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An integrative chronobiological-cognitive approach to seasonal affective disorder

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AN INTEGRATIVE CHRONOBIOLOGICAL-COGNITIVE APPROACH TO
SEASONAL AFFECTIVE DISORDER

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ABSTRACT

Seasonal affective disorder (SAD) is characterized by annual recurrence of clinical depression in the fall and winter months. The importance of SAD as a public health problem is underscored by its high prevalence (an estimated 5%) and by the large amount of time individuals with SAD are impaired (on average, 5 months each year). The specific cause of SAD remains unknown; however, researchers have identified possible chronobiological and psychological vulnerabilities to SAD. The study aimed to clarify psychological and chronobiological correlates of SAD in the first test of an integrative model of SAD.

The project used a longitudinal design to test the respective contributions of the chronobiological and cognitive vulnerabilities on winter depression severity in 31 SAD patients and 33 never-depressed controls at sites in Burlington, VT and Pittsburgh, PA. The measures selected for the cognitive vulnerability were established measures of vulnerability to nonseasonal depression with empirical support for their relevance to SAD: brooding rumination, dysfunctional attitudes, cognitive reactivity to an induced sad mood, and season-specific cognitions. The chronobiological vulnerability was measured as Phase Angle Difference (PAD) and deviation from PAD of 6 hours. All measures were completed once in the summer, when the SAD patients were remitted, and once in the winter, when patients were clinically depressed. Patients were distinguished from controls on most cognitive vulnerability measures (brooding, as well as rumination, dysfunctional attitudes, and seasonal beliefs). SAD patients exhibited shorter PAD than controls, but did not exhibit greater deviation from PAD-6. Results provide further support for specific cognitive, but not chronobiological, vulnerabilities in prediction of SAD. Limitations of the current sample are discussed.

Results hold implications for future SAD research bridging the chronobiological and psychological disciplines with the ultimate aim of improved understanding, assessment, treatment, and prevention of SAD.

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CHAPTER 1: Seasonal Affective Disorder (SAD)

Winter seasonal affective disorder (SAD) is a subtype of Major Depressive

Disorder, Recurrent characterized by a distinct seasonal pattern of major depressive

episodes in the fall and/or winter months that remit in the spring and summer months

(Rosenthal, Sack, & Gillin, 1984). In addition to the common symptoms of depression

(depressed mood, anhedonia, fatigue, low self-esteem), individuals with SAD often

experience 'atypical' symptoms, which present as a reversal of the vegetative symptoms

typical of nonseasonal depression, and include hypersomnia, weight gain, and

carbohydrate craving rather than insomnia, weight loss, and low appetite (Rosenthal et

al., 1984). To meet DSM-IV-TR criteria for SAD, an individual's current course of

depression must show a clear seasonal pattern over the past 2 years (APA, 2000). Of

individuals with recurrent major depression, an estimated 10-20% follow a seasonal

pattern (Magnusson, 2000). Some individuals experience the opposite seasonal pattern of

major depression exclusively in the summer months with remission in the winter months,

a syndrome referred to as summer SAD (Wehr et al., 1989). Summer SAD is thought to

be due to mood sensitivity to summer climate conditions (e.g., heat, humidity) and is

considered etiologically distinct from winter-type SAD. For the purpose of this study

investigating etiological factors in the annual recurrence of winter SAD, the generic term

"SAD" is used, herein, to refer to SAD-winter type.

The experience of some seasonal changes is very common, with only 8% of

individuals reporting no seasonal variation in mood or behavior (Kasper, Wehr, &

Bartko, 1989). A milder form of SAD, termed subsyndromal SAD (S-SAD) involves

similar symptoms to a lesser degree of severity and without significant impairment

(Bartko & Kasper, 1989). Individuals with SAD experience seasonal depressive symptoms to an extreme degree (i.e., full-blown major depression) with functional impairment. In the U.S. population, SAD affects an estimated 5% of adults, a total of 14.5 million Americans. SAD is associated with functional impairment for the individual within the family and at work for an average of 5 months per year, with typical onset in early adulthood (Magnusson, 2000). As in most other mood and anxiety disorders, SAD is more commonly reported in females, with an estimated gender ratio in SAD of 3:1 (Magnusson, 2000; Magnusson & Boivin, 2003).

Prevalence Across Latitude

Given that low light availability in winter is hypothesized as the environmental trigger of SAD episode onset, studies have examined whether SAD prevalence varies by latitude. Rosen, Targum, & Terman (1990) were the first to examine SAD and S-SAD prevalence across latitudes in the United States, comparing Nashua, NH, New York, NY, Montgomery County, MD, and Saratoga, FL. Participants were randomly selected via telephone directory and contacted to complete a seasonality questionnaire. Across locations, seasonality scores were significantly higher in females, and inversely related to age. After controlling for these demographic effects, seasonality scores were generally higher in NH and NY as compared to MD and FL, with SAD prevalence estimates highest in NH at 42.5°N (9.7%) and lowest in FL at 27°N (1.4%). Similar patterns were found for subscales measuring seasonal fluctuation in mood, sleep length, and weight. Additionally, a larger proportion of individuals at higher latitudes endorsed their seasonal changes as problematic as compared with individuals at lower latitudes (26.1% in NH vs. 13.5% in FL). Individuals at the three higher latitudes were also over two times more

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likely to identify winter months as the worst months than individuals in FL. Similar

investigations of latitude and prevalence were implemented in Scandinavia, with mixed

results, whereas no effect of latitude was found on SAD prevalence in Italy, Turkey, or

Australia, as reviewed by Magnusson (2000). In a study examining the prevalence of

SAD across eight degrees of latitude in Canada from 41.50°N to 49.49°N, latitude was

found to be only weakly negatively correlated with seasonal change in mood (Levitt &

Boyle, 2002). Thus, the strongest evidence for an effect of latitude on prevalence has

been found in U.S. populations (Mersch, Middendorp, Bouhuys, Beersma, & van den

Hoofdatter, 1999), suggesting that socio-cultural influences may impact SAD as well.

Environmental Triggers of SAD

Epidemiological studies examining SAD across latitude were indirectly testing

the effect of light availability on SAD. However, these studies did not control for

potentially confounding factors such as time spent outdoors, geographical climate, or the

tendency of individuals with SAD to migrate southward for symptom remission

(Magnusson, 2000; Mersch et al., 1999). Two survey studies in Japan compared the

effects of latitude and local hours of sunshine on SAD prevalence. Although both factors

significantly correlated with SAD prevalence, a regression analysis revealed that hours of

sunshine, but not latitude, was related to SAD prevalence (Okawa, Shirakawa, &

Uchiyama, 1996; Sakamoto, Kamo, Nakadaia, Tamura, & Takahaski, 1993). In a direct

test of environmental factors on SAD symptom severity, Molin, Mellerup, Bolwig,

Scheike, and Dam (1996) assessed depression severity biweekly from September to May

in a sample of SAD patients in Copenhagen, Denmark. Depression severity was found to

correspond to local meterological data, whereby light availability factors (e.g., minutes of

sunshine, global radiation, and photoperiod) inversely predicted depression severity

across the winter season in SAD patients. Young, Meaden, Fogg, Cherin, and Eastman

(1997) tested the effects of different environmental triggers on the annual timing of SAD

onset by pooling data on the timing of SAD symptom onset across seven fall seasons,

from 1988-1994 in SAD patients in Chicago, IL. Weekly onset risk for SAD was derived

using a survival analysis, and a multiple regression analysis was utilized to test the

relative impact of variations in weather (hours of sunshine, temperature, solar radiation)

and photoperiod (i.e., daylength from dawn to dusk) on the timing of SAD onset.

Photoperiod was the only significant predictor of onset risk, accounting for 26% of the

variance in risk (Young et al., 1997). Thus, despite being highly correlated with the

seasonal pattern of SAD risk, none of the other environmental variables, or their

interaction with photoperiod, accounted for significant variance in SAD risk above and

beyond that by photoperiod alone, supporting photoperiod as the primary environmental

predictor of SAD risk.

Chronobiological Vulnerability to SAD

To further explain the relation between photoperiod and seasonal depression

severity, psychiatric researchers have proposed several theories implicating circadian

rhythm abnormalities in SAD, suggesting that SAD patients demonstrate unique

chronobiological responses to the seasonal changes in photoperiod. In order to articulate

these theories, a brief description of the circadian pacemaker is needed.

The human circadian pacemaker, located in the suprachiasmatic nucleus (SCN) of

the anterior hypothalamus, is responsible for synchronizing physiological processes to the

external 24-hour light/dark cycle. The circadian clock is calibrated to the light/dark cycle

on a daily basis via input from external time cues, or zeitgebers, with light being the most potent zeitgeber. Ocular light input is projected to the SCN via the retinohypothalamic tract. The pacemaker, in turn, emits an endogenous neural signal of day length to regulate the timing of circadian rhythms in hormone secretion, sleep, alertness, and other behaviors (Wehr, 2001).

The human circadian system cannot be examined directly, thus, pacemaker output is measured by the timing of rhythms regulated by the daily resetting of circadian phase (e.g., core body temperature, melatonin, and cortisol release). Melatonin is secreted by the pineal gland at night, with daytime suppression by light. In humans, melatonin typically remains elevated for 10-12 hours at night, increasing significantly 2-3 hours prior to bedtime (Benloucif et al., 2008). The clock time of the onset of melatonin release captured under dim light conditions is referred to as the dim light melatonin onset (DLMO), and is the most commonly utilized biomarker for circadian phase as it appears to be relatively robust to changes in sleep, stress, and activity as compared to other measures of circadian phase such as core body temperature and cortisol (Arendt, 2005; Benloucif et al., 2008; Burgess & Fogg, 2008; Lewy, Wehr & Goodwin, 1980). See Figure 2 for an illustration of the temporal relation between DLMO and sleep.

Photoperiodic hypothesis. In mammals, the duration of nocturnal melatonin release varies by photoperiod and serves as a physiological signal of season for regulation of seasonal changes in physiology (e.g., thermoregulation, metabolism) and behavior (e.g., reproduction) where shorter photoperiods correspond to longer, and longer photoperiods correspond to shorter, melatonin release durations (Wehr, 2001). Therefore, the photoperiodic hypothesis proposes that people with SAD are like other

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mammals in that they have retained this circadian signal of season and uniquely exhibit prolonged duration of nocturnal melatonin release in response to the shortened photoperiod of winter (Wehr, 2001). This effect has been experimentally tested in studies examining circadian responses to natural and contrived variations in photoperiod in humans.

An initial investigation of the adaptation of melatonin duration to artificial photoperiods in healthy individuals exposed participants to two counterbalanced, contrived photoperiods: very short (10 hours of light/14 hours of darkness) and also very long (16 hours of light/8 hours of darkness) photoperiods corresponding to winter and summer day lengths, respectively (Wehr, Moul, Barbato, Giesen, & Seidel, 1993). Circadian rhythms were found to be expanded after exposure to the shortened photoperiod (long night) as compared to the same individuals exposed to longer photoperiods, as measured by the durations of nocturnal melatonin release, low core body temperature, and sleep. These effects retained after 24 hours in dim light conditions, providing further support to the circadian effects induced by photoperiod. These findings provide support that humans have retained the ability to track seasonal changes in this manner.

To test whether a unique response in melatonin duration was present in SAD, Wehr et al. (2001) compared SAD patients with healthy controls on duration of melatonin release in summer and winter. Patients exhibited longer active melatonin release durations during winter relative to themselves in summer (an average difference of 36 minutes), with the variance largely accounted (67%) for by a winter delay in timing of the offset of melatonin. However, control individuals did not show a significant seasonal

difference in the duration of melatonin release. This finding suggests that expanded

melatonin duration in winter relative to summer may be involved in SAD. However, this

is the only study to date comparing melatonin duration across seasons in SAD patients

and controls, the results need to be replicated.

Phase Shift Hypothesis. The Phase Shift Hypothesis (PSH) postulates that SAD

results from a seasonal misalignment between the circadian clock and the external

light/dark cycle or other biological rhythms (e.g., sleep/wake; Lewy, Sack, & Singer,

1988). Specifically, the PSH suggests that SAD patients become depressed in winter due

to the later dawn, which causes a circadian phase delay relative to the light/dark cycle

(clock time) or sleep/wake cycle. This hypothesis arose out of an observation that a

group of SAD patients exhibited more delayed circadian rhythms relative to

nondepressed controls in winter prior to treatment (Lewy, Sack, Singer, & White, 1987).

In this study, morning light therapy phase advanced SAD patients' circadian rhythms to

simulate those of the nondepressed controls, and was also shown to elicit a stronger

antidepressant effect than evening light administration (Lewy et al., 1987). Thus, Lewy

and colleagues inferred that SAD patients may exhibit phase-delayed circadian rhythms

in winter, and that morning bright light may reduce depressive symptoms by correcting

delayed circadian rhythms via advancing the circadian clock to simulate summer

rhythms. The theory has become one of the most widely studied in SAD (Lewy, 2015),

yet has yielded highly inconsistent findings, as reviewed below.

The PSH has largely been indirectly tested in bright light treatment trials

comparing antidepressant responses to light administered at various times of day. Light

is the primary zeitgeber for entrainment of the circadian system and has consistently been

shown to induce circadian phase resetting in humans according to a phase response curve (PRC; Czeisler et al., 1989). With the core body temperature minimum (t-min) marked as an estimator of the crossover point between the advance zone and delay zone of the PRC, studies have found the direction and magnitude of circadian phase shift achieved to be a sinusoidal function of the time of light administration relative to the circadian clock, with the largest phase shifts resulting from light exposure within 2 to 6 hours before (delay) and after (advance) the time of the t-min (as reviewed in Eastman & Martin, 1999). Consistent with the PRC to light, Terman, Terman, and Cooper (2001) found morning light to advance, and evening light to delay, melatonin onset in SAD patients.

According to the PSH, morning administration of bright light should elicit better treatment response, as compared to other administration times, because morning light advances the circadian clock per the phase response curve and is thought to correct the proposed pathophysiologic phase delay in SAD. Thalen, Morkrid, Kjellman, and Wetterberg (1995) reported no differences in degree of improvement associated with morning vs. evening light; however, a greater proportion of SAD patients exhibited a significant treatment response to light (defined as a 50% reduction in symptoms) than nonseasonally depressed patients, suggesting that SAD patients may have a unique physiological or psychological response to light. One meta-analysis reported that dual (morning-plus-evening) light exposure was superior to single exposures at morning, evening, or midday (Lee, Blashko, Janzen, Paterson, & Chan, 1997). Two early studies utilizing cross-over designs to compare the efficacy of morning versus evening light both reported that morning light administration elicited a superior antidepressant response to evening light (Avery, Khan, & Dager, 1991; Lewy et al., 1987). In a review of light

therapy trials, Terman, Terman, and Quitkin (1989) concluded that morning light

administration was associated with the greatest antidepressant response (53% remission

rate), relative to light administered in the evening (38%) or midday (32%), all superior to

placebo response (11%). Morning-plus-evening light exposure was not superior to

morning light alone. Three independent research groups published data in 1998 each

corroborating earlier findings that morning light is associated with better antidepressant

response than evening light (Eastman, Young, & Fogg, 1998; Lewy et al., 1998; Terman,

Terman, & Ross, 1998). Cool white fluorescent light exposure (10,000 lux) administered

in the morning daily for a minimum of 30 minutes is the current gold standard treatment

for SAD (Golden et al., 2005), with optimal administration on the advance zone of the

PRC, clinically derived as 2.5 hours after the midpoint of sleep (Terman et al., 2001).

According to the PSH, evening light would be expected to worsen SAD

symptoms due to inducing or exacerbating a circadian phase delay. However, Terman et

al. (1989) found that although morning light provided a stronger antidepressant response,

evening light alone was also associated with full remission in some (38%) patients, an

effect that directly opposes the phase delay theory of SAD and stands as a primary

critique of the PSH.

The superiority of response to morning light over evening indirectly supports the

PSH; however, this finding alone does not necessarily implicate a corrective phase

advance as the mechanism of the antidepressant response to light. Terman et al. (2001)

examined the relation between the antidepressant response and phase shift magnitude to

morning or evening light exposure utilizing a within-subject cross-over design with SAD

patients. The magnitude of phase advance with morning light was significantly

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positively correlated with symptom improvement, yet phase shifts with evening light were not significantly associated with antidepressant response. Similarly, Thompson, Childs, Martin, Rodin, and Smythe (1997) found SAD patients uniquely exhibited a phase advance of the melatonin rhythm to morning bright light treatment in winter; however, the degree of phase advance in patients did not correlate with symptom improvement. Eastman, Gallo, Lahmeyer, and Fogg (1993) found no association between the direction or magnitude of temperature rhythm phase shifts to morning light treatment and improvement in symptoms, nor were differences in phase shifts reported between SAD patients and controls. However, as noted by Eastman et al. (1993), the data were pooled across cross-over trials despite order in sequence of light treatments. Thus, the inconsistent findings could be due to the confound of carry-over effects. Rosenthal, Levendosky, and Skwerer (1990) also reported a nonsignificant relation between phase shift of the core-body temperature rhythm and antidepressant response to morning+evening light therapy. However, when analyzed by phase-type, individuals whose rhythms phase advanced during light treatment exhibited a greater antidepressant response. Studies testing phase shifts as a necessary component of the antidepressant response have largely indicated that phase shifts accompany, but may not be necessary for, an antidepressant response to light in SAD.

Bright light treatment trials have provided indirect tests of the PSH by comparing circadian phases at pretreatment (when depressed) and posttreatment (when nondepressed) during winter in patients to controls. Other studies have more directly tested the PSH by comparing circadian rhythms across seasons in untreated SAD patients and controls to examine whether SAD patients exhibit a unique seasonal misalignment of

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circadian rhythms. Checkley et al. (1993) compared the 24-hour melatonin release profiles during winter (November to March) in a sample of SAD individuals relative to nondepressed, healthy controls matched for age, sex, and month of study. The groups exhibited similar nocturnal melatonin profiles, such that there were no significant group differences found in the clock time of the onset, mean, amplitude, or acrophase (peak) of nocturnal melatonin release. The PSH predicts that the DLMO should be phase-delayed (shifted later) in SAD patients relative to controls in winter, which was not supported. Another study reported no differences in the timing of other 24/hour biological rhythms (cortisol, prolactin, and thyrotropin) between SAD patients when depressed and nondepressed controls (Oren, Levendosky, Kasper, Duncan, & Rosenthal, 1996), thus providing no evidence of other phase-delayed rhythms in SAD.

In 2001, Wehr et al. published a longitudinal study comparing 24-hour melatonin profiles of SAD patients and nondepressed controls in winter and in summer. There were no differences in the clock time of circadian phase (e.g., DLMO) in patients vs. controls. Therefore, this initial study of seasonal shift in the clock time of circadian phase did not support the posited phase delay in the DLMO as proposed by the PSH. However, Wehr et al. (2001) did not control for the timing of sleep, but did note in a secondary analysis that variation in wake time accounted for 7% of the variance in the winter duration of melatonin release in SAD patients. The lack of control for the effect of the rest/activity cycle (also referred to as sleep/wake cycle) on the clock time of circadian phase (e.g., DLMO) is a limitation across some naturalistic and treatment studies examining biological rhythms in SAD patients. Although light is the strongest zeitgeber to the circadian pacemaker, nonphotic zeitgebers informed by the timing of the sleep/wake

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cycle (e.g., sleep, activity) have been shown to alter the timing of circadian phase, thus possibly confounding or masking the influence of other factors of interest (e.g., season, psychopathology) on circadian phase.

Although the melatonin profile is more robust to influences from the sleep/wake cycle (i.e., activity and posture) than core body temperature or cortisol (Benloucif et al., 2012), there is a bidirectional relation between the sleep/wake cycle and circadian phase such that changes in sleep induce some shift in the timing of melatonin production and vice-versa, which reflects the dual oscillator model of the mammalian circadian rhythm (Arendt, 2005). Burgess and Eastman (2006) found that adjusting sleep times results in parallel phase shifts of the human melatonin rhythm, such that later wake times were shown to phase delay, and earlier wake times were shown to phase advance, the DLMO and dim light melatonin offset (DLMOff). The coupling of the timing of sleep with that of melatonin release has been recorded in healthy individuals as well, such that a 1-hour change in sleep time corresponded to a .87-hour (i.e., 52 min.) change in the timing of the DLMO (Sletten, Vincenzi, Redman, Lockley, & Rajaratnam, 2010; Wright, Gronifer, Duffy, & Czeisler, 2005).

Given the close coupling of the sleep/wake and circadian oscillators, studies examining the clock times of circadian biomarkers (e.g., DLMO) have not adequately controlled for effects of sleep variability on DLMO. Winkler et al. (2005) found the timing of wrist actigraph-measured sleep and activity in SAD patients was phase delayed (by an average of 50 minutes) in winter at baseline, prior to treatment with bright light relative to controls. This evidence of seasonal shift in sleep timing in SAD highlights the importance of controlling for the timing of the sleep/wake cycle when examining

circadian markers across individuals, for classification of circadian functioning in SAD. Additionally, morning light treatment has also been shown to phase advance sleep and activity patterns in SAD patients to match those of nondepressed individuals (Winkler et al., 2005), suggesting light exposure patterns phase shift sleep as well as circadian phase. The inter-individual variation in the timing of the rest/activity cycle is also reflected in sleep. This variation is due to inter-individual differences in activity demands (e.g., work schedules), light exposure patterns and diurnal variation (i.e., morning or evening type). Thus, comparing the DLMO across individuals without controlling for these factors does not accurately measure pure individual differences in circadian functioning. The effects of the sleep/wake cycle can be removed in extensive unmasking protocols that stabilize the timing of sleep in order to allow isolation of assessment of true effects on circadian phase.

The forced desynchrony protocol is the most extensive unmasking procedure, which requires participants to spend one week to one month in an inpatient temporal isolation chamber void of external zeitgebers while placed on artificial day lengths of either very short (20 hour) or long (28 hour) regimens that are incompatible with pacemaker functioning (Aschoff & Wever, 1976). The contrived "day" is spent in dim light, and the "night" is spent in darkness to avoid photic resetting of the circadian clock. This abnormal day length forces the endogenous circadian pacemaker to become desynchronized from the sleep/wake cycle and run at the natural rate of the individual's intrinsic period length (Czeisler et al., 1999). This uncoupling of the circadian oscillators allows measurement of an individual's circadian pacemaker functioning independent of the effects by sleep and activity, as captured via the intrinsic period length (assessed by

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the rate of shift in the timing of the DLMO or *t*-min from baseline to the end of the

desynchrony protocol).

To investigate the effect of circadian functioning on mood in SAD patients,

Koorengevel, Beersma, den Boer, and van den Hoofdakker (2003) studied seven SAD

patients and eight matched controls under forced desynchrony (20-hour day) for 10 days

across the following conditions: during a Major Depressive Episode in winter, upon full

remission from light treatment, and when naturally remitted in summer. Healthy

matched-control participants were assessed once in summer, once in winter. Circadian

phase was measured by serial salivary melatonin (DLMO) and continuous rectal core

body temperature *(t*-min) for one day at the start and end of the protocol. This protocol

revealed no significant group differences in circadian period or phase (assessed by

DLMO or *t*-min) and no significant within-subject changes in circadian period or phase

across conditions. Although the small sample size may have affected power to detect

minor fluctuations across conditions, this study did not support the PSH's assertion of

pacemaker abnormalities in SAD. However, significant mood-dependent circadian phase

shifts were reported in a patient with SAD studied under two forced desynchrony

protocols, when depressed and when euthymic (Koorengevel, Beersma, Gordijn, den

Boer, & van den Hoofdakker, 2000). A significant phase delay in the circadian

temperature rhythm (*t*-min) was observed during the depressed mood state, as compared

to the euthymic mood. This subject highlights possible inter-individual variation for

SAD patients to experience circadian misalignments when depressed.

A second unmasking protocol is referred to as a constant routine procedure, which

involves an inpatient stay where the exogenous factors (e.g., sleep, activity, food, light,

and temperature) are kept constant between all participants via bed rest, forced

wakefulness for 24 hours in dim light, and regularly-timed meals (Czeisler et al., 1985).

This protocol has been utilized by the majority of light therapy trials conducted to

indirectly test whether SAD patients exhibit circadian phase-shift corresponding to

treatment response. Avery et al. (1997) assessed the circadian response to light therapy

while controlling for the inter-individual differences in sleep times by utilizing a constant

routine protocol with standardized sleep schedules across all participants. The degree of

advance in the temperature minimum (t-min) correlated with degree of change in

Hamilton Depression Rating Scale scores from baseline to posttreatment in SAD patients

(Avery et al., 1997). Similarly, Dahl, Avery, and Lewy (1993) compared the DLMO and

core body temperature rhythms under constant routine conditions in six SAD patients and

six nondepressed healthy controls during winter. Both the DLMO and t-min

(temperature minima) were significantly phase-delayed in patients relative to controls,

providing support for winter phase-delayed circadian rhythms in SAD. However, as

noted by Avery et al. (1997), the imposed sleep schedule may differentially alter the

natural timing of circadian function between participants due to inter-individual variation

of previous circadian phase, sleep, and diurnal variation. These factors have been shown

to correspond to inter-individual variation in intrinsic period length, the endogenous rate

of circadian oscillation which is near 24-hours in humans (Czeisler et al., 1999; Duffy,

Rimmer, & Czeisler, 2001).

