve circannual variations with adaptive significance. Workman & Nelson (2011) hypothesize that circannual rhythms help animals functionally adapt to environmental challenges of seasons. For example, male Siberian hamsters exhibit more aggressive behaviors when exposed to short day patterns of melatonin secretion as compared to longer day melatonin secretion patterns, which may be helpful in procuring limited resources during the winter (Demas et al., 2004). In the context of the current study, it has been proposed that decreased hippocampal size in animals during the winter may be a result of decreased need for spatial memory in foraging behaviors (Pyter et al., 2005). Overall, seasonal variation in hippocampal volume may have been evolutionarily advantageous to divert resources from hippocampal neurogenesis to other brain areas needed for survival in winter months.

Applications to Experience and Exercise Literature

Recent studies in the experience and exercise literature have found similar or smaller percentages of variance explained in hippocampal volume change (2–4%: Erickson et al., 2011; Lövdén et al., 2011), suggesting the current study is consistent with other hippocampal plasticity estimates. Due to its highly plastic nature, even small changes in hippocampal volume have the potential to exert significant impact on hippocampal dependent processes. For example, hippocampal volume, as measured with MRI, has been associated with performance on memory tasks, both in adults and children (Ostby et al., 2012), as well as risk for dementia (Ikram et al., 2010; Stoub et al., 2010). It is likely that controlling for photoperiod in such studies would clarify interpretation of the results, and even uncover additional variance accounted for by the target variables.

Limitations

Despite its many strengths, the current study design includes some limitations. First, the current study was cross-sectional, measuring individuals once rather than during different seasons. In order to make a causal statement about individual seasonal hippocampal volume change, the current study question should be applied longitudinally, measuring within-individual seasonal variation in hippocampal volume in both summer and winter. Second, study measures were collected over several visits, which deviated from MRI scan collection by 0–30 days (i.e., BDI, CES-D, sleep, and physical activity), or more (i.e., blood pressure, BMI). Because the study question was concerned with the impact of photoperiod on brain volume, it was important to have participants complete study measures temporally proximal to the scan day. In an effort to limit the noise created by differences in photoperiod of scan and study measure day, the sample was restricted to those who completed measures within 30 days of scan. However, it is important to note that photoperiod can change by more than an hour during spring and fall months, which may mean that the photoperiod during study measure collection may differ from photoperiod during the scan. For this reason, future research should aim to collect all study measures on the day of scan and to repeat scans across the year in different photoperiods. Lastly, the study sample was limited to healthy midlife adults, which restricted the range of depression scores in the sample. Replication of the heightened seasonal change in hippocampal volumes in a sample with higher depression scores would extend these results to a clinical population.

In addition, study results may have been improved with the inclusion of additional measures. First, the current study focuses on the hippocampus; however, there may be other brain areas important to mood changes which may also exhibit seasonal plasticity. For example, one study found seasonal changes in amygdala in pre-pubertal Syrian hamsters (Romeo & Sisk, 2001), a structure which has also been implicated in the development of depression (Drevets, 2003). Secondly, associations between cognitive measures and hippocampal volume may suggest the importance for controlling for these measures in future studies. For instance, full scale IQ scores have been shown to be inversely related to hippocampal volume (Amat et al., 2008) and therefore may be important additional covariate to include in the novel photoperiod hippocampal volume relationship.

Conclusions

The current study is the first to demonstrate seasonal hippocampal volume differences based on photoperiod in humans. The reported seasonal variation is consistent with the animal literature, which has found that mammals under short photoperiod conditions exhibit smaller hippocampal volumes relative to those under long photoperiod conditions. These findings suggest that photoperiod may be an important value to analyze when studying brain volumes. Due to the similar variance explained in hippocampal volume by photoperiod compared to experience-dependent and exercise literature, results point to the importance of documenting photoperiod of scan day to ensure detected volume changes were a result of the intended intervention, rather than the day of testing. It is possible that some studies begin in winter and end in summer, yielding an increase in hippocampal volume due to photoperiod confounded with the target intervention. Beyond this contribution to the neuroplasticity literature, the current study provides insight into potential neurological mechanisms underlying seasonally varying phenomena, such as mood, alertness, and eating behavior. However, longitudinal studies are required in order to demonstrate causality between changes in hippocampal volume and seasonal variation in mood. If this heightened seasonal variation is further supported and the association between hippocampal volume and low mood replicated, then results may constitute a vulnerability to depression and point to a potential mechanism of action for bright light treatment, and a potential etiological factor in all disorders that respond favorably to bright light therapy, including mood, eating, and neurocognitive disorders.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Table 1