In addition to the constant routine procedures and forced desynchrony protocols

mentioned above, a third method to control for the effects of the sleep/wake cycle on

circadian phase in ambulatory conditions is to calculate the timing of circadian phase

relative to sleep. Phase Angle Difference (PAD) is defined as the temporal interval (in hours) between the circadian marker (e.g., DLMO) and sleep (e.g., midpoint of sleep). PAD is a better measure than clock time of circadian phase because PAD controls for the inter-individual variability in the timing of sleep, obviating the need to standardize sleep schedules across participants, thereby reducing noise in circadian phase assessment.

PAD measures the temporal relation of circadian phase to the sleep/wake cycle. The PSH postulated that SAD may involve a circadian misalignment between the pacemaker and the external light/dark cycle, or between the pacemaker and other biological rhythms such as the sleep/wake cycle (Lewy et al., 1988). The majority of the studies to date have tested the PSH as delays in circadian phase (e.g., DLMO) relative to the light/dark cycle (clock time). However, Lewy et al. (2003) proposed an optimal antidepressant phase angle between the circadian rhythm and sleep, as the DLMO in euthymic controls typically occurs 14 hours after wake time and 2 hours prior to sleep onset (Sletten et al., 2010). The 14-hour waketime-DLMO interval corresponds to a DLMO-midsleep interval of 6 hours, assuming an 8-hour sleep duration. Initial evidence for PSH was reported in an initial trial of exogenous melatonin for treatment of SAD (Lewy et al., 2003), whereby baseline-to-post-treatment reductions in mood were correlated with circadian shifts towards this proposed therapeutic window for phase-delayed SAD patients. To date, there have been two primary studies examining the relation between PAD and mood in SAD patients.

In 2006, Lewy et al. tested a placebo-controlled trial of exogenous melatonin as a phase shifting agent and potential treatment for individuals with SAD. SAD patients and controls were administered a low-dose of melatonin in the morning or afternoon/evening.

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DLMO and SIGH-SAD assessments were completed at baseline and post-treatment. PAD was found to be parabolically associated with pre-treatment depression severity, such that greater absolute deviations (either shorter or longer) from a PAD of 6 hours (DLMO to midsleep) were associated with significantly greater baseline symptom severity, accounting for 17% of the variance in pre-treatment Structured Interview Guide for the Hamilton Depression Scale – Seasonal Affective Disorder Version scores (Lewy et al., 2006). Neither parabolic, nor linear absolute deviation relations, were found between depression severity and DLMO or midpoint of sleep alone, suggesting the relevant marker is the circadian misalignment between these two oscillators. This study was based on the melatonin PRC that is 12 hours out of phase with the PRC to light, such that morning exogenous melatonin has been shown to induce phase delays, whereas evening melatonin induces phase advances of the circadian clock (Lewy, Ahmed, Jackson, & Sack, 1992; Lewy, et al., 1998). Consistent with the PRC, evening melatonin was shown to phase delay the DLMO and lengthen PAD; whereas morning melatonin did not significantly shift the DLMO or change PAD. In patients who received evening melatonin (the group that demonstrated the greatest phase shifts across treatment), individual absolute deviation (toward or away) from PAD-6 across treatment significantly predicted pre- to post-treatment change in depression severity, such that reduced deviation (shift toward) PAD-6 across treatment predicted greater reduction in depression severity. This study supports the PSH as depression severity in SAD patients corresponded to the degree of circadian misalignment relative to an optimally entrained circadian phase of 6 hours between the DLMO and midpoint of sleep (PAD-6), at baseline and across treatment with melatonin.

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Burgess, Fogg, Young, and Eastman (2004) further examined whether the antidepressant effect of light therapy is related to circadian timing of core body temperature, and the PAD between the core body temperature minimum (t-min) and sleep offset. Twenty-six patients with SAD were randomly assigned to receive 4 weeks of morning light, evening light, or placebo (deactivated negative ion generator). Circadian phase was captured via rectal core body temperature measured continuously for five weeks (baseline and during treatment). To minimize variation of circadian phase due to sleep changes throughout treatment, each participant kept an individualized stable sleep schedule (i.e., sleep timing and duration of 7-8 hours) for the four weeks of treatment. Average sleep duration and wake time did not differ between groups. Consistent with the phase response curve, morning light advanced, and evening light delayed, the t-min by 1 hour, resulting in lengthened with PAD with morning light, and shortened PAD with evening light. Yet, neither the degree of phase shift in the clock time of t-min nor the degree of shift in the interval between t-min and sleep offset, were signfiicantly correlated with the antidepressant response. However, Burgess et al. (2004) examined antidepressant response and PAD-3 (t-min to sleep offset), which corresponds to the proposed "sweet spot" of PAD-6 (DLMO to midsleep) in SAD. Patients with a t-min to sleep offset PAD of 3 hrs at week 4 exhibited the greatest improvement in mood. Further, SAD patients whose PADs moved closer to the proposed core body temperature "sweet spot" (PAD-3 hr) across the 4 weeks of treatment exhibited, on average, a two-fold reduction in symptoms as compared to patients whose PADs moved away from 3 hours from baseline to post-treatment. Absolute deviation from PAD-3 accounted for 33% of

the variance in SIGH-SAD scores at post-treatment (Burgess et al., 2004), with 38% of patients' PADs falling near 3 hrs (i.e., 2.5-3.5) hrs at week 4.

The findings of Lewy et al. (2006) and Burgess et al. (2004) elucidated the need to account for phase type (direction of shift) when assessing the relation between circadian phase shifts and depression severity in SAD. Lewy et al. (2006) reported that a majority (71%) of patients exhibited phase delays (PADs less than 6), and a minority (29%) exhibited phase advances (PADs greater than 6). The timing of melatonin treatment (morning or evening) was randomly assigned prior to phase-typing, and therefore, was not necessarily consistent with the direction of phase shift expected to be antidepressant (e.g., AM melatonin for phase-advanced patients and PM melatonin for phase-delayed patients). Before accounting for the confounding effect of phase type in response to exogenous melatonin treatment, there were no significant differences in percentage change in depression severity across treatment between morning melatonin, evening melatonin, or placebo treatment groups. However, when comparing treatment improvement across phase type (e.g., advance or delay), patients who received the "correct" treatment, as matched to their phase type, exhibited a significantly greater reduction (34%) in depression severity, as compared to those who received the incorrect (19%), or placebo (20%) treatments (Lewy et al., 2006). This effect indirectly supports the PSH because a treatment matched to the circadian misalignment was associated with better treatment response. Similarly, Burgess et al. (2004) reported null associations between degree of circadian phase shift (PAD between t-min and sleep offset) across treatment and antidepressant response to light treatment. However, direction of shift

toward or away from PAD-3 across treatment accounted for a significant proportion of variance (33.3%) in the antidepressant response.

These studies are yet to be replicated to provide more support for the role for circadian phase shifts assessed via PAD in SAD versus controls. However, these preliminary studies highlight that variability in PAD may relate to antidepressant response to bright light therapy by SAD patients. Although 75% of SAD patients were found to fall within the proximity of PAD-3 at post-treatment, 46% of patients had exhibited a PAD near 3 hrs at baseline (Burgess et al., 2004). This finding highlights possible variability in exhibited PAD and its possible relation to mood in SAD. Further, Wright et al. (2005) reported natural inter-individual variation in PAD (DLMO-sleep onset) in healthy individuals, related to inter-individual variation in the length of the intrinsic period, such that a shorter intrinsic period was associated with longer PAD, and a longer period with shorter PAD. The findings of Wright et al. (2005) further suggest that inter-individual variation in intrinsic period also may account for normative variation in PAD. The variability in PAD-6 (or PAD-3) within SAD patients, and as compared to controls, has yet to be determined.

There is preliminary evidence to suggest unique effects of circadian misalignments in nonseasonal depression. In a study of women with nonseasonal major depressive disorder assessed as mildly to moderately depressed, a strong negative correlation was found between PAD (DLMO-midsleep) and severity of depressed mood, such that a shorter PAD (more delayed circadian phase relative to sleep) was associated with greater depressive symptom severity as assessed by the Profile of Mood States-Brief Form (Emens, Lewy, Kinzie, Arntz, & Rough, 2009). In comparison to nondepressed

controls, nonseasonally depressed patients exhibited a greater *t*-min-midsleep PAD, consistent with the shorter DLMO-sleep PAD reported in prior studies (Hasler, Buysse, Kupfer, & Germain, 2010).

Additionally, there are a few studies to date that have supported a relation between circadian phase shifts and mood in healthy populations. Emens, Lewy, Rough, and Singer (2009) found PAD, assessed as DLMO to midpoint of sleep, was associated with mood ratings in healthy medical students, such that shorter PAD was associated with more depressed mood. This finding suggests a circadian misalignment to sleep may be a correlate of normative variation in mood. Whether the association between PAD and mood is stronger in SAD patients relative to controls has yet to be tested. Murray, Allen, and Trinder (2003) examined seasonal changes in self-reported diurnal preference (i.e., Morningness-eveningness as an indirect measure of circadian phase) within a sample of community sample of healthy adults in Melbourne, Australia. Murray et al. (2003) found that the majority of individuals exhibited a winter shift towards eveningness, the magnitude of which was associated with a lowering of mood from summer to winter within individuals. These studies support the possibility that circadian phase and/or diurnal preference may influence subtle mood shifts in healthy adults, as well, and thereby may not be an exclusive phenomenon in SAD.

In summary, the PSH has been controversial as there have been mixed results regarding the involvement of a circadian misalignment in SAD. However, many of these studies have examined the phase shift in the clock time of circadian rhythms without controlling for the effect of inter-individual variation in sleep. In an extension of the PSH, Lewy et al. (1988) suggested SAD may involve a circadian misalignment relative to

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the sleep/wake cycle. Studies examining the effect of the temporal relation between circadian rhythms and sleep (PAD) in SAD have shown that degree circadian misalignment to an optimal entrained PAD has correlated with depression severity in winter, and that degree of realignment of PAD after treatment with melatonin or bright light has been associated with SAD symptom improvement (Burgess et al., 2004; Lewy et al., 2003; 2006). Although circadian misalignment to sleep appears to be a correlate of SAD, causation has not been established. Additionally, a misalignment in PAD does not appear to fully account for the variance in SAD severity as not all patients exhibited misalignments when depressed (Burgess et al., 2004; Lewy et al., 2006). Given the limited number of studies examining PAD in SAD, important facets of the relation remain unknown, such as whether individuals with SAD exhibit a different degree of seasonal change in PAD than healthy, nondepressed individuals. More broadly, the mechanism linking a misalignment in circadian rhythms to a disruption in mood has yet to be elucidated as does the mechanism(s) of bright light treatment in symptom improvement.

Mechanisms linking photoperiod to circadian rhythmicity. There are several potential mechanisms to explain unique circadian responding to the short photoperiod of winter in SAD: seasonal variation in light exposure, retinal subsensitivity to light, or abnormal pathways in the circadian system (e.g., melanopsin photoreceptors, clock genes).

Light exposure patterns. Studies examining time spent outdoors across seasons as an indirect measure of light exposure found that SAD patients reported spending more time outside in summer and less time outdoors in winter (Eastman, 1990). Additionally,

patients spent significantly more time outdoors in summer than controls (Graw, Recker, Sand, Krauchi, & Wirz-Justice, 1999). This pattern is consistent with, although not direct evidence of, retinal subsensitivity to light in SAD suggesting SAD patients may require greater light exposure to maintain a euthymic mood, for which SAD patients compensate with greater time spent outdoors in summer, but are not able to do so in winter due to the weather. Oren, Moul, Schwartz, and Brown (1994) tested whether SAD patients exhibited unique light exposure patterns in winter as compared to controls. Actual ambient light exposure as experienced by SAD patients and controls was measured continuously via actigraphic wrist monitors. In this study, comparable light exposure intensity was reported by patients and controls during the winter; however, a significant correlation between depression severity and photoperiod was found for patients only, where shortened photoperiod was associated with greater depression severity. This finding suggests that SAD patients may exhibit a unique sensitivity to low light availability in winter.

      Retinal subsensitivity. Circadian responses to changes in photoperiod are partially mediated through the retina. There is research to suggest aberrant functions of the retinal photoreceptors (rods and/or cones) may contribute to the etiology of SAD and the response to light therapy. A healthy retina responds to low light levels with increased sensitivity to maintain visual acuity. There are two opposing theories of unique retinal sensitivities in SAD. The first posits that SAD patients may have a retinal subsensitivity or impaired retinal adaptation to low light levels, posing greater problems in winter when environmental light availability is low due to short photoperiods (Remé, Terman, & Wirz-Justice, 1990). The second theory suggests that SAD patients may experience a

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heightened sensitivity, or supersensitivity, to lower light levels, which may uniquely

affect circadian rhythms in SAD patients during winter (Beersma, 1990). Only a few

studies have examined retinal sensitivity across the seasons in SAD patients and

nondepressed controls. Ozaki, Rosenthal, Myers, Schwartz, and Oren (1995) measured

retinal sensitivity in summer and in winter in SAD patients and nondepressed controls via

the electrooculogram (EOG), an objective measure of retinal standing potential, with

higher ratios indicative of higher retinal sensitivity. Only controls were found to exhibit

an increased retinal sensitivity in winter, whereas SAD patients did not demonstrate a

seasonal difference in sensitivity, suggesting non-SAD individuals may be able to

compensate for low light conditions in winter whereas SAD patients are not (Ozaki et al.,

1995 A recent finding of diminished pupillary response in winter in SAD further supports

the retinal subsensitivity hypothesis (Roecklein et al., 2013). Specifically, SAD patients

had a smaller post illumination pupil response (PIPR; i.e., less pupil constriction

following a blue light stimulus) than controls in winter. The Roecklein et al. (2013)

study was cross-sectional with testing in winter only, so it remains unknown whether this

group difference persists at summer. Similarly, Lavoie et al. (2008) examined rod

sensitivity with electroretinogram (ERG) to light across seasons (summer and winter) in

SAD patients and controls and over four weeks of light treatment during winter in

patients. Only SAD patients demonstrated rod and cone retinal subsensitivity in winter

(at pre-treatment), as compared to their post-treatment levels when remitted with light

therapy. At summer, SAD patients were compared to controls, who did not exhibit

seasonal changes in retinal sensitivity. Hébert, Dumont, and LaChapelle (2006)

measured ERG in individuals with subsyndromal SAD (S-SAD) and healthy controls in

summer and winter. A group difference was observed in winter only, with lower

sensitivity in the S-SAD group, for whom the magnitude of decrease in rod sensitivity

from summer to winter was positively correlated with seasonality, the degree of seasonal

variability in an individual's mood and behavior. In contrast, Terman and Terman (1999)

found support for a retinal supersensitivity in SAD. SAD patients, but not controls,

exhibited a seasonal fluctuation in retinal sensitivity, with higher sensitivity in winter

relative to summer, and increased retinal sensitivity (faster rod recovery and lower cone

threshold) during a dark adaptation protocol in winter, as compared to controls. Given

the inconsistency of findings and multiple measures of retinal sensitivity utilized, more

research is needed to explicate whether SAD patients exhibit a heightened or impaired

retinal sensitivity and how retinal sensitivity aberrations may contribute to winter

depression severity (e.g., whether aberrant retinal function is tied to chronobiological or

psychological factors in SAD).

Melanopsin. Recently, a novel non-visual photopigment, melanopsin, has been

discovered in mammalian retinal ganglion cells (Provencio et al., 2000) and possibly

implicated in SAD (Roecklein et al., 2009). The photoreception detected by the non-

visual melanopsin system independently projects to the SCN via the retinohypothalamic

tract, supplementing the photic input from the ocular system (retinal rod and cone

receptors) in the regulation of circadian entrainment, melatonin production, sleep timing,

and pupillary response (Gooley, Lu, Chou, Scammell, & Saper, 2001; Gooley, Lu,

Fischer, & Saper, 2003). The melanopsin system has provided possible explanation as to

how circadian entrainment to the light/dark cycle is maintained in mammals without

visual light perception (Freedman et al., 1999; Provencio, Rollag, & Castrucci, 2002).

The melanopsin pathway appears to be critical for circadian function, as evidenced by

impaired circadian phase-setting observed in a breed of melanopsin-knockout mice

(Panda et al., 2002). Thus, abnormalities in the melanopsin system could underlie unique

responding to photoperiod in SAD as proposed in the photoperiodic or phase-shift

hypotheses. The first study examining the role of melanopsin in SAD found a single

missense variant in the melanopsin *OPN4* gene to be associated with increased risk for

SAD; specifically, individuals with the T/T genotype at P10L were 5.6 times more likely

to have SAD than were healthy controls (Roecklein et al., 2009). Given the low T/T

prevalence detected in this sample of SAD patients ($N = 130$, $n = 7$ or 5% of whom had

the T/T genotype), larger studies are needed to replicate results and clarify the role of

melanopsin deficiencies in SAD.

Clock genes. Genetic abnormalities in clock genes have been investigated as risk

factors for SAD. In a study comparing genotypes across SAD patients, controls, and

individuals high and low in seasonality; the Leu/Ser polymorphism in Npas2 was

associated with SAD, but not with high seasonality, but no other variants were associated

with SAD (Johannsson et al., 2003). However, Partonen et al. (2007) found single-

nucleotide polymorphisms in three clock genes (Per2, Arntl, and Npas2) central to

pacemaker functioning had additive effects on SAD, suggestive of a genetic risk profile.

Psychological Vulnerability to SAD

Cognitive models of SAD. Although Lewy, Sack, Singer and White (1987)

initially acknowledged that a circadian misalignment as proposed in the PSH may not be

sufficient for the development of SAD, psychiatric research has exclusively examined the

role of biology in SAD (e.g., biological rhythms, genes, neurotransmitters) to the

exclusion of psychological factors. Indirect evidence that cognitive and behavioral

vulnerabilities are also involved in SAD comes from a randomized clinical trial of a

cognitive-behavioral therapy (CBT) tailored to SAD (CBT-SAD). (CBT-SAD). CBT-

SAD is comparably efficacious to light therapy in acute reduction of SAD severity from

baseline to post-treatment (Rohan, Roecklein, et al., 2007; Rohan et al., 2015), and is

superior to light therapy in SAD recurrences and symptom severity at followups the next

winter (Rohan, Roecklein, Lacy & Vacek, 2009) and two winters later (Rohan et al.,

accepted). A recent wave of research conducted by clinical psychologists has revealed

that cognitive factors involved in nonseasonal depression are also implicated in SAD.

According to cognitive theories of depression, vulnerable individuals hold

negative cognitive processes (i.e., maladaptive thought patterns) that serve as underlying

vulnerabilities (i.e., diathesis), that when activated in periods of stress, contribute to

adverse emotional responses (i.e., depression). These studies have applied several

cognitive theories of depression to test whether specific cognitive vulnerabilities

implicated in nonseasonal depression also apply to SAD. In SAD, the occasion setter

(i.e., the stress) is operationalized as the onset of the winter season.

Rumination. The response styles theory (Nolen-Hoeksema & Morrow, 1991) of

depression proposes that an individual's response style (i.e., rumination or distraction) to

sad mood affects the duration and intensity of the ensuing depression symptoms.

Rumination is defined as the tendency to react to dysphoric mood by repetitively

focusing on negative mood, its causes, and consequences, whereas distraction involves

thoughts or behaviors aimed to disengage from mood. Degree of endorsement of

brooding rumination, a natural tendency to ruminate when distressed, has been shown to

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predict prolonged duration of depression symptoms in clinically depressed patients, as well as the development of depressive disorders (as reviewed by Nolen-Hoeksema, Wisco, & Lyubomirsky, 2008).

Rohan, Sigmon, and Dorhofer (2003) published a study in which women with a history of SAD and never-depressed age-matched controls were prospectively assessed in fall, winter, and summer on several cognitive factors. Controlling for initial depression severity in fall, rumination, but not distraction, in the fall was found to be a strong, significant predictor of winter depression severity. Similarly, Young and Azam (2003) reported that ruminative responses, but not distraction behaviors, as assessed via daily diaries over a period of two weeks in the fall predicted winter depression severity after controlling for initial levels of depression in SAD patients.

Treynor, Gonzalez, and Nolen-Hoeksema (2003) distinguished between subtypes of the ruminative response style: reflective pondering, defined as a purposeful reflection upon one's situation problem-solving, and brooding rumination, defined as "moody pondering" involving a passive comparison of one's situation with some unachieved standard. Brooding rumination is the maladaptive form of rumination, uniquely associated with current and predictive of future depression (Moberly & Watkins, 2008; Siegle, Moore, & Thase, 2004; Treynor, Gonzalez, & Nolen-Hoeksema, 2003) and other psychopathology (Watkins, 2009). Consistent with this distinction, Enggasser and Young (2007) found that only the brooding ruminative response style predicted winter depression severity in a sample of individuals with SAD symptoms. According to Kraemer, Kazdin, Offord, Kessler, Jensen, and Kupfers' (1997) criteria for a risk factor, a

brooding ruminative response style may constitute a cognitive risk factor for SAD

because it precedes episode onset and predicts symptom growth over time.

      Cognitive reactivity. Beck's cognitive model of depression (Beck, 1976)

proposes that dysfunctional attitudes stemming from maladaptive schemas constitute a

cognitive vulnerability to depression. Dysfunctional attitudes are learned maladaptive

attitudes or assumptions related to the negative cognitive triad. Rohan et al. (2003) found

that women with SAD endorsed more dysfunctional attitudes in fall and winter as

compared to themselves in summer when asymptomatic, whereas controls did not differ

across the seasons on dysfunctional attitudes. Of note, Rohan et al. (2003) did not detect

differences in the magnitude of endorsed dysfunctional attitudes between women with a

history of SAD (i.e., formerly depressed) and never-depressed controls in summer, when

patients are asymptomatic, suggesting a mood induction is needed to activate these

negative self-schemas in SAD patients. In a second longitudinal study examining

seasonal changes in dysfunctional attitudes in SAD patients and never-depressed

controls, SAD patients reported elevated dysfunctional attitudes in winter relative to

summer and endorsed more dysfunctional attitudes than controls in the winter (Golden,

Dalgleish, & Spinks, 2006). In a study comparing negative thought processes between

SAD patients, nonseasonally depressed individuals, and nondepressed controls in the

winter season, both patient groups endorsed greater dysfunctional attitudes than the

control group, with no significant differences between nonseasonally and seasonally

depressed patients (Hodges & Marks, 1998). Beck's theory of depression also

emphasizes the mechanism by which the activation of dysfunctional attitudes may

contribute to future relapse and recurrence of depression. The theory posits negative self-

schemas, as indicated by dysfunctional attitude endorsement, are activated by life stress

and/or sad mood (Beck, 1976). However, the relative ease with which dysfunctional

attitudes are activated by depressed mood states is termed "cognitive reactivity."

Cognitive reactivity can be assessed experimentally by inducing a sad mood when a

person is in a euthymic mood or is minimally symptomatic (e.g., during summer for SAD

patients) and measuring the change in dysfunctional attitudes before to after the mood

induction. The most commonly used dysphoric mood induction in tests of cognitive

reactivity involves reflecting on a personally-relevant sad memory while listening to a

piece of sad-suggestive orchestral music, Prokofiev's "Russia under a Mongolian Yoke"

played at half-speed, a procedure shown to reliably induce a sad mood (Clark &

Teasdale, 1985). Cognitive reactivity is theorized to model the activation of negative

schemas in response to stress-induced negative affect and, therefore, it should predict

increased risk to relapse and recurrence of depression (Segal, Williams, Teasdale, &

Gemar, 1996). Cognitive reactivity to a negative mood induction has been shown to be

greater in formerly depressed patients than never depressed (Gemar, Segal, Sagrati, &

Kennedy, 2001). Additionally, residual cognitive reactivity after successful treatment

with antidepressant medications or cognitive therapy has been shown to predict

depression relapse (69%) over an 18-month period in nonseasonally depressed

individuals (Segal, Kennedy, Gemar, Hood, Pedersen, & Buis, 2006). To date, there has

been one study examining cognitive reactivity in SAD. Enggasser and Young (2007)

utilized a prospective, longitudinal design to examine the effect of cognitive reactivity on

annual recurrence of winter depression symptoms in individuals with either SAD or sub-

syndromal SAD. Contrary to the nonseasonal depression literature, Enggasser and Young

(2007) did not find cognitive reactivity in response to a sad mood induction in the summer to be predictive of depressive symptoms the following winter. However, Enggasser and Young's findings have yet to be replicated.