Study Variable Means (SD) and Correlations

Variables	Means (SD)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
1. Age	42.85 (7.34)	1															
2. Gender	-	0.14**	1														
3. Race	-	0.11*	0.07	1													
4. Education	16.93 (2.85)	-0.08	-0.12*	-0.13*	1												
5. BMI	26.92 (5.20)	0.13**	-0.07	0.17**	-0.23**	1											
6. Systolic Blood Pressure (mm Hg)	115.02 (11.24)	0.13**	-0.19**	0.22**	-0.13**	0.32**	1										
7. Diastolic Blood Pressure (mm Hg)	72.14 (8.07)	0.15**	-0.09	0.14**	-0.11*	0.53**	0.68**	1									
8. BDI	4.41 (4.42)	0.00	0.06	0.01	-0.19*	-0.12*	0.03	0.05	1								
9. CES-D	8.40 (7.49)	-0.03	-.03	0.02	-0.09	0.04	-0.01	-0.02	0.69**	1							
10. Sleep Time (Hours)	6.78 (1.96)	0.01	0.08	0.02	-0.02	0.06	-0.03	-0.03	-0.12*	-0.06	1						
11. Physical Activity (Kilocalores)	2990.90 (2523.18)	-0.07	-0.17*	-0.06	0.04	-0.07	-0.06	-0.11	-0.18**	-0.16**	-0.02	1					
12. Photoperiod	12.51 (2.01)	-0.06	-0.06	-0.08	0.01	0.07	0.04	0.01	-0.12*	-0.12*	-0.03	0.05	1				
13. ICV	1339910.66 (260663.49)	-0.05	-0.72**	-0.16**	0.09	0.08	0.14**	0.03	-0.07	0.01	-0.09	0.16*	0.01	1			
14. Total Hippocampal Volume (mm³)	8340.47 (936.53)	-0.16**	-0.49**	-0.22**	0.07	-0.02	0.08	-0.03	-0.09	-0.06	0.01	0.12*	0.11*	0.60**	1		
15. Left hippocampal Volume (mm³)	4134.07 (511.36)	-0.12*	-0.46**	-0.20**	0.08	-0.05	0.08	-0.03	-0.08	-0.03	0.01	0.12*	0.12*	0.56**	0.95**	1	
16. Right Hippocampal Volume (mm³)	4206.40 (483.18)	-0.18**	-0.45**	-0.21**	0.05	-0.01	0.08	-0.03	-0.08	-0.07	0.00	0.11*	0.09	0.57**	0.94**	0.77**	1

Note: BMI= Body mass index: BDI = Beck Depression Inventory, CES-D = Center of Epidemiological Studies Depression Scale : ICV=Intracranial volume.

*
$p < 0.05$,

**
$p < 0.01$

Table 2

Model coefficients for exploring photoperiod predicting hippocampal volume

Variables	Total Sample (n=404)		
	Total	Left	Right
Age	−12.68 (−0.10)**	−4.49 (−0.07)	−8.18 (−0.12)**
	5.06	2.88	2.69
Sex	−190.14 (−0.10)	−121.69 (−0.12)*	−68.46 (−0.07)
	106.00	60.35	56.30
Race	−206.39 (−0.12)**	−104.29 (−0.10)**	−102.10 (−0.11)**
	70.02	35.35	37.18
ICV	0.002 (0.50)**	0.001 (0.45)**	0.001 (0.50)**
	>0.001	>0.001	>0.001
Photoperiod	37.79 (0.08)*	23.67 (0.09)*	14.10 (0.06)
	18.26	10.38	9.70
R^2	0.6%*	0.9%*	0.3%

Note: All statistics in this table are from block 2 of the analyses. Standardized coefficients listed in parenthesis. Standard error listed on the second line. ICV=Intracranial volume.

*
$p < 0.05$,

**
$p < 0.01$