Season-specific cognitions. In the Cognitive-Behavioral Integrative Model of SAD, Rohan (2008) proposes that individuals with SAD may hold rigid season-specific cognitions regarding how the weather impacts their mood. These cognitions are conceptualized as a domain-specific set of dysfunctional attitudes stemming from learned associations between negative mood or depression and the winter season, and may contribute to the maintenance of the annually recurrent seasonal pattern of depression experienced by SAD patients. Prior SAD studies have utilized the Seasonal Attitudes Scale (SAS; Sigmon, Rohan, Boulard, Whitcomb, & Dorhofer, 2000) as a measure of trait-like emotional and behavioral responses to the changing seasons, as well as specific attitudes about the seasons. The SAS has been shown to discriminate between individuals with moderate seasonality of mood, and nondepressed, low-seasonality controls (Rohan, Nillni, Mahon, Roecklein, Sitnikov, & Haaga, 2011). However, the SAS assesses an individual's attitudes about the changing seasons, as well as their typical emotional and behavioral responses across the seasons (i.e., SAD symptoms). In this respect, the SAS construct confounds seasonal attitudes with seasonality, measured by the SPAQ (Rosenthal et al., 1987). Conversely, the Seasonal Beliefs Questionnaire (SBQ; Rohan, Nillni, Lippy, Roecklein, & Hillhouse, 2007) was designed as a measure of season-specific cognitions that does not include items about symptoms. Rohan (2008)'s Integrative Cognitive-Behavioral Model of SAD implicates season-specific cognitions as a cognitive vulnerability of SAD.

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Behavioral models of SAD. According to Lewinsohn's (1974) behavioral model of depression (Lewinsohn, 1974), behavioral disengagement contributes to depression onset and maintenance because reduced activity reduces the potential to derive positive reinforcement from enjoyable activities. A diminished interest or pleasure in activities is a diagnostic symptom of depression per the DSM-IV-TR (APA, 2000). There has only been one study to date examining pleasant activity levels in SAD. In their longitudinal investigation across the seasons, Rohan et al. (2003) found that women with SAD engaged in significantly fewer pleasant activities in fall or winter relative to themselves in summer, and were less active in winter relative to controls whose frequency of engagement in pleasant activities did not differ across seasons. This study suggests that behavioral disengagement correlates with the seasonal pattern in SAD; however, clarification of the role of behavioral disengagement in the onset or annual recurrence of SAD warrants further study.

Integrative Models of SAD

Given the evidence for both biological and psychological factors in SAD, integrative etiological models propose that different types of vulnerabilities are mutually involved in SAD onset and maintenance. There are several models proposing an interplay of biological and psychological risk factors in SAD (Rohan, 2008; Young, Watel, Lahmeyer, & Eastman, 1991; Young, 1999). In the initial integrative model, Young (et al., 1991; 1999) proposed a dual vulnerability model of SAD, involving a psychological vulnerability, as reflected by the vegetative symptoms (e.g., changes in sleep, appetite, weight, and energy), and a separate psychological vulnerability, as evidenced by the cognitive-affective symptoms (e.g., depressed mood, anhedonia, and

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low self-esteem). Young's model proposes that the psychological vulnerability occurs concomitantly or in response to the vegetative symptoms. Young's dual vulnerability model emphasizes how these two vulnerabilities interact to influence the onset of specific SAD symptoms each fall/winter season.

Rohan's integrative cognitive-behavioral model of SAD (Rohan et al., 2008; Rohan, Rocklein, & Haaga, 2009) maintains Young's concept of dual biological and psychological vulnerabilities, yet elaborates the content of the psychological vulnerability to include specific cognitive (e.g., dysfunctional attitudes, rumination) and behavioral (e.g., behavioral disengagement) vulnerabilities to depression. See Figure 1 for Rohan's integrative cognitive-behavioral model of SAD. The model also postulates that SAD individuals hold negative core beliefs specific to the winter season, weather, and low light availability. The Seasonal Beliefs Questionnaire was developed to measure these possible SAD-specific cognitions (Rohan, Nillni, et al., 2007). In contrast to Young's model, Rohan's model does not tie the underlying vulnerabilities to specific symptom profiles.

Limitations of Current SAD Literature

The majority of SAD studies have indirectly tested the PSH by assessing phase shifts that accompany antidepressant response to light therapy. However, this type of design does not test the PSH assumption that SAD involves a natural shift in circadian rhythms across seasons. There have been two studies to date testing this effect (Koorengevel et al., 2003; Wehr et al., 2001), both of which reported a nonsignificant difference between summer and winter in SAD patients' circadian rhythms. However, methodological limitations confound the generalizability or certainty of these null

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findings. The latter study (Wehr et al., 2001) did not control for individual differences in the timing of sleep, a necessary measure to isolate true seasonal effects on the melatonin rhythm. The former study (Koorengevel et al., 2003) is the most stringent test of this effect to date in that it used forced desynchrony procedures; however, the protocol involved only 7 SAD patients due to the intensive and costly study procedures.

The greatest limitation of the current literature is the lack of empirical application of the integrative models of SAD. Despite recent theories that integrate psychological and biological vulnerabilities (Rohan, 2008; Young, 1991; 1999) and frequent acknowledgments in both literatures of the other vulnerabilities likely implicated in SAD, a major limitation of available research on SAD etiology is the examination of one vulnerability in isolation (i.e., biological or psychological) as opposed to analysis of both vulnerabilities within the same sample and statistical model. Studying one type of vulnerability in isolation has not allowed for comparison of the relative contributions of these vulnerabilities to SAD severity, controlling for effects of the other. This limitation is likely due to the disciplinary division in the field, such that the chronobiological research on SAD has been conducted by one "camp" (i.e., biological psychiatrists, physiological psychologists, and circadian biologists) whereas the psychological research has been conducted by a different "camp" (i.e., clinical psychologists with a cognitive-behavioral orientation) with little collaboration between them. Therefore, no study to date has tested an integrative model, which is needed to elucidate the specific roles that chronobiological and cognitive vulnerabilities play in the diathesis of SAD.

CHAPTER 2: The Current Project

The proposed project is the first study to integrate expertise from leading chronobiological and cognitive-behavioral SAD researchers to test an integrative model of SAD (Rohan, 2008), see Figure 1. The project aimed to clarify the etiological underpinnings of SAD by (1) comparing SAD patients and never-depressed controls on chronobiological and cognitive vulnerabilities at both summer and winter, (2) utilizing a prospective, longitudinal design to compare the relative contributions of the chronobiological and cognitive vulnerabilities in predicting winter depression severity in SAD patients versus controls.

The methodology of the current project improved upon the extant SAD literature in several ways. First, this project was the first to utilize measures of both the proposed cognitive and circadian correlates of SAD, such that relative contributions of these factors on SAD severity can be assessed. Second, all measures were assessed in summer and winter to accommodate longitudinal models of analyses. Third, the current study involved a novel examination of PAD as a correlate of SAD, with the assessment of variability in this relation across season and mood state. This provided a direct test of the PSH defined as a circadian misalignment to sleep rather than to the light-dark cycle.

Study Aims and Hypotheses

Aim 1: To test whether SAD patients and controls differ in the seasonal change of the chronobiological and cognitive vulnerabilities.

Hypothesis 1. SAD patients will show a greater degree of seasonal change in PAD from summer to winter than controls, with a mean shortening of PAD in winter

relative to summer, indicative of a phase delay. This group effect would suggest a seasonal circadian misalignment may be characteristic of SAD.

Hypothesis 2. SAD patients will exhibit comparable deviation from PAD-6 to controls in summer, and greater deviation from PAD-6 than controls in winter. A greater deviation from PAD-6 in winter among patients than controls would suggest a winter circadian misalignment in SAD.

Hypothesis 3. SAD patients will endorse higher values of brooding rumination than controls at both summer and winter assessments. This consistent group difference across time would reflect a greater trait tendency to respond to sad mood with maladaptive rumination in patients than controls.

Hypothesis 4. SAD patients will exhibit greater cognitive reactivity (i.e., an increase in endorsed dysfunctional attitudes across a negative mood induction) in summer than controls. Postulated as a maintenance mechanism of depression, this effect would suggest SAD patients are more prone to respond to dysphoric mood with more negative thought patterns.

Hypothesis 5. SAD patients will endorse more dysfunctional attitudes than controls at winter, but the groups will not differ at summer. This finding would suggest that SAD patients hold more rigid depressogenic attitudes than controls only when they are depressed.

Hypothesis 6. SAD patients will endorse more rigid seasonal beliefs than controls at both summer and winter assessments. This consistent group difference across time would reflect a greater trait tendency for patients to endorse rigid beliefs about seasons and light year-round, relative to controls.

Aim 2: To test the predictive effects of these group differences in chronobiological and cognitive vulnerabilities on seasonal change in depression severity.

Hypothesis 7. It is expected that the between-group effects of the vulnerabilities will account for variance in depression severity, above and beyond the unique effects of group, and the chronobiological and cognitive predictors.

CHAPTER 3: Method

Participants

Participants were adults (aged 18 to 65) community residents recruited from either the greater Burlington, Vermont or Pittsburgh, Pennsylvania areas. Specifically 31 individuals diagnosed with Major Depression Recurrent, with Seasonal Pattern (winter) and 33 age- and sex- matched never-depressed control participants were recruited for this study. General exclusion criteria for all participants included: 1) current psychological or psychiatric treatment (i.e. psychotropic medications, psychotherapy, light therapy) or plans to initiate treatment before study completion; 2) diagnosed sleep disorder (i.e. Obstructive Sleep Apnea, Periodic Limb Movement Disorder, or Narcolepsy); and 3) individuals with plans to travel outside New England within 2 weeks prior to a laboratory visit, to control for latitude effects on depressed mood and time-zone travel effects on circadian phase.

Study sites. Due to limited enrollment success in Burlington, VT (15.6% of phone screens, and 45.8% of diagnostic screens), data were pooled across two funded projects conducted simultaneously at the University of Vermont in Burlington, VT (44.5° N) and the University of Pittsburgh in Pittsburgh, PA (40.4° N). Data were collected concurrently from Pittsburgh and Burlington during the summer and winter seasons during three consecutive years, 2012-2014 using comparable study enrollment criteria and methods. Demographics and recruitment statistics are presented by site, below.

Criteria for the SAD patient group. At the time of initial in-person screening, inclusion criteria for the SAD patient group are: DSM-IV-TR criteria for Major Depression, Recurrent, with Seasonal Pattern for the past two winters as determined by

the Structured Clinical Interview for DSM-IV Axis I Disorders-Clinician Version (SCID-CV; First et al., 1996). Exclusion criteria for the SAD patient group are: 1) a current comorbid Axis I diagnosis, 2) Bipolar-type SAD, 3) summer-type SAD, and 4) acute or serious suicidal intent. At the summer laboratory visit, an additional exclusion of not having a full summer remission prior to lab visit 1 was applied (a score of ≥14 on the Beck Depression Inventory-Second Edition), indicative of minimal persisting depressive symptoms in summer. At the winter laboratory visit, an additional inclusion criterion of prospectively meeting DSM-IV-TR criteria for a current Major Depressive Episode (MDE) in the fall or winter months was applied. To do so, SAD patients were assessed by phone biweekly (twice monthly) starting in fall for current MDE criteria on the SCID-CV, and scheduled for Time 2 once criteria are met. Calls were audio recorded for reliability checks.

Criteria for the never-depressed control group. At the time of initial in-person screening, inclusion criteria for controls included: (1) no current Axis I diagnosis as ascertained by the SCID-CV, (2) no history of a Major Depressive Episode (MDE) on the SCID-CV, and (3) seasonality scores that fall in the normal range on the Seasonal Pattern Assessment Questionnaire (Rosenthal et al., 1984), indicating minimal seasonality and the absence of sub-syndromal SAD. Additional inclusion criteria applied just prior to each laboratory visit included: (4) DSM-IV criteria for a MDE on the SCID-CV and (2) scoring ≤ 14 on the BDI-II.

Procedure

Screening procedure. Individuals who respond to advertisements were screened for eligibility with a brief phone screen. Prior to study consent, the phone screen served

to preliminarily assess the inclusion/exclusion criteria: depression history (SAD status over past 2 winters for SAD patients, an absence of current depression or SAD history for control participants); known psychological and/or sleep diagnoses; current psychiatric treatment; interest and availability to participate in all study procedures. Eligible individuals were invited to the in-person screening visit. Potential participants first completed consent and HIPAA forms, then a diagnostic clinical interview, and lastly, the SCID-CV was administered to assess eligibility criteria. If exclusionary psychiatric diagnoses are met, the participant was informed and provided a referral list for psychological services. Qualified participants were scheduled for the time 1 assessment (May to September).

Ambulatory sleep schedule. Participants were asked to keep a consistent sleep schedule of their choosing (with duration parameters of 8 hours +/- 30 minutes at bedtime/waketime) for the 7 days prior to a laboratory visit to regulate sleep and circadian phase. Sleep/wake patterns were objectively measured with wrist actigraphy (Actiwatch 2, or Actiwatch Spectrum, Philips Respironics). Participants wore an actigraph wrist device continuously on their non-dominant wrist for the 7 days of sleep schedule leading up to the saliva collection time. Activity data were recorded in .5 min epochs. Sleep onset and offset times were derived with Actiware scoring software. In the event of watch malfunction (11%), sleep log times were substituted, as available. In order to maximize natural circadian phase and sleep timing, participants were asked to abstain from the use of melatonin and other sleep medications in the 2 weeks prior to a laboratory visit, and the consumption of alcohol was limited to 1 drink per day, and caffeine to 2 cups of coffee or caffeine equivalent daily before noon.

Saliva sample collection. Salivary melatonin has been shown to be a reliable, noninvasive measure of circadian phase (Voultios, Kennaway, & Dawson, 1997). There were two intended saliva collection days for each participant: one in late spring/summer (May to August) and one in late fall/winter (November to February). Participants completed serial (half-hourly) saliva collection for 6 hours (13 samples) on the 7th evening of the sleep schedule week. Sampling times were tailored for each participant based on their selected sleep schedule,, whereby the sampling window occurred 5.5 hours before to .5 hours after their habitual bedtime. This was intended to optimize capture of the DLMO, which typically occurs 2-5 hours prior to bedtime, yet which has been shown to vary by diurnal preference and timing of sleep (Emens, Yuhas, et al., 2009). Burlington, VT participants collected samples at home, whereas Pittsburgh, PA participants collected samples in the laboratory. The sampling methods are described in detail, below. All participants were instructed to brush their teeth, rinse their mouth, and abstain from all food or beverages 10 minutes prior to each sample. Participants were also asked to abstain from the following on the day of sampling: cranberry juice, chocolate, bananas, caffeinated and decaffeinated coffee, tea, soda, Aspirin, Ibuprofen, other non-steroidal anti-inflammatories, and toothpaste. All of these substances either coat the mouth or otherwise contaminate the saliva.

Burlington participants collected saliva samples at home on the 7th evening of the sleep schedule. At the laboratory visit, participants were provided sample materials [i.e., 13 Salivettes® (Sarstedt, AG & Co.) labeled with intended administration times, sample storage rack, saliva collection instructions, sunglasses, sample log and a toothbrush] and guided through a sampling tutorial. To control for lighting conditions, participants were

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fitted with a set of dark-colored goggles (Julbo® spectron 4 lens sunglasses) for 95%

light filtration to wear for 7 hours during the evening of saliva collection to avoid the

suppressant effects of light on melatonin production during sample collection (Lewy et

al., 1980). The participants were informed that the importance of recording the exact

sampling time (e.g., 6:32 pm) is much greater than sampling exactly at the intended time

(e.g. at 6:30 pm), with an example chart of clean melatonin data. This instructional

technique has been associated with sampling precision comparable to collection by in-

patient nursing staff (personal communication with Jonathan Emens, M.D., July 11,

2011).

Pittsburgh, PA participants collected 13 half-hourly saliva samples (Salivettes®;

Sarstedt, AG & Co.) starting from 5.5 hours before to 0.5 hour after their habitual

bedtime for the past week. Saliva samples were collected in the laboratory on the 7th

evening of the sleep schedule week, with the assistance of research staff. Participants

were allowed to ambulate and were not confined to constant postural conditions. Lighting

was controlled at ≤ 15 lux, as verified by spectrophotometer. Participants were provided

blue-light spectrum block glasses to wear if they needed to leave the unit during the

sample session.   Samples were centrifuged and stored at 2-8°C upon collection, and

stored at -80°C within 2 days of collection until shipped for assay.

Melatonin assay. Saliva samples collected in Burlington, VT were assayed for

melatonin in the Neuroscience Center of Biomedical Research Excellence Core

Laboratory at the University of Vermont Medical School using the Bühlmann Direct

Saliva Melatonin ELISA kit (ALPCO Diagnostics, Salem, NH). Saliva samples were

immediately stored at 2-8°C upon collection, and placed at -80°C within 4 days of

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collection for storage until assay (up to 6 months). The Burlington assays averaged an

intra-assay precision of .31 and an inter-assay precision of CV = .10. The intra-assay

precision was higher than the acceptable window (.15), although the interassay precision

was within acceptable range. Limitations of the former are discussed, below. Saliva

samples collected in Pittsburgh, PA were assayed for melatonin by SolidPhase, Inc.

(Portland, ME, USA) using the Bühlmann Direct Saliva Melatonin Radioimmunoassay

kit (ALPCO Diagnostics, Windham, NH, USA). SolidPhase, Inc. (Portland, ME, USA)

did not include duplicates in the assay despite using the Bühlmann Direct Saliva

Melatonin Radioimmunoassay kit (ALPCO Diagnostics, Windham, NH, USA).

Therefore, the intra-assay sensitivity for the Pittsburgh DLMO data are non-applicable

and the measure of reliability of concentrations estimates is unavailable. The inter-assay

sensitivity for Solidphase was within acceptable range at CV: .12.

Measures

Structured Clinical Interview for the DSM-IV Axis I Disorders-Clinical

Version (SCID-CV). The SCID-CV (First et al., 1996) is a structured diagnostic

interview, which assesses DSM-IV criteria for Axis I Disorders. The SCID-CV was

utilized as a screening instrument to verify SAD patient or never-depressed control status

for inclusion in the study. The SCID-CV was administered by the P.I., or other clinical

psychology graduate students, who have been trained in SCID administration and have

experience administering the SCID-CV. Of the Burlington SCID interviews, a subset, $n =$

10 (25.6%), were rated by a second rater for inter-rater reliability of SAD diagnosis, with

100% congruence.

Seasonal Pattern Assessment Questionnaire –SAD Version (SPAQ). The

SPAQ (Rosenthal et al., 1987) is a brief screening assessment for seasonality. Subjects

rate the degree to which they experience seasonal changes across 6 domains: sleep length,

social activity, mood, weight, appetite, and energy level rated on a scale of 0 "no change"

to 4 "extremely marked change." A global score $\geq$ 11, with a minimum of moderate

impairment from seasonal symptoms, is consistent with a diagnosis of SAD. Due to low

sensitivity, the SPAQ is recommended as a supplemental instrument to clinical interview

for diagnosis of SAD (Mersch et al., 2004).

Structured Interview Guide for the Hamilton Rating Scale for Depression–

Seasonal Affective Disorder Version (SIGH-SAD). The SIGH-SAD (Williams et al.,

1992) is a semi-structured clinical interview including the 21-item Structured Interview

Guide for the Hamilton Rating Scale for Depression (HAM-D) and a supplementary 8-

item subscale to assess atypical depressive symptoms associated with winter SAD. A

SIGH-SAD was administered at the Time 1 summer visit, when relatively asymptomatic,

and at the Time 2 winter laboratory visit when in a major depressive episode. The SIGH-

SAD (i.e., 29 items) demonstrated acceptable internal consistency in summer ($\alpha = .63$)

and excellent internal consistency when administered in winter ($\alpha = .91$). Intraclass

correlations (ICC) were calculated to assess the inter-rater reliability between trained

raters for SIGH-SAD total scores at each assessment. All Burlington SIGH-SAD

interviews were rated by a second rate, with an ICC = .838 for summer, and ICC = .993

for winter, SIGH-SAD scores. A random selection (10%) of Pittsburgh SIGH-SAD

interviews were rated by a second rater, selected randomly across patient group and

season. The Pittsburgh raters yielded an ICC = .941 for summer, and ICC = .998 for winter.

Beck Depression Inventory–Second Edition (BDI-II). The BDI-II (Beck, Steer, & Brown, 1996) is a 21-item measure of depressive symptom severity. The questionnaire consists of 21 groups of statements for which the responder must select the statement that best describes his/her experience in the past two weeks (e.g., for item 1, sadness: "I do not feel sad", "I feel sad much of the time", "I am sad all the time", or "I am so sad or unhappy that I can't stand it"). The BDI-II has demonstrated good test-retest reliability and convergent validity (Beck et al., 1996). The BDI-II served as an additional measure to verify depressive symptom severity at each laboratory visit. The BDI-II demonstrated excellent internal consistency at both summer ($\alpha = .97$) and winter ($\alpha = .91$).

Ruminative Response Scale (RRS). The RRS (Nolen-Hoeksema & Morrow, 1991) measures the tendency to ruminate in response to negative affect. The RRS consists of 22 responses to sad mood focused on the self and the causes and consequences of sad mood (e.g., "Go away by yourself and think about why you feel this way"), rated on a scale of 1 (almost never respond in this way) to 4 (almost always respond in this way). The RRS has three factor analytically-derived subscales: depression, brooding, and reflective-pondering. The RRS demonstrates a test-retest validity of .67 across 1 year, with good internal consistency for the reflective-pondering and brooding subscales, respectively ($\alpha = .72, .77$; Treynor et al., 2003).

Brooding rumination. The "brooding" subscale of the RRS has been particularly associated with depression (Joorman, Dkane, & Gotlib, 2006; Siegle et al., 2004; Treynor

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et al., 2003) and SAD (Enggasser & Young, 2007), and constituted the rumination, and

primary cognitive vulnerability, measure in this study. The RRS (total score)

demonstrated excellent internal consistency in summer ($\alpha = .95$) and winter ($\alpha = .97$).

The brooding rumination subscale score also demonstrated good internal consistency at

both summer ($\alpha = .81$) and winter ($\alpha = .89$) assessments.

Cognitive reactivity. The Dysfunctional Attitudes Scale (DAS; Weissman &

Beck, 1978) is a 40-item measure of common cognitive assumptions endorsed by

individuals with depression, such as, "If I fail at my work, then I am a failure as a

person." Ratings are given on a 7-point Likert scale with anchors of 7 = "totally agree"

to 1 = "totally disagree." Per research on the cognitive vulnerability to depression,

cognitive reactivity is measured by change in DAS score from before to after a dysphoric

mood induction, and constituted the measure of cognitive reactivity in the current study.

In the summer when non-depressed, participants underwent a dysphoric mood induction

by reflecting upon a time when they felt sad, while listening to the orchestral introduction

to 'Russia Under the Mongolian Yoke' by Prokofiev, at half-speed, for 10 minutes (Clark

& Teasdale, 1985). This procedure has been shown to effectively activate the

dysfunctional attitudes in remitted depressed individuals (Gemar et al., 2001). To

determine whether the induction of a sad mood was successful, Visual Analog Scales

(VAS) were administered at pre- and post-mood induction. The VAS consisted of a 146

mm line, with positive mood defined as distance (mm) from the center mark to the right

(maximum = +73 mm) and negative mood defined as distance from the center to the left

(maximum = -73 mm). DAS form A was completed at pre-mood induction, and DAS

form B completed at post-mood induction. DAS B demonstrated excellent internal

consistency (α = .94). DAS A also demonstrated excellent internal consistency, as measured at both summer (α = .92), and winter (α = .93).

Seasonal Beliefs Questionnaire (SBQ). The SBQ (Rohan, Nillni, et al., 2007) is a 26-item measure of season-specific cognitions in SAD (e.g. "I need sunshine to be happy"). For each item, respondents rate their level of agreement on a 7-point Likert scale from 7 "totally agree" to 1 "totally disagree." Although the SBQ is a relatively new measure, it is the only scale available to measure the SAD-specific cognitions proposed in Rohan's model. The SBQ has demonstrated high internal consistency (α = .98) and test-retest reliability (r = .89; Rohan, Nillni, et al., 2007). The SBQ demonstrated excellent internal consistency in the present study at both, summer (α = .94) and winter (α = .93) assessments.

Morningness – Eveningness Questionnaire (MEQ). The MEQ (Horne & Östberg, 1976) is a 19-item measure of diurnal preference, as a continuous scale of preferred morningness or eveningness. Total MEQ scores range from 16-86, with lower scores indicative of greater eveningness, and higher scores of greater morningness. Middle scores are reflective of an intermediate, or neither, morning- nor evening-type. The MEQ demonstrated relatively good internal consistency at both summer (α = .73) and winter (α = .69) assessments.

Phase Angle Difference (PAD). PAD is a measure of the relation between circadian phase and sleep, defined here as the difference in timing between the dim light melatonin onset (DLMO) and the midpoint of sleep, see Figure 2. The DLMO is the standard biomarker of circadian phase (Benloucif et al., 2012; Lewy et al., 1999) measured via serial saliva collections under dim light conditions (< 30 lux) in the

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evening, defined as the interpolated time between the last saliva sample with a melatonin concentration below 3pg/ml and the first sample above 3 pg/ml (Benloucif et al., 2008). The actigraphic sleep midpoints were averaged over the week prior to saliva collection. Deviation from PAD-6, proposed to be the "sweet spot" (Lewy et al., 2003; 2006), constituted the chronobiological predictor, calculated as an absolute value difference (in hours) from PAD of 6 hr. The absolute deviation was calculated to account for variation in direction of phase shift, as prior findings indicate that a minority (i.e., 1/3) of SAD patients exhibit a phase-advanced, whereas the majority exhibit a phase delayed, circadian rhythm when depressed (Lewy et al., 2006).

Data Analytic Method

Aim 1. A series of Linear Mixed Models were conducted in SPSS to examine the within- and between-subjects variation in the cognitive and chronobiological vulnerabilities. Within-subject effects were tested across time, categorized by season (i.e., summer and winter). Between-subjects effects were tested across groups (i.e., SAD patients and never-depressed controls). LMM offers several advantages over GLM for longitudinal designs, such as allowance for correlated repeated data (i.e., violation of the independence assumption of GLM), selection of flexible covariance matrices to allow variability in error across time and group, inclusion of all available data rather than requiring listwise deletion for repeated measures designs, as well as the allowance for variable timing of data collection across individuals (Raudenbush & Bryk, 2002). All vulnerability trajectories were presumed to be linear given the restriction of 2 waves of data. The time variable, Season, was dummy coded (1, 2), such that 1 corresponded to the

summer assessment as SAD remission (i.e., intercept) to preserve the baseline in a prediction of the onset of SAD recurrence from summer to winter.

Prior to testing the hypothesized effects of within- and between-subjects effects, the unconditional means model (i.e., intercept level) was examined for inter-individual variability of the outcome as a measure of independence of observations. The Intraclass Correlation (ICC) reflects the ratio of between-subject variance to the total variance, absent of any additional fixed effects. As generally recommended, mixed modeling was applied if the ICC was greater than .25, otherwise, GLM tests (e.g., regression or repeated measures ANOVA) were applied, as appropriate. Next, the unconditional growth model (i.e., intercept and time) was examined for random individual growth (i.e., random variation in individual slopes). For all the mixed models, the unconditional growth model did not converge, reflecting low random variation across time (i.e., restricted range of individual slopes), indicating that an individual growth model is not a good fit to the data. This result likely reflects restriction due to study design (i.e., selection of participants on the dichotomous presence or absence of SAD), with a dichotomized range of captured mood states across seasons (i.e., summer remission versus winter major depression in SAD patients). The study was designed as a stringent test of potential correlates of SAD recurrence. Due to the lack of random variation, the presented LMM results reflect average growth (i.e., group means) across time points, whereby regression coefficients indicate average degree of difference between summer and winter assessments, rather than individual rates of change. Participant was included in the model as a random factor to account for inter-individual variation in summer depression severity (i.e., intercept), as well as individual variation in SAD vulnerabilities. All mixed models were built

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sequentially starting from the unconditional means model, adding fixed effects in a stepped fashion across 4 additional models: Model 2 added the fixed main effect of season to the unconditional means model, Model 3 added the fixed main effect of patient status, and Model 4 added the interaction effect of patient status by season, entered as a fixed effect. Various covariance structures were fitted to the models. In all cases, an unstructured covariance matrix provided the best fit to the model, allowing covariances to vary across summer and winter. In order to account for unexpected error variance due to sample variability, factors shown to influence sample variability [e.g., study site, season order (i.e., summer or winter as Time 1), diurnal preference, attrition, age, or sex] were also tested for covariate effects on each vulnerability outcome measures. All significant variables were included in the final model as fixed covariates. The inclusion of significant covariates was intended to reduce error variance and associated Type I and Type II error rates, and thereby increase power for detecting true effects by the variables of interest. Prior to interpretation of model estimates, residuals were examined for linearity, normality, and detection of outliers. If violation of assumptions was detected, transformations of the dependent variable, and/or outlier diagnostics were applied. LMM does not yield effect size estimates for fixed effects. Therefore, fixed effect estimates (η^2) were calculated for Aim 1 analyses with GLM to facilitate interpretation of current and prior findings. Effect size estimates should be interpreted with some caution given that GLM estimates are not based on complete data due to listwise deletion.

Each cognitive vulnerability measure (i.e., Brooding Rumination subscale score, Ruminative Response Scale score, Seasonal Beliefs Questionnaire total score, Dysfunctional Attitudes Scale, and cognitive reactivity) was modeled as a linear function

of the fixed effects of season, patient status, and the interaction of patient status by season, as well as any significant sample bias covariate, including study site, season order, attrition, diurnal preference, or sex. The chronobiological vulnerabilities (DLMO, PAD, and PAD – 6) were modeled in the same way, with additional tests for fixed covariate effects of age and diurnal preference given established effects on circadian phase and/or sleep (Duffy, Rimmer, & Czeisler, 2001; Yoon et al., 2003). Significant 2- and 3-way interactions were explored graphically to determine the nature of the interaction and to test simple slopes, per Aiken & West (1991).

     Aim 2. A second series of Linear Mixed Modeling analyses was conducted to explore the integrative model of SAD recurrence, testing depression severity (i.e., BDI-II or SIGH-SAD total score) across seasons as a linear function of cognitive and chronobiological vulnerability effects. In a series of fixed effects linear mixed models, depression was tested as a linear function of participant (random effect) with season, patient status, and the patient status by season interaction as fixed factors. These SIGH-SAD and BDI-II models served as the base for comparison with subsequent models testing solo covariate effects of cognitive (brooding rumination, RRS, SBQ, cognitive reactivity, DAS) or chronobiological (PAD, PAD-6) vulnerability measures. The fixed covariate effects of the vulnerabilities were each tested in a stepped fashion across 4 additional models to the SIGH-SAD and BDI-II base model. Model 1 added the main effect of the vulnerability on depression. Model 2 added the 2-way interaction effect of vulnerability by patient status. Model 3 added the 2-way interaction of vulnerability by season. Model 4 added the 3-way interaction effect of vulnerability by patient status by season. The 2-way interaction terms test whether the effect of season or patient status on

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depression depends on level of the vulnerability. The 3-way interaction term tests whether the effect of patient status on average seasonal variation in depression severity depends on the level of the vulnerability. Interactions were explored graphically with planned simple slopes analyses and pairwise comparisons. Full maximum likelihood was employed to estimate parameters based on likelihood of model fit. Full maximum likelihood was selected over restricted maximum likelihood as the former provides more accurate estimates for comparison of models varying by fixed effects (Singer & Willett, 2003). To compare whether the inclusion of the vulnerability improved model fit, and to determine the best-fitting model, deviance chi-square tests were conducted between consecutive models, per Snijders and Bosker (2012). Examination of residuals of the base models revealed non-normality. Square-root transformations were found to correct the normality violation with correction of influential outliers. Therefore, the results of the transformed outcomes are presented, below.

The summer scores of RRS and brooding rumination were entered as trait cognitive predictors because the integrative model posits that these underlying cognitive vulnerabilities are stable across seasons in SAD, and contribute to depression via a diathesis-stress mechanisms, in the context of winter. The summer score of cognitive reactivity was also utilized as the negative mood induction was only administered in summer. DAS scores were entered for both summer and winter, in accordance with Beck's cognitive theory and prior research in depression and SAD supporting dysfunctional attitudes as mood state-dependent vulnerability that waxes and wanes with depressive episodes (Young & Yap, 2010). Seasonal beliefs were tested with both summer and winter scores due to the exploratory test of this proposed vulnerability.

Similar to the DAS, the summer and winter scores of the chronobiological vulnerability measures were entered to examine the effect of fluctuation of phase angle across mood states and seasons on SAD severity. This approach is intended to test the Phase Shift Hypothesis, which proposes that SAD patients may exhibit pathophysiologic shifting in circadian rhythms when depressed in winter.

Prior to inclusion in the model, grand mean centering was applied to all predictors to improve interpretability of intercepts, slopes, and interactions. Grand means were calculated based on all time points included in the model per predictor (i.e., summer only for RRS, brooding rumination, and cognitive reactivity). Grand mean centering of predictors was selected over group mean centering given that the between-groups differences in vulnerabilities are the effects of interest, rather than confounding effects. The dichotomous, between-subjects level 2 predictor, patient status, was not centered in order to retain interpretability, given that 0 is a meaningful value (i.e., absence of SAD). SPSS does not estimate effect size for time-varying covariates, therefore effect size estimates for Aim 2 predictors are not presented. Multiple imputation was applied to estimate missing cases, intended to improve power for hypothesis testing of Aim 2 given the number of parameters included in the models. Degrees of freedom in Aim 2 are based on the number of observations (128) due to multiple imputation and maximum likelihood estimation. Additionally, SPSS estimates degrees of freedom in LMM via the Satterhwaite approximation, which results in decimal estimates.

CHAPTER 4: Results

Participant Flow

Data were pooled across similar projects conducted simultaneously in Burlington, Vermont and Pittsburgh, Pennsylvania during the summer and winter seasons, 2012 – 2014 in Burlington, Vermont and Pittsburgh, Pennsylvania.

Burlington, **VT recruitment**. A total of $n = 373$ individuals completed the phone screen. After meeting phone screen criteria, 85 potential volunteers attended a screening visit and signed a consent form. Of those who attended a screening visit, $n = 26$ were excluded for the following reasons: $n = 7$ (8.2%) due to non-SAD axis I diagnosis, $n = 13$ (15.3%) due lack of fulfillment of DSM-IV criteria for SAD, and 2 (2.4.%) for medications, and $n = 4$ (4.7%) screened individuals were excluded as controls due to history of depression. Of the 59 subjects deemed eligible based on the screening visit, $n = 39$ were successfully scheduled and provided data. Of these 39, $n = 4$ (10.2%) patients were excluded from the analyses for not meeting SAD criteria at follow-up, defined as either moderate depression in summer (i.e., BDI-II ≥ 14) or lack of SAD recurrence in winter (i.e., never met full Major Depressive Episode per SCID criteria assessed biweekly via telephone). A total of $n = 35$ ($n = 21$ SAD patients, $n = 14$ controls) Burlington participants were included in analyses, comprising 59.3% of the pooled sample.

Pittsburgh, **PA recruitment**. From a dataset of 58 prospective participants enrolled after IRB approval and inclusion of the study measures, $n = 22$ patients (37.9%) were excluded due to current treatment, and $n = 7$ (12.1 %) were excluded due to SAD or

control exclusion criteria. A final sample of $n = 29$ ($n = 10$ SAD patients, $n = 19$ controls) were included from the Pittsburgh site, comprising 40.7% of the total pooled sample.

Sample Characteristics

The final pooled sample ($N = 64$) included 31 SAD patients, and 33 control participants, with 54.7% recruited in Burlington and 45.3% in Pittsburgh. The sample was predominantly female (81.3%) and Caucasian (81.2%), with a mean age of 45.51 years ($SD = 12.97$). See Table 1 for sample demographics and descriptives.

The sample of SAD patients ($n = 31$) was 74.2% female, consistent with the reported female gender ratio of 3:4 within the broader SAD patient population, and 71% Caucasian. The sample of controls ($n = 33$) was also predominantly female (87.9%) and Caucasian (90.9%). A significantly larger proportion of SAD patients than controls were members of racial/ethnic minority groups, 29.0% vs. 9.1%, respectively, $\chi^2(1) = 4.2$, $p = .041$. The SAD patient sample was also significantly older in age ($M = 49.0$, $SD = 11.2$) than the control group [$M = 42.2$, $SD = 13.8$), $t(62) = 2.15$, $p = .036$]. SAD patients had a mean SPAQ global seasonality score (GSS) of 15.76 ($SD = 4.72$), indicating moderate seasonality consistent with SPAQ criteria to estimate SAD diagnosis (GSS SAD cutoff score ≥ 11; Kasper et al., 1989). Consistent with inclusion of never-depressed, low-seasonality controls, controls' mean SPAQ GSS was 3.30 ($SD = 2.36$), indicating minimal seasonality (Kasper et al., 1989). Diurnal preference varied across groups whereby SAD patients endorsed more eveningness ($M = 51.61$, $SD = 8.26$) than controls, who endorsed more morningness ($M = 56.12$, $SD = 9.24$), $t(62) = -2.05$, $p = .044$.

Sample retention and missing data. Patterns of attrition were not different between patients and controls, $\chi^2(2) = 5.26$, $p = .072$, with 42 participants (65.6%)

providing data at both time points, $n = 10$ (15.6%) at summer only, and $n = 12$ (18.8%) at winter only. The degree of missing data varied by measure. The chronobiological data presented the most logistical challenges, and therefore the most missing data. However, patients and controls did not differ in the proportions with missing PAD data, $\chi^2(3) = 2.36$, $p = .502$. Of the sample as a whole, a detectable DLMO and viable sleep data for calculation of PAD was provided at both timepoints by $n = 28$ (43.8%), at the summer assessment only by $n = 5$ (7.8%), and at the winter assessment only by $n = 12$ (18.8%), however $n = 19$ (29.7%; $n = 11$ controls, $n = 8$ patients) did not provide valid PAD data at either assessment due to cases with a missed DLMO at Time 1 and attrition prior to Time 2. See Table 2 for valid data (%) per measure.

Assessment timing. SAD patients and controls did not differ in timing of assessments within season, as measured in absolute number of days between the SIGH-SAD interview and the seasonal solstice, in either the summer ($p = .312$) or winter ($p = .178$) assessments. The summer SIGH-SAD occurred an average of 49.64 ($SD = 31.29$) days (absolute) from the summer solstice (i.e., late May to mid-September). Similarly, the winter SIGH-SAD interview occurred an average of 47.07 ($SD = 21.05$) days (absolute) from the winter solstice (i.e., early December to mid-March).

Season order. Season order of enrollment (i.e., summer or winter as Time 1) was comparable across groups ($p = .462$), with $n = 30$ (46.9%; $n = 16$ patients, $n = 14$ controls) having completed Time 1 in summer, and $n = 34$ (53.1%; $n = 15$ patients, $n = 19$ controls) having completed Time 1 in winter.

Recruitment site. Sample demographics were compared across study sites to assess compatibility of sub-samples. A larger proportion of SAD patients included in the

analyses were recruited in Burlington ($n = 21$; 67.7%) than Pittsburgh ($n = 10$; 32.3%),

and, conversely, a larger proportion of controls included in the analyses were recruited in

Pittsburgh ($n = 19$; 57.6%) than Burlington ($n = 14$; 42.4%), [$\chi^2(1) = 4.14$, $p = .042$].

There were significantly fewer male SAD patients recruited in Pittsburgh ($n = 2$; 6.9%) as

compared to Burlington ($n = 10$; 28.6%), [$\chi^2(1) = 4.89$, $p = .027$]. There were no

between-site demographic differences within the patient or controls groups in age ($p =$

.419; $p = .562$), seasonality as indexed by SPAQ GSS ($p = .268$; $p = .487$), or diurnal

preference measured as MEQ score ($p = .125$; $p = .843$). Proportion of seasonal

enrollment order significantly varied by study site [$\chi^2(1) = 7.92$, $p = .005$], whereby the

majority of Burlington participants completed the summer assessment at Time 1 (62.9%),

however the majority of Pittsburgh participants completed the winter assessment at Time

1 (72.4%).

Depression severity. The validity of the following analyses was contingent upon

the accurate recruiting of SAD patients and low-seasonality, never-depressed controls

during contrasting mood states at winter. To verify validity of SAD patient vs. control

status (i.e., presence of SAD symptoms in patients and absence of depression in controls),

preliminary independent samples *t*-tests were conducted at summer and winter between

SAD patients and controls to examine levels of depression on the BDI-II. As expected,

SAD patients endorsed moderate depression severity on the BDI-II in winter ($M = 26.52$,

$SD = 6.69$), as compared to controls whose winter depression severity fell within the

minimal range of the BDI-II ($M = 1.13$, $SD = 1.91$), $t(23.59) = 13.77$, $p < .001$. Both

groups fell within the minimal depression severity range on the BDI-II in summer,

although SAD patients scores were slightly higher ($M = 4.68$, $SD = 4.32$) than controls

($M = 1.32$, $SD = 2.14$), $t (40.84) = 3.70$, $p < .001$. The full patterns of within- (i.e.,

season) and between-subjects (i.e., group) effects on seasonal change in depression were

examined within a linear mixed model for BDI-II and SIGH-SAD scores, as presented

under results for Aim 2 analyses. See Table 3 for depression scores across group and

season.

Aim 1: **To test whether SAD patients and controls differ in cognitive or**

chronobiological vulnerabilities across seasons

   Chronobiological vulnerability results. Due to the related mechanisms of

sleep/wake cycle, correlations were examined between sleep and circadian factors prior

to testing within-and between-subjects factors in PAD or PAD-6. See Table 4 for the

estimated marginal means of sleep and chronobiological measures.

   In order to properly interpret group and season effects on PAD, within- and

between-subjects variability in sleep (midsleep) and melatonin timing (DLMO) were

examined separately prior to analysis of PAD. In addition to examining season and

patient group effects, the chronobiological measures were also tested for the following

effects shown to be associated with variability in circadian function: age, diurnal

preference, and study site (i.e., proxy for latitudinal difference in photoperiod).

Additionally, chronobiological measures were also tested for sampling effects due to

completer status and season order.

   The average clock time of midsleep, as occurring across the 7 days prior to

DLMO collection, was examined for individual-level variability to assess for fit to a

linear mixed model. The unconditional means model yielded an ICC of .87, indicating

87% of variance in midsleep is attributable to variation at the individual level. The

unconditional growth model indicated a nonsignificant random variation across time ($p =$ .487). Therefore, a fixed effects linear mixed model was applied. The model was built in a stepped fashion from the intercept, including significant effects. Initial tests of potential covariates revealed that midsleep times were not influenced by season order ($p = .646$), or completer status ($p = .188$). These factors were dropped from the model. However, there were significant fixed effects of age ($p < .001$), study site ($p = .033$), and MEQ ($p = .024$), and sex ($p < .001$) on midsleep timing. There were no significant interaction effects between the covariates and patient status or season. To reduce unknown error, age, study site, MEQ, and sex were jointly included in the final model as fixed covariates. The final model tested midsleep as a linear function of season with participant entered as a random effect; season, patient status, and the interaction of patient status by season entered as fixed factors; and with age, study site, MEQ, and sex included as fixed covariates. The effects of MEQ and sex became nonsignificant in the final model ($p = .826$; p = .059, respectively). There was a significant fixed covariate main effect of age [$F(1, 56.36) = 23.05, p < .001, \eta^2 = .434$], whereby older age was associated with earlier midsleep times ($b = -.04, SE = -.01$). The effect of study site also remained significant, [$F(1, 53.69) = 9.76, p = .003, \eta^2 = .108$], indicating that Burlington participants averaged later midsleep clock times ($M = 3.10, SD = 1.02$) than Pittsburgh participants ($M = 2.48, SD = 0.80$). Average midsleep occurred at $M = 2.92$ ($SD = 1.00$). Of note, there were no significant interactions of age or site by patient status or season. The model did not yield significant effects of interest for season ($p = .426$), patient status ($p = .813$), or the interaction of patient status by season ($p = .769$), reflecting comparable timing in midsleep between patients and controls at summer, at winter, as well as comparable degrees of seasonal

variation in midsleep across groups. See Table 4 for the estimated marginal means by group and season, as adjusted for the effects of age and site.

An unconditional model for DLMO clock time was also examined for fit to the linear mixed model, which yielded an ICC of .58, indicating 58% of the variance in DLMO occurs at the individual level. The unconditional growth model yielded a nonsignificant random variation by season, which implicated application of a fixed effects model. A linear mixed model was built sequentially testing effects of season, patient status, and the patient status by season interaction, and influences by confounding factors related to circadian rhythms (e.g., study site, age, diurnal preference as MEQ score) or sample variability (e.g., completer status and season order). There were no effects of season order ($p = .138$), completer status ($p = .463$), or sex ($p = .080$), or MEQ ($p = .364$). There were significant effects of study site ($p = .023$), and age by season ($p = .006$). There were no significant interactions of site or age by patient status. Site, age, and age by season were included in the model. An unstructured covariance structure was selected for the final model. The model tested DLMO as a linear function of participant (random effect), with season, patient status, and patient status by season included as fixed factors, and study site, age, and age by season included as fixed covariates. The model did not reveal significant differences across seasons ($p = .080$) or patient status ($p = .095$), or an interaction of patient status by season ($p = .450$), indicating similarity in DLMO timing across groups and stability across seasonal assessments. The main effect of site remained significant, [$F(1, 47.50) = 4.26$, $p = .044$, $\eta^2 = .081$], indicating later DLMO times in the Pittsburgh sample ($b = .73$ hrs, $SE = .36$), with the average Burlington DLMO occurred at 20:22 ($SD = 1.29$), and the average Pittsburgh DLMO

occurred at 21:05 (SD = 1.50), as averaged across seasons. There was not a significant

site difference by season. However, descriptively, the Pittsburgh DLMOs occurred an

average of 36.96 minutes later than Burlington in summer, and an average of 49.63

minutes later than Burlington in winter. The direction of site variability in summer

DLMO difference was consistent with documented difference between laboratory and at-

home saliva collection. Prior research has found that laboratory DLMOs occur an average

of 37 (+/- 19) minutes later than at-home collection in the same participants (Pullman,

Roepke, & Duffy, 2012). The DLMO difference across sites, which was larger in winter,

may reflect the compound effects of sampling method differences and the shorter winter

photoperiod in Vermont. There was also a significant effect of age by season [F(1, 37.80)

= 4.51, p = .040, η^2 = .105] on DLMO clock times. The simple slopes analysis revealed

that older participants averaged later DLMO times (i.e., 45 minutes) in winter than older

participants in summer [(b = .75), t = 2.06, p = .045], whereas younger participants did

not exhibit significant seasonal variation (p = .670). See Table 4 for the estimated

marginal means for DLMO by group and season, adjusted for effects of age and site.

      Hypothesis 1: **PAD**. The unconditional model for PAD yielded an ICC of .54,

indicating 54% of the variance in PAD is attributable to inter-individual variation. The

unconditional growth model revealed a nonsignificant effect of season, indicating a fixed

effects model is appropriate. Therefore, a fixed effects linear model was applied to

examine the within- and between-subjects patterns of PAD. The model was built in a

stepped fashion adding the effects of season, patient status, patient status by season, and

potential covariates sequentially. Study site, age, MEQ, season order, and completer

status were all examined as covariates for potential inclusion in the model. The model

building yielded nonsignificant effects for age (p = .567), sex (p = .785), MEQ (p = .674), season order (p = .160), and completer status (p = .786). Consistent with the site differences in DLMO, there was a significant fixed effect for study site (p = .001) on PAD. Therefore, site was included in the final model as a fixed covariate. An unstructured covariance structure was applied to the model to allow maximum flexibility across observations. The final model tested PAD as a linear function of participant (random effect), with season, patient status, and the patient status by time interaction term as fixed factors, and study site included as a fixed covariate. Contrary to the hypothesized effects, the model yielded nonsignificant effects for season (p = .836) and patient status (p = .161), and patient status by season (p = .836), indicating comparable PAD across seasons and group, with a sample average PAD of M = 6.32 hours (SD = 1.27). There was a significant fixed effect of site [$F(1$, 49.18) = 13.61, p = .001, η^2 = .086], whereby Burlington participants exhibited longer PAD collapsing across seasons (M = 6.63, SD = 0.94) than Pittsburgh participants (M = 5.57, SD = 1.64), (b = -1.27, SE = 0.36). The longer PAD in Vermont appears to be due to both earlier occurring DLMO and later occurring midsleep times, relative to the Pittsburgh sample. Of note, the effect of patient status was nonsignificant (p = .638) prior to adding study site to the model, which suggests that the effect of site is not masking an effect of patient status. Examination of the model residuals revealed one influential outlier (z = -3.51), a control participant who exhibited a uniquely short PAD in winter (PAD = 2.47 hr) relative to the other control participants, M = 6.73 (SD = 1.29). A square root transformation did not correct for non-normality associated with the outlier due to the degree of departure from the mean. Removal of this outlier corrected the normality of residuals. The outlier was removed to

improve precision of the group mean for the sample, given the lack of individual growth resolution in the current statistical model. However, the outlier is deemed a valid data point to be noted as variability within the control population. The reduced model revealed a significant main effect for season [$F(1, 30.50) = 7.04$, $p = 013$, $\eta^2 = .001$], whereby winter PADs averaged longer ($M = 6.61$, $SE = .16$) than summer PADs ($M = 6.24$, $SE = .15$)., with winter PADs averaging 25 minutes longer than summer PADs ($b = -0.41$, $SE = .20$). There was also a main effect of patient status [$F(1, 43.19) = 4.51$, $p = 039$, $\eta^2 = .016$] whereby controls exhibited longer PADs, collapsing across seasons, ($M = 6.73$, $SE = .20$) than patients ($M = 6.12$, $SE = .20$), with control PADs averaging 38 minutes longer than patient PADs ($b = -.64$, $SE = .32$). There was not a significant interaction of patient status by season ($p = .811$). The aforementioned effect of site remained significant in the reduced model [$F(1, 45.91) = 13.86$, $p = .001$, $\eta^2 = .163$]. There were not interaction effects of site by season or patient status. See Table 4 for estimated marginal means of PAD by group and season after removal of the outlier.

Hypothesis 2: **PAD-6**. The unconditional model yielded an ICC of .25, indicating that 25% of the variance in PAD-6 is attributable to variability at the individual level. The unconditional growth model yielded a nonsignificant effect of season, implicating a fixed effects model. A fixed effects linear model was utilized to test within- and between-subjects effects of PAD-6. There were no significant effects of site ($p = .204$), completer status ($p = .338$), season order ($p = .684$), sex ($p = 227$), or age ($p = .246$). PAD-6 was modeled as a linear function of patient status, season, and the interaction. Examination of residuals revealed outlier influence by the same case as identified in the PAD analysis ($z = 1.88$). Contrary to the PAD analysis, a square-root transformation performed on the

PAD-6 outcome measure corrected non-normality of residuals for retention of the outlier. MEQ remained the only significant covariate, and was included in the final model. Testing for MEQ confounding effects is of particular importance when comparing patterns of PAD and PAD-6 given that chronotype is associated with inter-individual variation in intrinsic period and natural phase angle of entrainment to light (Duffy, Djik, Hall, & Czeisler, 1999; Duffy, Rimmer, & Czeisler, 2001; Emens et al., 2009). The inclusion of MEQ significantly improved model fit. An unstructured covariance structure was fitted to the model given that PAD-6 was expected to vary differently by season for patients and controls. The final model tested PAD-6 (absolute deviation) as a linear function of participant (random effect), with season, patient status, and patient status by season entered as fixed factors, and with MEQ included as a fixed covariate. The Linear Mixed Model results revealed nonsignificant effects of season ($p = .135$), and season by patient status ($p = .233$). The effect of patient status remained significant, yet diminished with the addition of MEQ, [$F(1, 40.46) = 4.09$, $p = .039$, $\eta^2 = .166$], whereby controls exhibited greater deviation from PAD-6 ($M = .99$ hrs, $SE = .06$) than patients ($M = .80$ hrs, $SE = 06$) collapsing across seasons. The significant covariate main effect for MEQ [$F(1, 51.36) = 4.67$, $p = .035$, $\eta^2 = .122$] revealed that greater morningness was associated with greater deviation from PAD-6 ($b = .01$, $SE = .01$), whereby a 1 point increase in morningness was associated with a 1-minute increase in deviation from PAD-6. The patterns of significant results do not support the hypothesis for greater deviation from PAD-6 in SAD patients than controls. See Table 4 for estimated marginal means of PAD-6, adjusting for the covariate effect of MEQ, and Figure 6 for illustration of PAD-6 by patient status and season.

Cognitive Vulnerability Results. See Table 5 for descriptive statistics for the cognitive vulnerabilities by patient status and season.

Hypothesis 3**: Brooding rumination**. It was hypothesized that SAD patients would endorse greater brooding rumination relative to controls. An effect of season was not expected, as rumination has been conceptualized and previously examined as a trait tendency to ruminate (and in this case, brood) in response to sad mood. Rumination in the fall has been shown to be predictive of depression severity the following winter in SAD (Rohan, Sigmon, & Dorhofer, 2003; Young & Azam, 2003), and this finding has been replicated for brooding rumination, specifically (Enggasser & Young, 2007). The unconditional means model for the brooding rumination subscale score of the RRS (Treynor et al., 2003) yielded an ICC of $r = .69$ at the participant level, indicating 69% of the variance in brooding rumination is attributable to inter-individual variation. The unconditional growth model yielded a nonsignificant random effect of season ($p = .202$) indicating that a fixed effects model is warranted over a random effects model. A fixed effects linear model was applied to test the effects of season, patient status, and the interaction of patient status by season on brooding rumination subscale score.

Prior to finalizing the model, season order (i.e., season of Time 1) and completer status (i.e., attrition) were separately tested as possible fixed effects to determine whether these factors should be included as fixed covariates in the model. These models did not yield significant effects for study site ($p = .172$), completer status ($p = .622$), or sex ($p = .065$). There was a significant covariate effect of season order by patient status ($p = .007$), indicating variability in the effect of patient status by season order. This effect was included as a covariate in the final model, which included participant entered as a random

effect, with season, patient status, and the interaction, patient status by season, entered as fixed factors, and season order and season order by patient status as fixed covariates. An unstructured covariance structure was selected given the expectation for covariances to differ between SAD patients and controls across seasons. Examination of residuals revealed significant non-normality (i.e., leptokurtosis) with two outliers, a patient in winter with extreme low ($z = -6.21$; raw score: 0) and a patient in winter with extreme high ($z = 6.87$; raw score: 13). Normality was not corrected by transformation of the outcome, so the raw values were examined. The outliers were retained in the model as their removal did not change the pattern of results and the points were deemed valid. However, the exact estimates of the model should therefore be regarded with some caution, due to violation of normality. There was a significant fixed covariate interaction of season order x patient status [$F(1, 61.93) = 9.61$, $p = .003$, $\eta^2 = .102$. A simple slopes analysis revealed that participants enrolled in winter as Time 1 endorsed greater mean levels of brooding rumination than participants enrolled initially in summer. The effect was significant within both the patient [$b = 7.74$, $t = 10.96$, $p < .001$] and control groups [$b = 4.68$, $t = 2.98$, $p = .004$], however the interaction effect indicates that the effect was stronger in patients. There were also significant main effects of season, [$F(1, 48.29) = 17.68$, $p < .001$, $\eta^2 = .150$], and patient status [$F(1, 63.56) = 34.10$, $p < .001$, $\eta^2 = .578$], and a significant interaction effect of patient status by season, [$F(1, 48.29) = 17.68$, $p < .001$, $\eta^2 = .174$], indicating differential average patterns of brooding rumination across seasons between patients and controls. The interaction was explored graphically and via paired comparisons to determine the nature of the effects. The simple slopes analysis revealed significant seasonal variation in brooding rumination across summer and winter

(i.e., significantly different from zero) for patients, [$b = 3.01$ ($SE = .53$), $p < .001$], but not controls, $p = 1.00$. Paired contrasts revealed that SAD patients endorsed greater brooding rumination than controls at summer [$b = 3.33$ ($SE = .60$), $p < .001$], and winter [$b = 5.88$ ($SE = .68$), $p < .001$]. Taken together, these results indicate that SAD patients endorse a greater tendency to engage in brooding rumination in response to sad mood year-round relative to controls, and also exhibit unique, significant seasonal variation across seasons, with greater tendency to brood in winter, when depressed. These results support the hypothesis that SAD patients would report more tendency to brood, which supports brooding rumination as a cognitive risk factor in SAD. This finding is novel in documenting the trait elevation of brooding rumination in SAD patients, relative to a never-depressed control group, as well as by observing the significant seasonal elevation of brooding rumination in winter in patients. See Table 5 for estimated marginal means of brooding rumination adjusted for season order, and Figure 7 for a graphical representation of brooding rumination estimated marginal means by patient status and season.

For direct comparison to the extant literature, the total score of the RRS (Treynor et al., 2003) was also examined for patterns occurring across season and patient status, as the full RRS scale been the most widely used within the SAD literature to date, with replicated support for the predictive effect of general rumination on winter depression severity. The same model, as for brooding, was run with the RRS total score. The unconditional model of the total score revealed yielded an ICC of .64 at the participant level, indicating 64% of the variance in RRS is attributable to inter-individual variation. The individual growth curve model yielded a nonsignificant random effect of time on

individual growth trajectories ($p = .197$), implicating a fixed effects linear model. Prior to

finalizing the model, study site, completer status, and season order were tested as possible

covariates due to variability in the sample. There were not significant effects for

completer status ($p = .423$) or sex ($p = .721$). There were initial significant effects of

study site ($p = .012$) and season order ($p = .021$). There was an additional effect of season

order by patient status ($p = .018$). Therefore, site, season order, and season order by

patient status were jointly included as fixed covariates in the final model. The final model

tested RRS as a linear function with participant entered as a random effect; and season,

patient status, and the interaction of patient status by season entered as fixed factors, and

with site, season order and season order by patient status included as fixed covariates. An

unstructured covariance structure was fitted to the model. Including the covariates in the

final model improved model fit per the AIC and BIC indices. Examination of residuals

revealed significant violation of normality, as well as numerous outliers. A square-root

transformation corrected normality and outlier bias, and retained the same pattern of

results, and was therefore considered the final RRS model. The square-root RRS model

revealed significant covariate effects of site [$F(1, 66.69) = 7.77$, $p = .007$, $\eta^2 = .015$],

whereby Burlington participants averaged greater rumination than Pittsburgh participants

($b = -.76$, $SE = .27$). There was also a significant interaction effect of season order by

patient status [$F(1, 64.49) = 6.03$, $p = .017$, $\eta^2 = .044$]. A simple slopes analysis revealed

that participants enrolled in winter as Time 1 endorsed greater mean levels of rumination

than participants enrolled in summer. The effect was significant for patients ($b = 4.37$, $t = 12.26$, $p < .001$), as well as controls ($b = 3.61$, $t = 4.06$, $p < .001$), with the interaction

indicating a stronger effect within the patient group. Regarding the hypothesized effects,

there was a significant fixed effect of season [$F(1, 47.10) = 32.55, p < .001, \eta^2 = .262$],

and a large effect of patient status [$F(1, 65.02) = 37.02, p < .001, \eta^2 = .892$]. There was

also a significant patient status by season interaction [$F(1, 47.28) = 26.43, p < .001, \eta^2 = .224$], indicating differential rates of seasonal variation in RRS by patient status. The

nature of the interaction was explored graphically. A simple slopes analysis revealed that

SAD patients averaged significantly greater RRS scores in winter relative to summer ($p < .001$), in contrast to the control group, which did not exhibit significant seasonal variation

($p = .675$). Further, SAD patients averaged greater RRS than controls at both summer and

winter, with respective differences as $M = 2.14$, $SE = .31$, $p < .001$; $M = 3.74$, $SE = .27$, $p < .001$. This supports the broad construct of rumination in SAD as depressed mood state-

dependent, as was observed for brooding-specific rumination. See Table 5 for the RRS

estimated marginal means, adjusted for covariate effects. Figure 8 illustrates average

group means by season.

Hypothesis 4: **Cognitive reactivity**. It was hypothesized that SAD patients would

exhibit greater cognitive reactivity (i.e., an increase in endorsed dysfunctional attitudes

across a negative mood induction) in summer than controls.

Prior to examining model effects, a manipulation check was conducted to confirm

that the dysphoric mood induction was successful in producing a negative mood, as

measured by the Visual Analog Scale (VAS). On average, the sample endorsed a mean

positive mood (i.e., defined as above the midpoint mark) at pre-induction ($M = 99.81$, $SD = 14.78$), and a mean negative mood (i.e., defined as below the midpoint mark) at post-

induction ($M = 51.11$, $SD = 23.13$). All participants evidenced an increase in VAS from

pre- to post-mood induction with a mean change in VAS of 50.00 mm ($SD = 27.74$).

Accordingly, a GLM 2 by 2 Mixed ANOVA ($n = 35$) revealed a significant effect of time, whereby post-induction VAS scores were significantly lower (i.e., more negative) than pre-induction VAS scores. There was not a significant main effect of patient status ($p = .405$) or a significant interaction of patient status by mood induction timepoint (pre- and post-induction; $p = .717$), indicating that the mood induction procedure was comparably effective at inducing a negative mood for both groups.

The degree of mood reactive negative thinking (i.e., cognitive reactivity; change in DAS score from pre- to post-mood induction) across SAD patients and controls was examined with a linear mixed model analysis. Mood induction (pre- to post-induction) constituted the time variable. LMM was employed due to non-independence of the observations across time. The unconditional means model revealed an ICC of .26, indicating that 26% of the variability in cognitive reactivity was accounted for by inter-individual variability. Similar to the other analyses examining change across season, the unconditional growth model did not converge; therefore, a fixed effects model was applied. There were no significant covariate effects of completer status, season order, sex, or site. Therefore, the final model tested cognitive reactivity as a linear function of participant (random effect) by patient status and mood induction (i.e., time), with the interaction of patient status by mood induction, included as fixed factors. Examination of residuals revealed violation of the linearity assumption with the identification of three outliers, all SAD patients with extreme (high or low) reactivity. Transformations did not correct linearity. Joint removal of the outliers resulted in correction of the model, as indicated by improvement in model fit and visual inspection of residual plots. The reduced model revealed a significant effect of mood induction [$F(1, 32.66) = 11.98$, $p =$

.002, $\eta^2 = .146$], and a significant main effect of patient status [$F(1, 49.86) = 9.77, p <$ .001, $\eta^2 = 164$]. There was also a significant interaction of patient status by mood induction [$F(1, 32.66) = 4.77, p = .003, \eta^2 = .059$]. The interaction was explored with a simple slopes analysis to examine the average degree of change in DAS from pre- to post-induction between patients and controls. The simple slopes analysis revealed that SAD patients exhibited significant cognitive reactivity in response to the negative mood induction [$b = 27.68 (SE = 5.72), p < .001$], whereas the effect was not observed in controls ($p = .437$). Patients showed higher DAS scores relative to controls at post-induction only [$b = 34. 58, SE = 10.94, p = 003$]. Regarding the removal of outliers, inclusion of one patient with an extreme low cognitive reactivity score (raw score = -29; z = -80.36) masked the mean interaction effect represented by the sample. Two other outliers exhibited extreme cognitive reactivity (raw scores of 248, 186, and residuals of z = 108.64, z = 75.31, respectively). Although inclusion of these cases did not change the pattern of results, these cases were found to significantly skew mean estimates of change. These cases were not included in the model due to disproportionate influence on group change estimates; however, the data are deemed valid, and these outliers highlight likely important variability in cognitive reactivity within the SAD patient population.

Hypothesis 5: **Dysfunctional attitudes**. It was hypothesized that SAD patients would endorse more dysfunctional attitudes than controls at winter, but the groups will not differ at summer. This finding would suggest that SAD patients hold more rigid depressogenic attitudes than controls only when they are depressed. The DAS measured in summer (prior to the mood induction) and winter was also examined for within- and between-subjects effects, as a measure of cognitive vulnerability across the seasons in

SAD. The unconditional means model was tested for cross-level variation at the individual level, and revealed an ICC of .69, indicating 69% of variance in DAS scores is attributable to variation at the individual level (level 2). The unconditional growth model yielded a nonsignificant random effect of season, indicating that a fixed effects model is implicated. There were no significant effects of completer status ($p = .760$), season order ($p = .529$), or study site ($p = .564$), therefore, these factors were dropped from subsequent models. An unstructured covariance structure provided the best fit to the model. The final model tested DAS as a linear function of participant (random effect), with season, patient status, and the interaction of patient status by season (fixed factors). Examination of residuals met model assumptions. The final model revealed significant fixed effects of season [$F(1, 44.34) = .18$, $p = .004$, $\eta^2 = .144$], and patient status [$F(1, 61.76) = 12.18$, $p = .001$, $\eta^2 = .314$]. There was also a significant interaction of season by patient status [$F(1, 44.31) = 9.58$, $p = .003$, $\eta^2 = .157$], indicating that degree of seasonal variation in DAS depended upon level of patient or control status. The interaction was examined graphically with a simple slopes analysis to further test whether one or both slopes were each significantly different from zero. As hypothesized, the interaction indicated significantly greater seasonal variation in DAS across seasons unique to the patient status [$b = 18.55$ ($SE = 6.14$), $t = 4.14$, $p < .001$], whereby SAD patients endorsed more rigid dysfunctional attitudes in winter ($M = 127.48$, $SE = 4.89$) than summer ($M = 109.13$, $SE = 4.94$). However, control participants did not exhibit significant variation in dysfunctional attitudes across seasons ($p = .964$). SAD patients and controls significantly differed in DAS scores across seasons, with greater mean discrepancy in winter [$b = 26.30$, $SE = 5.89$, $p = .002$] than in summer [$b = 11.69$, $SE = 5.67$, $p = .004$]. See Table 5 for the DAS

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estimated marginal means by patient status and season. Figure 10 provides a graphical

representation of this interaction effect. This finding supports the hypothesis that SAD

patients would more strongly endorse dysfunctional attitudes in winter, within the context

of depression, supporting Beck's cognitive theory and DAS as a correlate of SAD.

Hypothesis 6: **Seasonal beliefs**. It was hypothesized that SAD patients would

endorse more rigid seasonal beliefs than controls at both summer and winter assessments.

This consistent group difference across time would reflect a greater trait tendency for

patients to endorse rigid beliefs about seasons and light year-round, relative to controls.

The unconditional means model was initially tested for repeated measures variation at the

individual level (level 2). The unconditional means model yielded an ICC of $r = .94$ at the

participant level, indicating 94% of the variance in Seasonal Beliefs Questionnaire (SBQ)

score is attributable to inter-individual variation. The unconditional growth model yielded

a nonsignificant random effect of time on individual trajectories, indicating that a fixed

effects model is warranted. Therefore, a fixed effect linear model was utilized to examine

the within- and between-subject patterns of seasonal beliefs. Prior to finalizing the model,

study site, completer status, and season order were tested as possible covariates due to

variability in the sample. There were no significant effects for study site ($p = .626$),

season order ($p = .086$), sex ($p = .815$), or MEQ ($p = .094$). There was a significant

covariate effect of completer status ($p = .002$), which was then included in the final

model to account for sampling bias. An unstructured covariance structure was applied to

the model due to expected varying covariance across season. The final model tested SBQ

as a linear function of participant (random effect), with season, patient status, and patient

status by season as fixed factors, and completer status as a fixed covariate. The effect of

completer status was retained in the model [$F(1,60.89) = 10.103$, $p = .002$], whereby

participants who completed the study averaged greater seasonal beliefs ($M = 101.61$, SD

$= 35.95$) than non-completers ($M = 108.68$, $SD = 34.24$), $b = 14.24$ ($SE = 4.60$). Of the

primary variables of interest, there was a significant main effect of season [$F(1, 44.78) =$

18.82, $p < .001$, $\eta^2 = .059$], with higher SBQ scores in winter ($M = 111.95$, $SE = 2.38$)

than in summer ($M = 105.22$, $SE = 2.17$). There was also a large significant main effect

of patient status [$F(1, 60.38) = 206.63$, $p < .001$, $\eta^2 = .834$], whereby SAD patients

endorsed more seasonal beliefs ($M = 138.74$, $SE = 3.08$) than controls ($M = 78.3$, $SE =$

2.91), collapsing across seasons. There was not a significant interaction of patient status

by season ($p = .382$) indicating comparable patterns of change in SBQ in patients and

controls. See Table 5 for estimated marginal means of SBQ by patient status and season.

See Figure 11 for a graphical depiction of the main effects of season and patient status.

Aim 2: **To test the respective, predictive effects of cognitive and chronobiological**

vulnerabilities on SAD depression severity across seasons.

        Hypothesis 7: **Between-group effects of the vulnerabilities on depression**

severity. It was hypothesized that the between-group effects of the vulnerabilities would

account for variance in depression severity, above and beyond the unique effects of

patient status (SAD patient vs. control) and the main effects of the chronobiological and

cognitive predictors.

        Base models were examined for the SIGH-SAD and BDI-II separately, examining

the effects of season, patient status, the interaction of patient status by season, as well as

potential confounding covariate effects due to sampling variability. The unconditional

means and growth models were examined initially. Nonsignificant random variation in

depression severity for the SIGH-SAD and BDI-II indicated a fixed effects model would provide the best fit to the data. Prior to analysis of the data, residuals were examined for model assumptions. The base model residuals for both the SIGH-SAD and BDI-II raw scores exhibited significant non-normality. Square-root transformations on the outcome measures corrected the normality violation of the residuals. See Table 3 for SIGH-SAD and BDI-II depression severity mean scores (raw and transformed) by group and season for the imputed data, with means of the original data for comparison.

To determine the effects of potential confounding factors due to the sample variability in: study site, season order, attrition, age, sex, and diurnal preference (MEQ); zero-order correlations were examined between these factors and the depression severity outcome measures (SIGH-SAD and BDI-II SQRT scores); see Table 6 for correlation coefficients. If significant, these factors were tested as fixed covariates in the last step of base model testing. Any significant fixed covariate was included in the base model for subsequent analyses. The SIGH-SAD SQRT scores were correlated with MEQ, such that less morningness (i.e., more eveningness) was associated with greater depression per the SIGH-SAD ($r = -.18$, $p = .043$). The BDI-II was significantly correlated with study site ($r = -.18$, $p = .047$), sex ($r = -.20$, $p = .023$), and age ($r = .19$, $p = .037$). These factors were each tested as fixed effects, separately and combined.

SIGH-SAD. The imputed unconditional means models of the SIGH-SAD total scores yielded an average ICC of .21, estimating 21% of the variance in SIGH-SAD was due to variability between individuals. Although the ICC below the recommended threshold for application of LMM over GLM (ICC = .25), LMM was deemed a better fit to the structure of the data due to nested and non-independent observations. The

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unconditional growth model with season added as a Random effect did not converge, indicating that a fixed effects LMM was appropriate. The base SIGH-SAD model was built over a series of steps, incrementally adding one fixed effect parameter of season, patient status, and the interaction of patient status by season. When included as a fixed covariate, MEQ did not significantly predict SIGH-SAD scores, nor were there significant interactions of MEQ by patient status, or season. Therefore the final model included participant as a random effect, with season, patient status and the interaction as fixed factors. An unstructured covariance matrix provided the best model fit.

The SIGH-SAD base model revealed a significant main effect of season [$F(1, 67.37) = 69.41$, $p < .001$, $\eta^2 = .374$], and a significant main effect of patient status [$F(1, 67.37) = 141.81$, $p < .001$, $\eta^2 = .678$]. As expected, there was a also a significant patient status by season interaction, indicating differential seasonal variation in depression severity for patients and controls [$F(1, 67.37) = 48.17$, $p < .001$, $\eta^2 = .260$]. A simple slopes analysis was conducted to examine the nature of the interaction, and revealed that only SAD patients exhibited significant seasonal variation between summer and winter [$b = 2.22$ ($SE = .23$) $p < .001$], whereas controls did not ($p = .348$). Paired comparisons further revealed that SAD patients averaged greater SIGH-SAD scores than controls at both summer [$b = 0.98$, ($SE = 0.15$), $p < .001$] and winter [$b = 3.01$ ($SE = 0.16$), $p < .001$]. However, the degree of depression endorsed by patients on the SIGH-SAD in the summer was within the normal range of mood (i.e., SIGH-SAD ≥ 20 has been used as a cutpoint for a major depressive episode). Figure 12 provides a graphical display of averaged SIGH-SAD SQRT patterns across seasons between groups. This effect

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corroborates successful capture of seasonal depression in SAD patients, and the absence of depression in controls, per the SIGH-SAD.

BDI-II. The patterns of the BDI-II were congruent with those exhibited by the SIGH-SAD. The imputed unconditional means models of the BDI-II total scores (SQRT) yielded an average ICC of .20, indicating 20% of the variance in BDI-II is due to variability between individuals. Convergence was not met with the unconditional growth model, when season was entered as a random effect, indicating that slopes between individuals did not significantly randomly vary. Therefore, a fixed effect model was employed in which season was identified as a repeated effect for model structure, whereby the effect of time on BDI-II was tested as a fixed effect. Participant was entered as a random effect. Therefore, BDI-II scores were tested as a linear function of season, patient status, and patient status by season (fixed effects), participant (random effect), and sex, site, or age (fixed covariates). Tests for significant confounds did not reveal significant covariates effects for site, sex, or age, *ns*. There were also no significant interactions of these potential covariates by patient status or season. Therefore these factors were dropped from subsequent models.

The base model for the BDI-II included participant entered as a random factor, with patient status, season, and the interaction of patient status by season entered as fixed factors. An unstructured covariance matrix provided the best model fit, The BDI-II base model revealed a significant main effect of season [$F(1, 64) = 73.55$, $p < .001$, $\eta^2 = .330$], a significant main effect for patient status [$F(1, 64) = 135.35$, $p < .001$, $\eta^2 = .678$], and a significant patient status by season interaction, indicating differential seasonal variation in average depression severity across season by group [$F(1,64,) = 83.99$, $p < .001$, $\eta^2 =$

.378]. A simple slopes analysis was conducted to examine the nature of the interaction. The degree of depression difference between summer to winter was significantly different from zero for patients only $b = 2.87$ ($SE = 0.23$), $p < .001$, not for controls ($p = .666$). Pairwise comparisons also revealed that SAD patients averaged higher BDI-II scores than controls at both summer [$b = 0.92$ ($SE = 0.26$), $p = .002$] and winter [$b = 3.89$ ($SE = .27$), $p < .001$]. Summer BDI-II scores for SAD patients were within the normal (euthymic mood range), with a cutpoint of BDI-II ≥ 13 used to define mild depressive symptoms (Beck et al., 1996). See Figure 13 for a graphical illustration of the BDI-II patterns by patient status and season. This further corroborates successful capture of seasonal depression in SAD patients and the absence of SAD in controls per the BDI-II.

Zero-order correlations. Prior to hypothesis testing the effects of vulnerabilities on depression, zero-order correlations were computed among independent vulnerability variables and outcome depression variables (SIGH-SAD and BDI-II SQRT scores), see Tables 7 and 8 for correlations between chronobiological and cognitive predictor variables with depression outcome measures, respectively. The cognitive vulnerability measures that remain elevated across season were all positively correlated with depression severity (i.e., BDI-II and SIGH-SAD SQRT scores) at summer and winter at $p < .01$. The state-like cognitive vulnerabilities (e.g., DAS scores) were consistently positively correlated with depression at winter ($p < .01$), although cognitive reactivity was not significantly correlated with BDI-II or SIGH-SAD at summer or winter, *ns*. The chronobiological measures were less consistently related to depression outcomes. Average midsleep clock time, DLMO clock time, and PAD were not correlated with either BDI-II or SIGH-SAD SQRT scores in summer or winter. Absolute deviation from

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PAD-6 in winter was significantly negatively correlated with winter scores on both the BDI-II and SIGH-SAD (p < .01).

Cognitive Vulnerability Models. The Linear Mixed Modeling results examining effects of vulnerabilities on depression severity are presented below, by each vulnerability measure, with results for SIGH-SAD and BDI-II (SQRT) presented in succession. The model coefficients reflect the effect of grand-mean centered predictors on square root-transformed outcomes. All models retained significant effects of patient status, season, and the interaction of patient status by season. Reported below, are findings for the additional effects of the respective vulnerabilities.

Brooding rumination. The effects of trait brooding rumination (i.e., summer score) on SIGH-SAD (SQRT) severity was tested across a series of 4 models. Model 1 significantly improved the fit to the data beyond the base SIGH-SAD model [$\chi^2(1) =$ 2518.80, $p < .001$]. Model 1 yielded a significant main effect of brooding rumination in summer on SIGH-SAD severity, collapsing across group and season [$F(1, 64) = 5.33, p =$ .033], whereby greater brooding rumination predicted greater SIGH-SAD depression severity ($b = .83$, $SE = .04$). See Table 9 for the LMM results of trait brooding rumination (i.e., summer score) on SIGH-SAD (SQRT).

Of the BDI-II analyses with summer brooding scores, Model 1 provided the best fit, with significantly improved fit from the BDI-II base model [$\chi^2(1) = 47.10, p < .001$]. Model 1 yielded a nonsignificant effect for brooding rumination summer score ($p = .271$). There were no significant interaction effects for trait brooding rumination by patient status or season on BDI-II scores. See Tables 9 and 10 for LMM results for the effect of trait (i.e., summer) brooding rumination on SIGH-SAD, and BDI-II scores, respectively.

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Due to the significant seasonal variation in brooding rumination in SAD patients in Aim 1 analyses, reported above, a follow-up analysis examined whether there were differential effects when including brooding rumination scores at both summer and winter, thereby testing the effects of concurrent brooding rumination (i.e., state brooding rumination) on depression severity. The follow-up analysis conducted the same series of LMM, modeling SIGH-SAD and BDI-II (SQRT) as linear functions of brooding, entered with both summer and winter scores. Of the SIGH-SAD models, Model 1 provided the best fit, with significantly improved fit beyond the base model, $[\chi^2(1) = 32.09, p < .001]$. Model 1 revealed a significant main effect for brooding rumination $[F(1, 114.92) = 19.48, p < .001]$, whereby greater brooding predicted higher SIGH-SAD (SQRT) scores $(b = .14, SE = .03)$. See Table 11 for state brooding rumination effects on SIGH-SAD (SQRT).

Brooding rumination summer and winter scores were also tested for predictive effects on BDI-II (SQRT). Similar to the SIGH-SAD results, Model 1 was the best fitting model for the BDI-II, whereby the inclusion of the main effect of brooding rumination significantly improved model fit beyond the BDI-II (SQRT) base model, $[\chi^2(1) = 30.29, p < .001]$. There was a significant main effect of brooding rumination on BDI-II (SQRT) as well, $[F(1, 112.13) = 24.72, p < .001]$. Models 2 also yielded a significant interaction effect of state brooding rumination by patient status $[F(1, 120.92) = 11.12, p = .008]$. The interaction remained significant across Models 1-4. There was a trend toward an interaction effect with state brooding rumination by season $(p = .054)$ at Model 3, although there was not a significant three-way interaction of brooding rumination by season by patient status $(p = .577)$ at Model 4. The effect of state brooding rumination by

patient status was examined graphically with a simple slopes analysis as an exploratory analysis. The analysis revealed significant slopes for both patients [$b = 0.70$, $t = 4.05$, $p < .001$] and controls [$b = 0.41$, $t = 4.87$, $p < .001$], whereby higher state brooding rumination predicted greater levels of concurrent depression in both groups. Contrary to the hypothesized effect, controls evidenced a significantly steeper slope ($b = 0.29$, $SE = .09$) than patients, indicating increased potency for brooding rumination for controls relative to SAD patients, within the minimal range of depression endorsed by the control sample. Implications for SAD vulnerabilities are discussed, below. See Figure 14 for a graphical representation of the interaction. See Table 12 for LMM results for state brooding rumination on average BDI-II (SQRT) scores.

Ruminative Response Scale (RRS). The series of SIGH-SAD models examining trait rumination included the summer score of the RRS as a predictor of depression. The SIGH-SAD analyses significantly improved model fit at Model 1, [$\chi^2(1) = 16.90$, $p < .001$]. However, there were no significant effects of trait rumination on SIGH-SAD severity ($p = .089$, Model 1). See Table 13 for the LMM estimates for trait rumination (i.e., RRS, summer score) on SIGH-SAD severity across models.

The BDI-II LMM analyses testing the summer RRS score as a covariate of depression also failed to yield a significant effect for RRS. The inclusion of RRS in the model significantly improved model fit with Model 1 [$\chi^2(1) = 1\text{-}.50$, $p < .001$]. Congruent with the SIGH-SAD findings, there were no significant effects of trait rumination on BDI-II scores, *ns*. See Table 14 for trait rumination (i.e., RRS, summer score) effects on BDI-II SQRT scores. Taken together, these findings do not provide

support for trait rumination, or trait brooding rumination, as a contributing vulnerabilities to SAD severity, as measured by either the SIGH-SAD or the BDI-II.

As an exploratory aim to test the role of concurrent (i.e., state) ruminative responding with current depression severity, a series of LMM was conducted with RRS scores including both summer and winter scores on SIGH-SAD and BDI-II SQRT scores. Model 1 of the SIGH-SAD analyses provided significant better fit than the base model, and the best fitting model, $[\chi^2(1) = 36.75, p < .001]$. There was also a significant main effect for RRS $[F(1, 118.68) = 26.00\ p < .001]$, indicating that endorsed tendency to ruminate was associated with concurrent mood ($b = .04$, $SE = .01$), for both patients and controls. There were no significant interactions of state rumination by patient status or season on SIGH-SAD scores. See Table 15 for the LMM results of state rumination on SIGH-SAD (SQRT) scores.

Model 3 of the BDI-II analyses yielded the best fit, $[\chi^2(1) = 5.98, p = .032]$. Model 3 also revealed a significant main effect of RRS $[F(1, 125.60) = 42.80, p < .001]$, as well as significant interaction effects of rumination by patient status $[F(1, 121.92) = 11.73, p = 004]$, and rumination by season $[F(1, 84.82) = 8.53, p = .006]$. There was not a significant 3-way interaction between rumination, patient status, and season in Model 4 ($p = .572$), therefore the 2-way interactions were examined with simple slopes analyses. Regarding the effect of rumination by patient status, the simple slopes analysis revealed that rumination had a stronger association with depression severity (BDI-II SQRT scores) in patients, yet the effect was significant in patients $[b = 0.2, t = 4.36, p < .001]$ and controls $[b = 0.1, t = 5.52, p < .001]$. The evidence for association of rumination with depression in both patients and controls may indicate that rumination is related to

depression severity, regardless of threshold (i.e., severe or minimal). Given, that this

analysis included both summer and winter scores of depression and rumination, this

effect is likely masking variability in SAD severity across seasons, as well. See Figure 15

for the interaction of state rumination and patient status on BDI-II depression severity

(SQRT). The significant interaction of rumination by season indicated that the effect of

RRS on BDI-II scores varied by season. The simple slopes analysis revealed that

rumination significantly predicted greater depression severity in winter [$b = 0.07$, SE

$=0.01$, $t = 7.18$, $p < .001$], with only a trend toward a similar effect in summer ($p = .051$).

Figure 16 illustrates of the seasonal variation in the magnitude of effect of rumination on

BDI-II depression. Table 16 presents for the LMM effects for state rumination on BDI-II

(SQRT).

Cognitive reactivity. Cognitive reactivity was added to the base models for

SIGH-SAD and BDI-II. The inclusion of cognitive reactivity significantly improved

model fit at Model 1 for both SIGHSAD [$\chi^2(1) = 14.23$, $p < .001$] and BDI-II [$\chi^2(1) =$

10.56, $p < .001$]. However, neither the SIGH-SAD, nor the BDI-II, series revealed

significant covariate effects of cognitive reactivity at Model 1 or across the models, *ns*.

See Tables 17 and 18 for LMM results for cognitive reactivity.

Dysfunctional Attitudes Scale (DAS). Inclusion of the DAS as a covariate to the

SIGH-SAD model significantly improved model fit at Model 1, [$\chi^2(1) = 24.47$, $p < .001$].

Model 1 revealed a significant main effect for DAS [$F(1, 101.19) = 11.52$, $p = .001$],

indicating that higher DAS scores were predictive of higher depression scores overall (b

$= 0.01$, $SE = 0.03$), collapsing across group and season. The main effect was maintained

across Models 1-4. However, the SIGH-SAD models did not yield significant interaction

effects of DAS by patient status or season. See Table 19 for LMM results of DAS on SIGH-SAD (SQRT).

The inclusion of DAS as a covariate significantly improved model fit, with Model 1 providing the best fit to the data [$\chi^2(1) = 18.60$, $p < .001$]. There was a significant main effect of DAS [$F(1, 108.25) = 9.94$, $p = .002$]. Model 2 also yielded a significant interaction for DAS by patient status [$F(1,114.38) = 6.04$, $p = .015$. This effect was retained in Models 2-3. Model 4 revealed a significant 3-way interaction of DAS by patient status and season [$F(1, 84.99) = 5.15$, $p = .028$]. Because model fit estimates may be influenced by power, the 3-way interaction in Model 4 was explored. The nature of the 3-way interaction was explored graphically and probed with a simple slopes analysis. The interaction revealed that the effect of dysfunctional attitudes on depression significantly varied across season in patients ($p = .006$), but not in controls, *ns*. For patients, dysfunctional attitudes significantly predicted greater depression in winter [$b = 4.38$, *SE* = .20, $t = 21.66$, $p < .001$], but not summer ($p = .236$). In contrast, dysfunctional attitudes were significantly predictive of greater depression severity in controls year-round, i.e., in both summer ($b = 0.02$, *SE* = .01, $t = 2.75$, $p = .010$] and winter [$b = 0.97$, *SE* = .18, $t = 5.38$, $p < .001$]. The interaction of DAS by patient status by season is displayed in Figure 17. Additionally, see Table 20 for LMM results of DAS on BDI-II (SQRT) scores.

Seasonal Beliefs Questionnaire (SBQ). The SIGH-SAD analyses for the SBQ revealed significantly improved model fit at Model 3 relative to Model 2 [$\chi^2(1) = 28.59$, $p < .001$]. Model 3 yielded a significant main effect of seasonal beliefs on SIGH-SAD [$F(1, 123.18) = 21.58$, $p < .001$, a significant interaction of SBQ by season [$F(1, 91.73) = 11.82$, $p = .002$], and Model 4 revealed a significant 3-way interaction of seasonal beliefs

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by patient status [$F(1, 94.63) = 4.93$, $p = .043$]. The 3-way interaction was interpreted despite best fit in Model 3 due to possible power confounds. The interaction indicated differential seasonal variation in the effect of SBQ on depression between patients and controls. The simple slopes analysis revealed that SBQ was a significant predictor of BDI-II score for patients, in winter [$b = .03$, $SE = .01$), $t = 5.00$, $p < .001$], but not summer ($p = .162$). The pattern was reversed for controls, for which there was a significant effect of SBQ on BDI-II in summer only [$b = .03$, $SE = .01$, $t = 2.81$, $p < .001$], but not winter ($p = .070$). Pairwise comparisons of slopes indicated that the difference between summer and winter slopes was significant for patients [$b = -.04$, $SE = .01$, $p = .001$], but not controls ($p = .548$). Figure 18 presents a graphical display of the interaction effect. See Table 21 for LMM results of SBQ on SIGH-SAD (SQRT).

The BDI-II models for the SBQ yielded a significantly improved model fit at Model 1 [$\chi^2(1) = 28.59$, $p < .001$]. Model 1 yielded a significant main effect of SBQ [$F(1, 124.96) = 22.17$, $p < .001$], indicating that greater endorsement of rigid seasonal beliefs predicted greater levels of depression per the BDI-II, collapsing across groups and seasons ($b = .02$, $SE = .004$). See Table 22 for the LMM results of SBQ on BDI-II (SQRT).

Chronobiological Vulnerability Models.

PAD. The LMM analyses examining the effects of PAD on SIGH-SAD (SQRT) yielded an improved fit with Model 1 [$\chi^2(1) = 14.81$, $p < .001$]. However, there were not significant effects of PAD on SIGH-SAD detected across the models, *ns*.

The BDI-II model series for PAD retained the significant effects for season and the interaction of patient status by season. Model 1 significantly improved model fit

beyond the BDI-II (SQRT) base model, $[\chi^2(1) = 11.93, p = .002]$. However, PAD was not a significant predictor of BDI-II scores, as evidenced by nonsignificant effects across all models. See Table 24 for LMM results for PAD on BDI (SQRT).

PAD-6. The SIGH-SAD analysis for PAD-6 revealed significant improved fit at Model 1 $[\chi^2(1) = 16.10, p < .001]$. The models did not reveal significant effects for PAD-6 as a predictor of SIGH-SAD scores, *ns*. See Table 25 for the LMM results of PAD-6 on SIGH-SAD.

Of the BDI-II analyses for PAD-6, Model 1 yielded the best fit relative to the base model $[\chi^2(1) = 12.20, p = .001]$. However, none of the models yielded significant main effects of PAD-6, or interactions of PAD-6 by patient status or season on BDI-II scores. Table 26 presents the LMM results for PAD-6 on BDI-II (SQRT). Taken together, these null findings do not support the role of season variation in PAD or PAD-6 as predictive of SAD severity. Limitations and implications are addressed, below.

CHAPTER 5: Discussion

The current study aimed to extend the current literature in the field of SAD by investigating the presence and prominence of proposed chronobiological and cognitive vulnerabilities to inform a more comprehensive understanding of seasonal depression. The state of the current literature presents a paucity of direct evidence implicating chronobiological vulnerabilities in SAD. The majority of available evidence indirectly infers a chronobiological mechanism based on the efficacy of light therapy as a SAD treatment. A greater limitation of the literature, and one that this study intended to address, is the disparateness of studies examining chronobiological and cognitive vulnerabilities despite evidence implicating both vulnerabilities in SAD. In favor of integrating evidence across the disciplines of clinical psychology and chronobiology, the current project aimed to compare patterns of chronobiological and cognitive vulnerabilities across the summer and winter between SAD patients and never-depressed controls to determine the distinct effects in SAD. A secondary aim was to examine the respective effects of these vulnerabilities in prediction of seasonal depression. To achieve these aims, the project enrolled a group of SAD patients and never-depressed controls to complete cognitive vulnerability questionnaires and collect saliva data to test chronobiological biomarkers once during summer, when SAD patients are characteristically euthymic, and once during winter, when SAD patients are significantly depressed. The timing of assessments were confined to summer and winter to capture the presence and absence of a depressive episode in the SAD group. The study design served as a stringent test of the between-groups differences in vulnerabilities and the within-

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subjects change in vulnerability across the change in seasons (i.e., a proxy for mood state in SAD).

Aim 1: **To test whether SAD patients and controls differ in the seasonal change of the chronobiological and cognitive vulnerabilities**.

Hypothesis 1: SAD patients will show a greater degree of seasonal change in PAD from summer to winter than controls, with a mean shortening of PAD in winter relative to summer, indicative of a phase delay. This group effect would suggest a seasonal circadian misalignment may be characteristic of SAD.

Prior to examining PAD, the timing of midsleep and DLMO were examined. Regarding midsleep times, the model did not reveal significant difference in midsleep timing across seasons, or significant variation in midsleep between groups. Midsleep timing in the sample was significantly influenced by age, with older age associated with earlier midsleep times. This effect is consistently supported in the literature and is regarded as established, as recently reviewed by Adan et al. (2012). Of note, age-related advances in sleep timing (i.e., sleep/wake cycle) are not reflective of shifts in circadian functioning or diurnal preference (Duffy & Czeisler, 2002). In the current sample, Burlington participants exhibited later midsleep times than Pittsburgh participants. Similarly, the Burlington sample yielded earlier DLMOs in both summer and winter. The summer DLMOs collected in Burlington were an average of 36.5 minutes earlier than those collected in Pittsburgh, a difference on par with the documented difference (37 minutes) between laboratory (i.e., Pittsburgh) and at-home (i.e., Burlington) salivary DLMO collection methods (Pullman, Roepke, & Duffy, 2012). DLMOs collected in winter were even more discrepant by site in timing, with an average difference of 49.5

minutes. The increased magnitude of the site difference in DLMO at winter is likely due to the combined effects of these sampling method differences as well as shorter winter photoperiod in Vermont. Later midsleep and earlier DLMO timing in Vermont resulted in longer observed PAD in the Burlington sample relative to Pittsburgh, collapsing across seasons. This direction is consistent with the expected effects of latitude and sampling method.

The findings of the current study do not support distinct circadian misalignment in PAD as proposed by the Phase Shift Hypothesis (PSH). Even after removal of an influential outlier masking significant main effects of season and patient status, the effects were inconsistent with the PSH. As a whole, the sample exhibited an average lengthening of PAD in winter relative to summer, with an average difference of 25 minutes longer PAD in winter. Further, the main effect of patient status revealed that controls in the current sample averaged longer PADs than patients, with an average PAD difference of 38 minutes longer in controls. Rather, $n = 19$ (61.3%) of SAD patients exhibited a phase advance in winter relative to summer. This is near opposite that reported in the literature, whereby an estimated minority 1/3 of SAD patients were predicted to phase advance, rather than delay, in winter (Lewy et al., 2006). The control group exhibited a more balanced directions of shift, with $n = 18$ (54.5%) exhibiting a phase advance. It should be noted that although the PSH posits that phase delays are more common in SAD, comparison of mean seasonal shift in PAD across individuals is not an ideal measure to examine abnormality of circadian functioning due to the inter-individual individual variability in intrinsic period length (i.e., cancelling out abnormal phase advances and delays), as exhibited by opposing directions of shift. However, these effects

were tested to examine whether the SAD patients averaged more delay than controls in winter regardless of some variability. This sample exhibited more variability in direction of seasonal shift in patients than has been documented in the prior literature, highlighting important variability within the SAD population. The current findings did not support the PSH, as patients did not exhibit unique phase delays in winter, relative to summer. In contrast, patients and controls did not differ on PAD in either season. Although this data cannot determine whether a pathophysiologic phase delay possibly occurs for SAD patients outside of this sample. As the first test of seasonal shift in PAD in SAD, the effects ought to be retested. However, the proposed PSH winter delay was not observed within this sample of SAD patients.

Hypothesis 2: SAD patients will exhibit comparable deviation from PAD-6 to controls in summer, and greater deviation from PAD-6 than controls in winter. A greater deviation from PAD-6 in winter among patients than controls would suggest a circadian misalignment in winter in SAD.

As a more robust test of the PSH, the absolute deviation from PAD-6 (hrs.) was calculated for PAD in summer and winter. PAD-6 has been associated with near 24-hour circadian oscillation and a naturally entrained circadian phase, as well maximum response to light therapy in winter in SAD (Burgess et al., 2004; Duffy et al., 2001; Lewy et al., 2006). Contrary to the hypothesized effects, the results did not yield significant effects of season, or an interaction of season and group. There was a significant effect of patient status in the opposite direction of the PSH, whereby controls exhibited greater mean deviation from PAD-6 than patients. This finding is inconsistent with SAD theory positing closer proximity to PAD-6 as related to antidepressant response to light therapy

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in SAD, as well as prior theory and findings that PAD-6 is associated with stable circadian entrainment (Duffy et al., 2001). In the current sample, there was also a significant covariate effect of MEQ, whereby morningness was related to increased deviation from PAD-6. This sample of SAD patients averaged intermediate chronotype, or "neither type," rather than the typical "evening type" (Murray, Allen, & Trinder, 2003), whereas the controls averaged moderate morning type. The between-groups discrepancies in morningness-eveningness and deviation from PAD-6 are consistent with the literature that associates more extreme chronotypes with greater degrees of phase shift due to intrinsic periods that are longer or shorter than 24 hrs (Duffy & Czeisler, 2002; Emens et al., 2009; Wright et al., 2005). Thus, in this sample, a greater degree of deviation from PAD-6 in controls may reflect a greater departure from a 24 hr circadian period, as indicated by their moderate morningness. Given that prior reports of SAD patients show significant departures from PAD-6 in winter (Burgess et al., 2004; Lewy et al., 2006), the present finding of greater deviation in controls, may be confounded by group differences in chronotype. The current inverse finding also brings to light the importance of matching controls and patients on chronotype for an accurate comparison of true circadian misalignment, by controlling for inter-individual variability in phase angle due to individual variation in intrinsic period length. Targeted recruitment of SAD patients who identify as evening-types may ensure enrollment of patients with longer intrinsic periods, which is consistent with delayed sleep phase syndrome in SAD (Lee, Rex, Nievergelt, Kelsoe, & Kripke, 2011). These patients may be more prone to exhibit significant phase delays from summer to winter, and may be the desired sample to examine whether abnormal seasonal phase delays are associated with greater depression

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for some SAD patients. Similarly, enrolling patients with more extreme morningness may also allow more adequate testing of whether significant seasonal circadian phase advances are truly associated with SAD in a minority subset of SAD patients, as proposed by Lewy et al. (2006). Additionally, the current sample supports the variability of PAD-6 within the SAD group (i.e., the minimal deviation of PAD-6 during winter depression, at least in some SAD patients), as consistent with the Burgess et al. (2004) finding that 46% of the SAD patient sample exhibited a healthy phase angle at baseline of light therapy, during a full Major Depressive Episode. Taken together, these findings indicate that significant circadian misalignment is not a necessary condition for SAD recurrence.

Hypothesis 3: SAD patients will endorse higher brooding rumination than controls at both summer and winter assessments.

The current study tested whether brooding rumination, a maladaptive subtype of rumination closely linked to depression severity and relapse, was also a correlate of SAD. To date, there has been one prior study examining brooding rumination in SAD. Enggasser and Young (2007) reported that trait brooding rumination endorsed during summer remission was prospectively predictive of depression severity the following winter. However, no published study to date had yet examined whether SAD patients endorsed a distinctive tendency to brood in response to sad mood relative to never-depressed controls. This was Aim 1 of the current study. The hypothesized effect was that SAD patients would endorse higher brooding rumination than controls at both summer and winter assessments, indicating a trait tendency to ruminate, and specifically, brood (i.e., dwell on the causes, consequences, and symptoms associated with sad mood) when

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sad. The results of the current study support the hypothesis that brooding rumination is distinct in SAD, as patients endorsed elevated brooding rumination in summer and winter as compared to controls. The residual elevation in brooding rumination in SAD during remission may reflect habitual learning, based on their history of depression and the strengthening of brooding rumination as habit over the course of depressive episodes (e.g., more opportunities to brood with more frequent depressive symptoms). Contrary to the hypothesis, SAD patients also endorsed significant seasonal variation in brooding rumination, with an greater endorsed tendency to brood in response to sad mood during depression in winter, relative to remission in summer. This effect was not observed in controls. The Response Styles Theory posits rumination as a trait tendency to ruminate in response to sad mood (Nolen Hoeksema & Morrow, 1991), with documented stability of rumination over time (Smith & Alloy, 2009). This trait tendency has been characterized by a tendency to engage in rumination in the presence of, or after exposure to, a traumatic or psychosocial stressor, whereby rumination is considered a reactive response. In addition to demonstrating that brooding rumination magnitude is distinct in SAD, the current study provided preliminary evidence highlighting that SAD patients exhibit significant seasonal fluctuation of brooding rumination relative to controls.

Within the current sample, the same pattern of results was found for the broader construct of ruminative response style (Nolen-Hoeksema & Morrow, 1991), as measured by the total Rumination subscale score on the Ruminative Response Scale (RRS). Patients did not endorse the expected stability of a ruminative tendency across time, but endorsed increased tendency to ruminate in response to sad mood, when feeling sad in winter, relative to summer. Taken together, the findings of brooding rumination and more

general rumination, may indicate that a tendency to ruminate or brood in response to sad mood remains a latent vulnerability year-round in SAD, but that it is the fluctuation that occurs within the context of seasonal depression that most strongly predicts concurrent depression severity. These findings support the implication that these styles of maladaptive coping (i.e., brooding and rumination) may intensify with SAD episodes and remain activated to a lesser degree year-round in SAD. The extensive literature on brooding rumination in nonseasonal depression has found brooding rumination to be associated with increased depression and related vulnerabilities (i.e., rejection sensitivity, intrapersonal submissiveness, and increased suicidal ideation; Moberly & Watkins, 2008; Pearson, Watkins, Mullan, & Moberly, 2010; Siegle, Moore, & Thase, 2004; Treynor, Gonzalez, & Nolen-Hoeksema, 2003). Whether these vulnerabilities are associated with brooding among SAD patients remains unknown.

Hypothesis 4: SAD patients will exhibit greater cognitive reactivity (i.e., an increase in endorsed dysfunctional attitudes across a negative mood induction) in summer than controls.

In Beck's cognitive theory, sad mood induction replicates stress, under which activation of negative core schema and negative core beliefs are activated. Beck's cognitive theory has been supported by the findings that remitted non-seasonally depressed individuals exhibit greater cognitive reactivity than never-depressed controls (Gemar, Segal, Sagrati, & Kennedy, 2001), and cognitive reactivity has also been found to mediate the relationship between neuroticism and depression severity in nonseasonally depressed patients (Barnhofer & Chittka, 2009; Segal, Kennedy, Gemar, Hood, Pedersen, & Buis, 2006). To date, only one published study had examined cognitive reactivity in

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SAD (Enggasser and Young, 2007), and found evidence for significant cognitive reactivity in SAD. The current study was the first study to compare SAD patients and controls on cognitive reactivity and found SAD patients to exhibit a distinct increase in dysfunctional attitudes in response to a negative mood induction. In contrast, never-depressed controls did not exhibit significant cognitive reactivity, despite endorsing increased sad mood to the mood induction.

Hypothesis 5: SAD patients will endorse more dysfunctional attitudes than controls at winter, but the groups will not differ at summer. This finding would suggest that SAD patients hold more rigid depressive attitudes than controls only when they are depressed.

The current study replicated this effect in SAD. SAD patients in the current study endorsed higher dysfunctional attitudes in winter relative to summer. Additionally, patients endorsed greater dysfunctional attitudes relative to controls in both summer, when remitted, and in winter when depressed, although the between-groups difference was greater in winter. These findings indicate significant seasonal variation in DAS, as consistent with Beck's cognitive theory proposing that increased activation of negative self-schema in response to depression is a vulnerability of recurrent depression. Taken together with prior literature, this pattern of mood suggests state-dependent endorsement of dysfunctional attitudes are distinct in SAD relative to never-depressed controls (Golden, Dalgleish, & Spinks, 2006; Hodges & Marks, 1998; Rohan et al., 2003), and that DAS scores wax and wane with SAD episodes (Hodges & Marks, 1998). Of importance, the current findings also highlight residual elevation of dysfunctional attitudes during remission in summer between SAD episodes indicating that the

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vulnerability is not entirely latent in nature. These findings further support dysfunctional attitudes as a cognitive vulnerability to nonseasonal depression appears to generalize to seasonal depression.

Hypothesis 6. SAD patients will endorse more rigid seasonal beliefs than controls at both summer and winter assessments. This consistent group difference across time would reflect a greater trait tendency for patients to endorse rigid beliefs about seasons and light year-round, relative to controls.

As a potentially SAD-specific cognitive vulnerability, the study provided a novel test of the Seasonal Beliefs Questionnaire (SBQ) between patients and controls. Relative to other cognitive measures designed for SAD such as the Seasonal Attitudes Scale, the SBQ was designed as a measure of rigid beliefs about the seasons and light that is less confounded with SAD symptoms (Rohan, Nillni, Lippy, Roecklein, & Hillhouse, 2007). In support of the hypothesis, the current study found a significant effect of patient status, whereby SAD patients endorsed significantly greater seasonal beliefs across both seasons than controls. Both patients and controls endorsed higher SBQ scores in the winter than in the summer, suggesting that seasonal beliefs may be more activated within the environmental conditions of winter for humans living at latitudes with significant seasonal climate fluctuations. Unlike the DAS which waxes and wanes with episodes nonseasonal depression as well as SAD (i.e., mood state-like), seasonal beliefs assessed by the SBQ were proposed to be trait-like across the seasons. The seasonal variation indicates that these beliefs are not entirely static across seasons; yet SAD patients maintained consistently higher levels of seasonal beliefs year-round relative to controls, indicating some chronicity in the vulnerability across the year. The sustained elevation of

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seasonal beliefs in patients relative to controls may be reflective of reinforcement of these beliefs both in and out of a SAD episode. SBQ items reflect the assumptions that mood is contingent on season and lighting conditions, and that the likelihood of reinforcement depends on current context of seasonal conditions. For example, the SBQ belief, "I need sunshine to be happy," is likely reinforced for patients during the longer photoperiod in summer, when euthymic, albeit not as much, as well as during the shorter photoperiod of winter, when depressed. In contrast, it makes intuitive sense that endorsement of DAS items such as, "If I do not do well all the time, people will not respect me" and "If others dislike you, you cannot be happy" would escalate within the context of depression, but return to normative levels when euthymic. Given the large effect size between patients and controls in the endorsement of SBQ beliefs, these findings further support the SBQ as a valid measure for SAD-specific rigid beliefs about the seasons and light, which are specifically targeted in CBT for SAD.

Aim 2: **To test the predictive effects of these group differences in cognitive and chronobiological vulnerabilities on seasonal change in depression severity.**

Hypothesis 7: the between-group effects of the vulnerabilities will account for variance in depression severity, above and beyond the unique effects of group and the chronobiological and cognitive predictors.

Chronobiological Vulnerabilities. Contrary to expectation, the current study did not find predictive effects of PAD or deviation from PAD-6 on BDI-II or SIGH-SAD scores. The current study examined whether PAD, or absolute deviation from PAD-6, was associated with mood state across seasons in patients. PAD did not yield significant correlations or predictive relations to depression severity per the BDI-II or SIGH-SAD at

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summer or winter. Due to the variability in direction of circadian shift in the measure of PAD, absolute deviation from PAD-6 was examined as a fixed factor on depression severity. PAD-6 has been proposed as the optimal PAD (i.e., DLMO to midsleep) in humans, based on evidence that PAD-6 is associated with an intrinsic period close to 24 hrs and natural entrainment in healthy adults (Duffy, Rimmer, & Czeisler, 2001). Additionally, two SAD studies to date have provided indirect evidence implicating deviation from PAD-6 (or equivalent) as a vulnerability in SAD (Burgess et al., 2004; Lewy et al., 2006) based on the observation that reduced deviation from PAD-6 after light therapy was associated with better treatment response in 75% of patients. In the current study, PAD-6 was inversely correlated with BDI-II depression severity in winter, indicating greater PAD-6 deviation in controls. This evidence is in opposition of the hypothesis and suggests that deviation from PAD-6 is not exclusive to SAD. The minimal observed deviation from PAD-6 in the SAD group also highlights variability within the SAD population regarding this proposed vulnerability. This is consistent, however, with the prior report by Burgess et al. (2004) that a significant minority (46%) had exhibited healthy phase angles (within 1 *SD* of PAD-6) at pretreatment, when clinically depressed. Taken together, the results from the current study suggest that deviation from PAD-6 is not a necessary or exclusive condition of SAD. Given the limited number of studies examining PAD and PAD-6 in SAD, it remains unknown whether these samples of patients are representative of the broader SAD population. One interesting finding is that the SAD patients did not exhibit the distinct eveningness characteristic of SAD. PAD-6 was associated with morningness, as consistent with prior reports that morningness is associated with longer phase angles (Emens et al., 2009). Consistent with the effect of

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chronotype on phase shift, phase delays would be expected by individuals with more evening-type chronotype. Therefore, the effect may not have been applicable in this sample of patients with intermediate chronotype. The question remains whether the influence of circadian misalignment in SAD varies by chronotype. To explore this effect, future studies ought to aim to recruit patients and controls, matched across a broad range of chronotype in order to clarify potential circadian variability and vulnerability in SAD.

Cognitive Vulnerabilities. The current study examined whether the between-groups effects of the cognitive vulnerabilities, as documented in Aim 1, significantly predicted between-groups differences in seasonal depression severity. The current study yielded a significant effect for dysfunctional attitudes, which revealed that more rigid dysfunctional attitudes were predictive of depression severity by patients in winter, but not in summer. Conversely, controls did not exhibit seasonal variation in the effect of dysfunctional attitudes, although dysfunctional attitudes were predictive of depression, albeit to a lesser degree, in controls year-round. The differential findings in the effect of dysfunctional attitudes on depression severity in patients and controls are consistent with the observed seasonal variation in endorsement of dysfunctional attitudes by patients only, as well as with Beck's cognitive theory which proposes that activation of negative automatic thoughts and negative core schemas within the context of stressful experience precipitates, and ultimately maintains depression severity and duration (Beck et al., 1979). For SAD patients, winter constitutes a recurrent, external stressful context. Contrary to the hypothesis and Beck's cognitive theory, the current study did not provide significant results for cognitive reactivity to a SAD mood induction as predictive of depression severity in winter despite unique cognitive reactivity exhibited by the SAD

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group. This is the second study, to date, to test an association between cognitive reactivity and winter depression severity in SAD. The first test of cognitive reactivity in SAD, Enggasser and Young (2007) also failed to find support for cognitive reactivity as predictive of SAD severity in individuals with SAD and subsyndromal SAD. Therefore, the current finding serves as replication of the prior report by Enggasser & Young (2007).

However, Enggasser and Young (2007) were also the first to test brooding subtype of rumination as predictive of SAD severity. They reported a significant effect of trait brooding (i.e., summer score) on winter depression, but a nonsignificant finding for reflective pondering, or broader rumination. Contrary to the prior report, the current study did not yield significant effects for trait brooding or rumination scores. Rather, the inclusion of the summer and winter scores, as the examination of the covariation in brooding tendency with concurrent mood state, revealed a significant main effect of brooding rumination and general ruminative response style. These findings highlight the importance of examining the magnitude of the current ruminative response, in this case, by self-report, as a vulnerability measure for current depression. Although SAD patients exhibited an elevated baseline in brooding rumination relative to controls, the seasonal variation – as additional fluctuation in rumination – was the significant predictor of depression in the current sample.

The current findings also highlight the role of specific dysfunctional attitudes regarding seasonal beliefs and depression severity. This theme of rigid negative attitudes was endorsed to a greater degree in SAD patients, relative to controls, in both summer and winter, yet both groups endorsed increased rigid seasonal beliefs in winter, within the context of the shortened photoperiod. Consistent with the hypothesis, seasonal beliefs

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uniquely predicted depression for patients in winter. The finding of residual elevation of

seasonal beliefs in summer may reflect reinforcement of rigid seasonal beliefs in summer

and winter, as they experience recurrent pairing of summer with remission and winter

with depression over the annual course of SAD recurrence. These thoughts are currently

the targets of CBT-SAD, as they are considered to maintain seasonal patterns of

experiential avoidance, behavioral disengagement, and depression in winter. The latter

association is supported by the current study, although future research should further

examine the possible influence of seasonal cognitions on behaviors across seasons in

SAD, as well.

In summary, the current study found further evidence for rumination and

dysfunctional attitudes as predictive of depression severity. Novel findings included the

documentation of elevated brooding rumination in SAD patients, relative to controls, as

well as the contribution of state brooding rumination and rumination to depression

severity. Seasonal beliefs, as measured by the SBQ, were also significantly predictive of

depression severity, indicating these beliefs are important contributors to depression in

SAD. The between-groups differences in the cognitive vulnerabilities complicated

testing the hypothesis that between-groups differences (i.e., interactions of vulnerability

by patient status) would explain additional variance in depression severity above and

beyond the main effect of patient status, or the effect of patient status and season in the

linear mixed model. It is possible that Aim 2 main effects reported above (i.e., brooding

rumination, RRS, or DAS on SIGH-SAD; or SBQ on BDI-II,) in part reflect the between-

groups differences in vulnerability across patient status groups., although this needs to be

retested in a larger sample. As a whole, the present study provides further support for

cognitive vulnerabilities are significant contributing factors to depression severity, and in this instance, SAD.

Of additional note is that rumination and brooding rumination were also predictive of depression in controls. Despite reported elevated levels of brooding relative to controls, brooding rumination was more predictive of depression in controls. This finding is contrary to the hypothesized effects, and may indicate that these vulnerabilities may be more potent for minimal levels of depression, as endorsed by the current control group. Additionally, dysfunctional attitudes were predictive of depression within the control group, to a lesser degree, year-round. These effects within the control group indicate that although cognitive vulnerabilities may be distinct in seasonal variation and potency of influence on depression in winter in SAD, non-clinically depressed individuals are not immune to the influence of cognitive vulnerabilities on mood.

Study Limitations

The current sample presented a number of noteworthy limitations. First, the absence of a third (i.e., fall) assessment precluded the examination of true individual growth curve analysis. All effects were assumed to be linear, but it is possible that the slope of change in depression or corresponding vulnerabilities may vary nonlinearly across season depending on internal (i.e., psychological) and/or external (i.e., environmental) cues for seasonal mood changes.

Second, the inclusion of Pittsburgh data was intended to increase sample size and generalizability across locations/latitude. However, the introduction of another site for the purposes of increased power introduced unbalanced sample variability. Although there were no between-site differences in age, sex, or ethnicity for the entire sample, or within

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either the patient or control groups, a greater number of controls were recruited in Pittsburgh, and a greater number of patients were recruited in Burlington. Pooling of data and condensed seasonal enrollment compromised feasibility of enrolling a truly matched sample. The current study attempted to control for sample variability within each analysis, although this does not replace true matching for the purposes of comparing magnitude of vulnerabilities.

There were significant site differences in DLMO collection methods. Pittsburgh participants completed salivary laboratory DLMO collections, whereas Burlington participants collected salivary melatonin samples at-home. Recent research suggests relative compatibility of laboratory and at-home sampling methods, yet with some difference in DLMO. The study with methods most comparable to the current study compared at-home and laboratory DLMO as collected on consecutive nights in a small sample ($n = 18$) of healthy adults with sleep complaints (Pullman, Roepke, & Duffy, 2012). Comparable to the current study, participants were provided a set of dark goggles and instructed to remain in dim light conditions from 7 hours prior, to 1 hour after, their typical bedtime. The study revealed successful detection of DLMOs using the 3 pg/ml threshold in 62% of individuals at-home, yet less than the 88% detected with laboratory collection. The DLMO times significantly correlated between laboratory and at-home collection ($r = 0.85$, $p = .0001$), yet the collection methods yielded an average difference in DLMO timing of 37 minutes (+/- 19 minutes). The success rate of at-home DLMO detection in the current study (i.e., 83.6 % in the Burlington sample) was comparable to those reported in prior studies (i.e., 76% in Keijzer, Smits, Peeters, Looman, Endenburg, Klein, 2011 and 62.5% in Pullman, Roepke, & Duffy, 2012). Laboratory DLMO

detection in the Pittsburgh sample (83.8%) was comparable to the at-home DLMO detection in the Burlington sample. Newly published research has revealed the development of a salivary collection kit with an object time stamp compliance measure for dim light and half-hourly saliva collection, which has yielded improved at-home DLMO results, with DLMO times comparable ($p < .05$) to laboratory collection (Burgess, Wyatt, Park, & Fogg, 2015). This new procedure provides promise in preserving the reliability of circadian phase detection when collected at-home. This can affect the validity of the saliva data, and may have compromised the validity of the saliva data in Burlington and/or further confounded comparison of the DLMO results. Further, the intra-assay sensitivity in the Burlington sample was below the acceptable threshold (CV: .31) indicating variability between original and duplicate samples likely due to low precision laboratory technique by study staff. This may have compromised the validity and the observance of effects in the Burlington sample. Additionally, assays conducted by SolidPhase, Inc. (Portland, ME, USA) did not include duplicates despite using the Bühlmann Direct Saliva Melatonin Radioimmunoassay kit (ALPCO Diagnostics, Windham, NH, USA). Therefore, the intra-assay sensitivity for the Pittsburgh DLMO data are unknown.

Initial study procedures for Time 1 assessment in summer and Time 2 assessment in winter were relaxed for recruitment feasibility by allowing initial enrollment of subjects in either summer or winter, introducing further sample variability in direction of observed SAD episode (i.e., summer 1st measuring SAD recurrence onset, and winter 1st measuring SAD recurrence offset). The models tested for effects of season order on patterns of vulnerabilities and depression. Of note, there were no detected effects of

season order on the magnitude of seasonal depression, on the cognitive or chronobiological vulnerabilities, or on the effects of the vulnerabilities on depression severity.

Lastly, the lack of broader variation in seasonal mood precluded examination of individual growth across seasons. Future studies ought to include broader range of variability in SAD, by perhaps including a subsyndromal-SAD (i.e., high seasonality, lower depression group), or a nonseasonally depression comparison (i.e., low seasonality, higher depression group) to examine the moderation of these vulnerabilities across depression and SAD. Further, the current sample size likely further restricted resolution of detected effects due to the number of parameters included in Aim 2 analyses. For example, controlling for the large effects of patient status, and moderate effects of patient status by season on depression severity is expected to have diminished power for detection of effects by the vulnerability covariates.

Future Directions

Cognitive Vulnerabilities. Aim 1 results replicated support for cognitive vulnerabilities to depression in SAD, for rumination on the RRS, seasonal beliefs on the SBQ, and dysfunctional attitudes on the DAS. The study provided further evidence for unique endorsement of brooding-type rumination, specifically in SAD versus controls, and new evidence for the effect of mood-state concurrent brooding and ruminative responses that predict depression severity. Future studies ought to further examine the possible role of cognitive vulnerabilities in SAD, as well as to replicate the findings of brooding rumination and seasonal beliefs in SAD. Additionally, the evidence for state rumination supports the notion of examining current ruminative behaviors, perhaps in

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response to seasonal or darkness cues, to further the theory and evidence for cognitive vulnerabilities specific to SAD. These efforts further refine our understanding of the maladaptive cognitive processes specific to SAD, and thereby identify potentially important targets to address in treatments, such as CBT-SAD.

For example, given the prominence of rumination in prediction of SAD recurrence, targeting rumination in treatment may further bolster the treatment response. Evans et al. (2013) found that SAD treatment (LT or CBT) was associated with acute reductions in negative automatic thought frequency and intensity, and ruminative tendency. However, only the reductions in the content (negative automatic thoughts) were prescriptive of reduction in SAD severity the following winter (Evans, et al., 2013). One possible explanation may be that ruminative process is not targeted directly by CBT mechanisms, whereby the reduction in rumination over the course of CBT-SAD may be a consequence, rather than a cause, of the reduction in depressive severity. Mindfulness-based cognitive therapy (MBCT) has been shown to reduce relapse in nonseasonally depressed patients with a history of 3+ major depressive episodes (Teasdale, Segal, Williams, Ridgeway, Soulsby, & Lau, 2000); and a recently published review of the mechanisms for MBCT (van der Velden et al., 2015) revealed some evidence that reduction in rumination mediated the effect of MBCT on depressive relapse. One study to date (Fleer et al., 2014) has recently pilot-tested MBCT for SAD with treatment delivered during summer remission consistent with MBCT for nonseasonal depression (Segal et al., 2012). The SAD trial did not find significant effects between MBCT and wait-list control (Fleer et al., 2014). However, it remains to be tested whether the application of

mindfulness component to CBT-SAD delivered in winter, and targeted at rumination in response to seasonal cues may further buffer SAD recurrence.

Chronobiological Vulnerabilities. The most important implication of these findings for future studies examining chronobiological vulnerabilities between SAD patients and controls is the demonstrated need to control for diurnal preference, or intrinsic period, when comparing phase angle difference or deviation from PAD-6 across SAD patients and controls. There is extensive evidence linking diurnal preference, and intrinsic period, to phase angle of entrainment. Morningness, or shorter intrinsic periods are associated with longer phase angle differences (i.e., a longer interval between melatonin release and sleep; Duffy, Dijk, Hall, & Czeisler, 1999; Duffy, Rimmer, & Czeisler, 2001; Mongrain, Lavoie, Selmaoui, Paquet, & Dumont, 2004). Controlling for either intrinsic period, or the related behavioral trait, diurnal preference, by group matching would improve accuracy of the between-groups comparison to determine whether abnormal phase angle entrainment is truly indicative of SAD, rather than confounded by natural individual variability in intrinsic period. Given that the current sample was uniquely morning-type relative to other SAD samples (Lee, Rex, Nievergelt, Kelsoe, & Kripke, 2011), it remains unclear whether SAD patients who endorse greater eveningness, and more intrinsic circadian delays, may also exhibit abnormal deviation from PAD-6.

A second implication, in the context of null findings for PAD abnormalities in SAD, is the need to include multiple markers of possible chronobiological vulnerabilities to balance the model that includes multiple measures of cognitive vulnerability. This study served as a further step in refining the proposed vulnerabilities; however, the field

is still in the exploratory phase in determining potential circadian biomarkers of SAD. For example, there is recent research supporting aberrant pupillary response in SAD, as assessed by the post illumination pupil response (PIPR; Roecklein, et al., 2013). This study provided preliminary evidence to suggest that SAD may involve deficient retinal response to low light levels in winter, as observed in SAD patients, but not in never-depressed controls. These findings suggest that some SAD patients may have low light intake in winter, which may affect the circadian photoentrainment and melatonin release in winter. However, the influence of these effects on annual SAD recurrence remains unknown.

Integrative Chronobiological-Cognitive Model. Future research should also test the integrative model of SAD with a larger sample to adequately power examination of the relative, and possible interactive, effects of chronobiological and cognitive vulnerabilities in SAD within one model to further our understanding of the maintenance mechanisms in SAD. Ultimately, this research could explore the possible heterogeneity in profiles of chronobiological and cognitive risk factors in SAD (i.e., whether some load higher on one type of vulnerability over another, versus the combination). Doing so may improve precision of SAD assessment, and treatment referral for appropriate treatment (i.e., light therapy vs. CBT- SAD) matched to prominent underlying vulnerabilities (e.g., light therapy for pronounced circadian misalignment; CBT-SAD for prominent cognitive vulnerability), consistent with personalized medicine.

Conclusions

The current study served as a first test of the chronobiological and cognitive components in the integrative chronobioloigcal-cognitive model of SAD. Findings

supported that SAD patients could be distinguished from controls on the basis of several cognitive vulnerabilities (ruminative response style, brooding, seasonal beliefs, cognitive reactivity, and dysfunctional attitudes). The reported effects replicate prior findings on rumination and dysfunctional attitudes, and newly implicate brooding rumination, cognitive reactivity, and seasonal beliefs as characteristic of SAD relative to controls. Vulnerabilities that vary across seasons (i.e., rumination, dysfunctional attitudes, and seasonal beliefs) were more strongly related to depression severity than proposed latent (i.e., cognitive reactivity), or trait (i.e., residual ruminative tendency during summer remission) vulnerabilities. The patterns of effects in the current study highlight the importance of measuring concurrent vulnerabilities with the seasonal variation in SAD severity to fully capture the resolution of season-varying vulnerability effects. Understanding the dynamic interplay between vulnerabilities and depression severity across seasons in SAD may ultimately improve SAD assessment and treatment. The current findings suggest that these maladaptive cognitive constructs and processes vary in magnitude and potency for SAD over the annual course of seasonal change.

Contrary to the hypothesized effects, and despite the observed distinct cognitive reactivity in SAD patients, cognitive reactivity did not predict SAD severity in the current sample. This is the second study to date to report a null relationship between cognitive reactivity to an induced negative mood and seasonal depression. Additionally, the current results were inconclusive regarding a seasonal circadian phase misalignment as a vulnerability for SAD. The variability in the sample regarding chronotype and assay sensitivity limited the generalizability of these findings. Although the present results did not support the phase shift hypothesis, more stringent tests are needed. Of importance, the

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current sample further indicates the importance of controlling for confounding influence of chronotype when investigating the presence of abnormal circadian functioning in SAD versus healthy controls.

As the chronobiological and cognitive vulnerabilities continue to be refined, subsequent tests of an integrative chronobiological- or physiological-cognitive model for SAD should continue to be explored. Furthered understanding of the interplay between cognitive-behavioral and chronobiological vulnerabilities to SAD may lead allow better informed treatment referrals (i.e., light therapy or CBT-SAD) based on the prominent underlying vulnerabilities of the SAD patient, and ultimately improve treatment for SAD.

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APPENDIX A

Subject ID # _____   Date_____

Ruminative Response Scale

People think and do many different things when they feel depressed. Please read each of the items below and indicate whether you never, sometimes, often, or always think or do each one when you feel down, sad, or depressed. Please indicate what you <u>generally</u> do, not what you think you should do.

0	1	2	3
Almost Never	Sometimes	Often	Almost Always

_____ 1. Think about how alone you feel.

_____ 2. Think "I won't be able to do my job/work if I don't snap out of this."

_____ 3. Think about your feelings of fatigue and achiness.

_____ 4. Think about how hard it is to concentrate.

_____ 5. Think "What am I doing to deserve this."

_____ 6. Think about how passive and unmotivated you feel.

_____ 7. Analyze recent events to try to understand why you are depressed.

_____ 8. Think about how you don't seem to feel anything anymore.

_____ 9. Think "Why can't I get going."

_____ 10. Think "Why do I always react this way."

_____ 11. Go away by yourself and think about why you feel this way.

_____ 12. Write down what you are thinking and analyze it.

_____ 13. Think about a recent situation, wishing it had gone better.

_____ 14. Think "I won't be able to concentrate if I keep feeling this way."

_____ 15. Think "Why do I have problems other people don't have?"

_____ 16. Think "Why can't I handle things better?"

_____ 17. Think about how sad you feel.

_____ 18. Think about all your shortcomings, failings, faults, mistakes.

_____ 19. Think about how you don't feel up to doing anything.

_____ 20. Analyze your personality to try to understand why you are depressed

____ 21. Go someplace alone to think about your feelings.

_____ 22. Think about how angry you are with yourself.

APPENDIX B

DAS – Form A

Subject ID # _____   Date _____

This inventory lists different attitudes or beliefs which people sometimes hold. Read <u>EACH</u> statement carefully and decide how much you agree or disagree with the statement.

For each of the attitudes, show your answer by placing a checkmark under the column that BEST DESCRIBES HOW YOU THINK. Be sure to choose only one answer for each attitude. Because people are different, there is no right answer or wrong answer to these statements.

To decide whether a given attitude is typical of your way of looking at things, simply keep in mind what you are like MOST OF THE TIME.

Remember that your answers should describe the way you think MOST OF THE TIME.

ATTITUDES	TOTALLY AGREE	AGREE VERY MUCH	AGREE SLIGHTLY	NEUTRAL	DISAGREE SLIGHTLY	DISAGREE VERY MUCH	TOTALLY DISAGREE
1. It is difficult to be happy unless one is good looking, intelligent, rich, and creative.							
2. Happiness is more a matter of my attitude towards myself than the way other people feel about me.							
3. People will probably think less of me if I make a mistake.							
4. If I do not do well all the time, people will not respect me.							

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ATTITUDES	TOTALLY AGREE	AGREE VERY MUCH	AGREE SLIGHTLY	NEUTRAL	DISAGREE SLIGHTLY	DISAGREE VERY MUCH	TOTALLY DISAGREE
5. Taking even a small risk is foolish because the loss is likely to be a disaster.							
6. It is possible to gain another person's respect without being especially talented at anything.							
7. I cannot be happy unless most people I know admire me.							
8. If a person asks for help, it is a sign of weakness.							
9. If I do not do as well as other people, it means I am an inferior person.							
10. If I fail at my work, then I am a failure as a person.							
11. If you cannot do something well, there is little point in doing it at all.							
12. Making mistakes is fine because I can learn from them.							
13. If someone disagrees with me, it probably indicates that he does not like me.							
14. If I fail partly, it is as bad as being a complete failure.							
15. If other people know what you are really like they will think less of you.							

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ATTITUDES	TOTALLY AGREE	AGREE VERY MUCH	AGREE SLIGHTLY	NEUTRAL	DISAGREE SLIGHTLY	DISAGREE VERY MUCH	TOTALLY DISAGREE
16. I am nothing if a person I love doesn't love me.							
17. One can get pleasure from an activity regardless of the end result.							
18. People should have a reasonable likelihood of success before undertaking anything.							
19. My value depends greatly on what others think of me.							
20. If I don't set the highest standards for myself, I am likely to end up a second rate person.							
21. If I am to be a worthwhile person, I must be truly outstanding in one major respect.							
22. People who have good ideas are more worthy than those who do not.							
23. I should be upset if I make a mistake.							
24. My own opinions of myself are more important than others' opinions of me.							

ATTITUDES	TOTALLY AGREE	AGREE VERY MUCH	AGREE SLIGHTLY	NEUTRAL	DISAGREE SLIGHTLY	DISAGREE VERY MUCH	TOTALLY DISAGREE
25. To be a good, moral, worthwhile person, I must help everyone who needs it.							
26. If I ask a question, it makes me look inferior.							
27. It is awful to be disapproved of by people important to you.							
28. If you don't have other people to lean on, you are bound to be sad.							
29. I can reach important goals without slave driving myself.							
30. It is possible for a person to be scolded and not get upset.							
31. I cannot trust other people because they might be cruel to me.							
32. If others dislike you, you cannot be happy.							
33. It is best to give up your own interests in order to please people.							
34. My happiness depends more on other people than it does on me.							

ATTITUDES	TOTALLY AGREE	AGREE VERY MUCH	AGREE SLIGHTLY	NEUTRAL	DISAGREE SLIGHTLY	DISAGREE VERY MUCH	TOTALLY DISAGREE
36. If a person avoids problems, the problem tends to go away.							
37. I can be happy even if I miss out on many of the good things in life.							
38. What other people think about me is important.							
39. Being isolated from others is bound to lead to unhappiness.							
40. I can find happiness without being loved by another person.							

DAS – Form B

Subject ID # _____   Date _____

This inventory lists different attitudes or beliefs which people sometimes hold. Read EACH statement carefully and decide how much you agree or disagree with the statement.

For each of the attitudes, show your answer by placing a checkmark under the column that BEST DESCRIBES HOW YOU THINK. Be sure to choose only one answer for each attitude. Because people are different, there is no right answer or wrong answer to these statements.

To decide whether a given attitude is typical of your way of looking at things, simply keep in mind what you are like MOST OF THE TIME.

Remember that your answers should describe the way you think MOST OF THE TIME.

ATTITUDES	TOTALLY AGREE	AGREE VERY MUCH	AGREE SLIGHTLY	NEUTRAL	DISAGREE SLIGHTLY	DISAGREE VERY MUCH	TOTALLY DISAGREE
1. You can be a happy person without going out of your way in order to please other people.							
2. I have to impress new acquaintances with my charm, intelligence, or wit or they won't like me.							
3. If I put other people's needs before my own, they should help me when I want them to do something for me.							
4. It is shameful for a person to display his weaknesses.							

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ATTITUDES	TOTALLY AGREE	AGREE VERY MUCH	AGREE SLIGHTLY	NEUTRAL	DISAGREE SLIGHTLY	DISAREE VERY MUCH	TTALLY DISAGREE
5. People will like me even if I am not successful.							
6. People who have the marks of success (good looks, fame, wealth) are bound to be happier than people who do not.							
7. I should try to impress other people if I want them to like me.							
8. If a person I love does not love me, it means I am unlovable.							
9. I ought to be able to solve my problems quickly and without a great deal of effort.							
10. If a person is indifferent to mean, it means he does not like me.							
11. I should be able to please everybody.							
12. Others can care for me even if they know all my weaknesses.							
13. If people whom I care about do not care for me, it is awful.							
14. Criticism need not upset the person who receives the criticism.							
15. My life is wasted unless I am a success.							

ATTITUDES	TOTALLY AGREE	AGREE VERY MUCH	AGREE SLIGHTLY	NEUTRAL	DISAGREE SLIGHTLY	DISAGREE VERY MUCH	TOTALLY DISAGREE
16. People should prepare for the worst or they will be disappointed.							
17. I must be a useful, productive, creative person or life has no purpose.							
18. A person should think less of himself if other people do not accept him.							
19. I do not need other people's approval for me to be happy.							
20. I can enjoy myself even when others do not like me.							
21. My value as a person depends greatly on what others think of me.							
22. If I make a foolish statement it means I am a foolish person.							
23. If a person has to be alone for a long period of time, it follows that he has to feel lonely.							
24. A person should be able to control what happens to him.							

ATTITUDES	TOTALLY AGREE	AGREE VERY MUCH	AGREE SLIGHTLY	NEUTRAL	DISAGREE SLIGHTLY	DISAGREE VERY MUCH	TOTALLY DISAGREE
25. If a person is not a success, then his life is meaningless.							
26. A person doesn't need to be well liked in order to be happy.							
26. A person doesn't need to be well liked in order to be happy.							
27. If someone performs a selfish act, this means he is a selfish person.							
28. I should always have complete control over my feelings.							
29. I should be happy all the time.							
30. If people consider me unattractive it need not upset me.							
31. Whenever I take a chance or risk I am only looking for trouble.							
32. A person cannot change his emotional reactions even if he knows they are harmful to him.							

ATTITUDES	TOTALLY AGREE	AGREE VERY MUCH	AGREE SLIGHTLY	NEUTRAL	DISAGREE SLIGHTLY	DISAGREE VERY MUCH	TOTALLY DISAGREE
33. I may be able to influence other people's behaviour but I cannot control it.							
34. People will reject you if they know your weaknesses.							
35. People should be criticized for their mistakes.							
36. One should look for a practical solution to problems rather than a perfect solution.							
37. If I do well, it is probably due to chance; if I do badly, it is probably my own fault.							
38. The way to get people to like you is to impress them with your personality.							
39. Turning to someone else for advice or help is an admission of weakness.							
40. A person should do well at everything he undertakes.							

Seasonal Beliefs Questionnaire

Subject ID # _____   Date_____

<u>Directions</u>: Below is a list of <u>thoughts, attitudes, and beliefs about the seasons</u> that people might have. Please read each statement carefully and decide how much you agree or disagree with it. For each item, write the number that corresponds to how much you agree or disagree with that statement in the blank space in front of it. Answer each statement based on HOW YOU GENERALLY THINK.

1	2	3	4	5	6	7
Totally Disagre	Disagree Very Much	Disagree Slightly	Neutral	Agree Slightly	Agree Very Much	Totally Agree

___ 1. Winter is the best season of the year.

___ 2. I can't be productive on dark, dreary days.

___ 3. Dark, gloomy days are depressing.

___ 4. I look forward to winter.

___ 5. Everything is easier in the summertime.

___ 6. I don't pay much attention to the changing seasons.

___ 7. Spring is no better than any other season.

___ 8. It's difficult to feel good on dark, dreary days.

___ 9. I'm in a fog all winter long.

___ 10. It's hard to get up in the dark.

___ 11. I love winter.

___ 12. Sunlight doesn't affect my mood.

___ 13. There's something wrong with me in the winter.

___ 14. All is well if the sun is shining.

___ 15. I don't expect much of myself in the winter.

___ 16. Dark, dreary days exhaust me.

___ 17. I can't seem to get going on dark, dreary mornings.

___ 18. I'm a failure in the winter.

___ 19. I welcome cold winter days.

___ 20. I'm stuck in a rut in the winter.

___ 21. How I feel is irrelevant to the weather.

___ 22. I am going to have the winter blues every year.

___ 23. I'm not a winter person.

___ 24. I'm always happier when it's warmer.

___ 25. I can't snap out of my winter funk.

___ 26. I'm ineffective in the winter.

APPENDIX D

Daily Diary Form

Subject ID # _____   Date _____

Instructions: Complete one diary per day, start a new form each morning.

Date: [   ]   Day of the Week: [   ]

Morning questions (complete first time upon awakening):

1. What time did you fall asleep last night?   [   ]
   (Note: this may be different from the time you got into bed)

2. What time did you wake up this morning?   [   ]
   (Note: this may be different from the time you got out of bed)

3. Please rate the quality of last night's sleep on a scale of one to ten,   [   ]
   with one being defined as restless and ten being very sound.

4. How rested do you feel? Please rate this on a scale of one to ten,   [   ]
   with one being exhausted and ten being very refreshed.

Evening questions:

1. On a scale of one to ten, how did you feel during the day with one   [   ]
   defined as extremely tired and ten being rested and full of energy.

2. How many naps did you take today?   [   ]

3. If so, what time did you take the naps?   _____

4. What was the total amount of time you were asleep during those naps? [   ]

5. How much caffeine and alcohol did you have today?   _____

6. What medications did you take today?

Medication	Dose	Time(s) Taken

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Beck Depression Inventory-II

Subject ID # _____   Date_____

Instructions: This questionnaire consists of 21 groups of statements. Please read each group of statements carefully, and then pick out the **one statement** in each group that best describes the way you have been feeling during the **past two weeks, including today**. Circle the number beside the statement you have picked. If several statements in the group seem to apply equally well, circle the highest number for that group. Be sure that you do not choose more than one statement for any group, including Item 16 (Changes in Sleeping Pattern) or Item 18 (Changes in Appetite)

1. Sadness
  0   I do not feel sad.
  1   I feel sad much of the time.
  2   I am sad all the time.
  3   I am so sad or unhappy that I can't
       stand it.

2. Pessimism
  0   I am not discouraged about my future.
  1   I feel more discouraged about my future
       than I used to be.
  2   I do not expect things to work out for me.
  3   I feel my future is hopeless and will only
       get worse.

3. Past Failure
  0   I do not feel like a failure.
  1   I have failed more than I should have.
  2   As I look back, I see a lot of failures.
  3   I feel I am a total failure as a person.

4. Loss of Pleasure
  0   I get as much pleasure as I ever did
       from the things I enjoy.
  1   I don't enjoy things as much as I used to.
  2   I get very little pleasure from the things I
       used to enjoy.
  3   I can't get any pleasure from the things I
       used to enjoy.

5. Guilty Feelings
  0   I don't feel particularly guilty.
  1   I feel guilty over many things I have
        done or should have done.
  2   I feel quite guilty most of the time.
  3   I feel guilty all of the time.

6. Punishment Feelings
  0   I don't feel I am being punished.
  1   I feel I may be punished.
  2   I expect to be punished.
  3   I feel I am being punished.

7. Self-Dislike
  0   I feel the same about myself as ever.
  1   I have lost confidence in myself.
  2   I am disappointed in myself.
  3   I dislike myself.

8. Self-Criticalness
  0   I don't criticize or blame myself more than
       usual
  1 I am more critical of myself than I used to
      be.
  2   I criticize myself for all of my faults.
  3   I blame myself for everything bad that
       happens.

9. Suicidal Thoughts or Wishes
  0   I don't have any thoughts of killing
       myself.
  1   I have thoughts of killing myself, but I
       would not carry them out.
  2   I would like to kill myself.
  3   I would kill myself if I had the chance.

10. Crying
  0   I don't cry anymore than I used to.
  1   I cry more than I used to.
  2   I cry over every little thing.
  3   I feel like crying, but I can't.

11.

11. Agitation
0   I am no more restless or would up than usual.
1   I feel more restless or wound up than usual.
2   I am so restless or agitated that it's hard to stay still.
3   I am so restless or agitated that I have to   keep moving or doing something.

12. Loss of Interest
0   I have not lost interest in other people or activities.
1   I am less interested in other people or things than before.
2   I have lost most of my interest in other people or things.
3   It's hard to get interested in anything.

13. Indecisiveness
0   I make decisions about as well as ever
1   I find it more difficult to make decisions than usual.
2   I have much greater difficulty in making decisions than I used to.
3   I have trouble making any decisions.

14. Worthlessness
0   I do not feel I am worthless.
1   I don't consider myself as worthwhile and useful as I used to.
2   I feel more worthless as compared to other people.
3   I feel utterly worthless.

15. Loss of Energy
0   I have as much energy as ever.
1   I have less energy than I used to have.
2   I don't have enough energy to do very much
3   I don't have enough energy to do anything.

16. Changes in Sleeping Pattern
0   I have not experienced any change in my sleeping pattern.
1a I sleep somewhat more than usual.
1b I sleep somewhat less than usual.
2a I sleep a lot more than usual.
2b I sleep a lot less than usual
3a I sleep most of the day.
3b I wake up 1-2 hours early and can't get back to sleep.

17. Irritability
0   I am no more irritable than usual.
1   I am more irritable than usual.
2   I am much more irritable than usual.
3   I am irritable all the time.

18. Changes in Appetite
0   I have not experienced any change in my appetite.
1a My appetite is somewhat less than usual.
1b My appetite is somewhat greater than usual.
2a My appetite is much less than before.
2b My appetite is much greater than usual.
3a I have no appetite at all.
3b I crave food all the time.

19. Concentration Difficulty
0   I can concentrate as well as ever.
1   I can't concentrate as well as usual.
3   It's hard to keep my mind on anything for very long.
4   I find I can't concentrate on anything.

20. Tiredness or Fatigue
0   I am no more tired or fatigued than usual.
1   I get more tired or fatigued more easily than usual.
2   I am too tired or fatigued to do a lot of the things I used to do.
3   I am too tired or fatigued to do most of the things I used to do.

21. Loss of Interest in Sex
0   I have not noticed any recent change in my interest in sex.
1   I am less interested in sex than I used to be.
2   I am much less interested in sex now.
3   I have lost interest in sex completely

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Structured Interview for the Hamilton Depression Rating Scale—
Seasonal Affective Disorder Version (SIGH-SAD)

Subject ID # _____ Date_____

Have you been physically sick or ill over the last week?

YES   NO

If yes, explain:

_____

Have you taken any trips outside of the area since you were last here in the lab?

YES   NO

If yes, where did you go?:

_____

What dates were you there?

_____

Is the climate of (that location) tropical or summer-like this time of year?   YES   NO

OVERVIEW: I'd like to ask you some questions about the past week, since last (DAY OF WEEK). How have you been feeling since then?

H1.   What's your mood been like this past week (compared to when you feel OK)?

DEPRESSED MOOD (sadness, Hopeless, helpless, worthless):

Have you been feeling down or depressed?

Sad? Hopeless? Helpless? Worthless?

In the last week, how often have you felt (OWN EQUIVALENT)? Every day? All day?

Have you been crying at all?

0 = absent
1 = indicated only on questioning
2 = spontaneously reported verbally
3 = communicated non-verbally, i.e. facial expression, posture, voice tendency to weep
4 = VIRTUALLY ONLY; this in spontaneous verbal and non-verbal communication

IF SCORED 1-4 ABOVE, ASK: How long have you been feeling this way?

H2.   IF OUTPATIENT: Have you been working this week (in or out of the home)?
IF NOT: Why not?

IF WORKING: Have you been able to get as much (work) done as you usually do (when you're feeling OK)?

How have you been spending your time this past week (when not at work)?

Have you felt interested in doing (THOSE THINGS), or do you feel you have to push yourself to do them?

Have you stopped doing anything you used to do? IF YES: Why?

Is there anything you look forward to?

WORK AND ACTIVITIES:

0 = no difficulty
1 = thoughts and feelings of incapacity, fatigue or weakness related to activities, work or hobbies
2 = loss of interest in activity, hobbies or work – by direct report of the patient or indirect in listlessness, indecision And vacillation (feels he has to push self to do work or activities)
3 = decrease in actual time spent in activities or decrease in productivity. In hospital, patient spends less than 3 hours/day in activities (hospital job or hobbies) exclusive of ward chores
4 = stopped working because of present illness. In hospital, no activities except ward chores, or fails to perform ward chores unassisted

A1. In the last week, have you been as social as when you feel well? IF NO: Tell me which fits you best. (READ DOWN ANCHOR DESCRIPTIONS AND RATE ACCORDINGLY.)

*SOCIAL WITHDRAWAL:

0 = interacts with other people as usual
1 = less interested in socializing with others but continues to do so
2 = interacting less with other people in social (optional) situations
3 = interacting less with other people in work or family situations (i.e., where it is necessary)
4 = marked withdrawal from others in family or work situations

H3. This week, how has your interest in sex been? (I'm not asking about actual sexual activity, but about your interest in sex – how much you think about it.)

Has there been any change in your interest in sex (from when you were not depressed)?

Is it something you've thought much about? IF NO: Is that unusual for you compared to when you feel well? (Is it a little less or a lot less?)

GENITAL SYMPTOMS (such as loss of libido, menstrual disturbances):

0 = absent
1 = mild
2 = severe

H4. How has your appetite been this past week? (What about compared to your usual appetite?)

Have you had to force yourself to eat?

Have other people had to urge you to eat? (Have you skipped meals?)

Have you had any stomach or intestinal problems? (Have you needed to take anything for that?)

SOMATIC SYMPTOMS GASTROINTESTINAL:

0 = none
1 = loss of appetite but eating without encouragement
2 = difficulty eating without urging: requests or requires laxatives or medication for G.I. symptoms

H5. Have you lost any weight since you started feeling depressed or down? IF YES: Did you lose any weight this last week? (Was it because of feeling depressed?) How much did you lose?

IF NOT SURE: Do you think your clothes are any looser on you?

LOSS OF WEIGHT (Rate either A or B):

A. When rating by history:
0 = no weight loss
1 = probable weight loss due to current depression
2 = definite (according to patient) weight loss due to depression
3 = not assessed

B. When actual weight changes are measured:
0 = less than 1 pound loss in week
1 = greater than 1 pound loss in week
2 = greater than 2 pounds loss in week
3 = not assessed

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A2.   Have you gained any weight in the   *WEIGHT GAIN:
        last week? IF YES: Was it because
        of feeling depressed or down? How   0 = no weight gain
        much did you gain?   1 = probable weight gain due to current
                                                       depression
                                                   2 = definite (according to patient) weight
                                                       gain due to depression

A3.   In the past week, has your appetite   *APPETITE INCREASE:
        been greater than when you feel well
        or OK? IF YES: Do you want to eat a   0 = no increase in appetite
        little more, somewhat more, or much   1 = wants to eat a little more than usual
        more   than when you feel well or OK?   2 = wants to eat somewhat more than
                                                       normal
                                                   3 = wants to eat much more than usual

A4.   In the past week, have you actually   *INCREASED EATING
        been eating more than when you feel
        well or OK? IF YES: A little more,   0 = is not eating more than usual
        somewhat more, or much more than   1 = is eating a little more than usual
        when you feel well or OK?   2 = is eating somewhat more than usual
                                                   3 = is eating much more than normal

A5.   In the last week, have you been   *CARBOHYDRATE CRAVING OR
        craving or eating more starches or   EATING (in relation to total amount of
        sugars?   food desired or eaten)
        IF YES: Have you been eating
        or craving starches or sugars more   0 = no change in food preference or
        than when you feel well or OK, much   consumption
        more, or has it been irresistible?   1 = craving or eating more
                                                       carbohydrates (starches or sugars)
                                                       than before
                                                   2 = craving or eating much more
                                                       carbohydrates than before
                                                   3 = irresistible craving or eating of
                                                       sweets or starches

        Has it been mainly starches or mainly   CIRCLE ONE   Mainly   Mainly   Both
        sweets? Which specific foods have you   OR BOTH: starches   sweets
        been craving?
        LIST:
                                                   CIRCLE ONE
        Have you actually been eating more   OR BOTH: Craving   Eating   Both
        starches or sweets, or just craving them?
                                                   USUAL TIME OF CRAVING OR EATING:
        Has the (CRAVING OR EATING)
        occurred at any particular time of day?   0 = it comes and goes at various times
        (_____o'clock)   1 = usually morning
                                                   2 = usually afternoon or evening
                                                   3 = virtually all the time
                                                   RATER NOTE: IF BOTH CRAVING
                                                   AND EATING, RATE TIME OF EATING.
                                                   DO NOT COUNT ABOVE SCORE IN
                                                   TOTALS.

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H6.	I'd like to ask you now about your sleeping during the past week. Have you had any trouble falling asleep at the beginning of the night? (Right after you go to bed, how long has it been taking you to fall asleep?) How many nights this week have you had trouble falling asleep?	INSOMNIA EARLY (INITIAL INSOMNIA): 0 = no difficulty falling asleep 1 = complains of occasional difficulty falling asleep – i.e., more than ½ hour 2 = complains of nightly difficulty falling asleep
H7.	During the past week, have you been waking up in the middle of the night? IF YES: Do you get out of bed? What do you do? (Only go to the bathroom?) When you get back in bed, are you able able to fall right back asleep? Have you felt your sleeping has been restless or disturbed some nights?	INSOMNIA MIDDLE: 0 = no difficulty 1 = complains of being restless and disturbed during the night 2 = waking during the night – any getting out of bed (except to void)
H8.	What time have you been waking up in the morning for the last time, this past week? IF EARLY: Is that with an alarm clock, or do you just wake up yourself? What time do you usually wake up (that is, when you feel well)?	INSOMNIA LATE (TERMINAL INSOMNIA): 0 = no difficulty 1 = waking in early hours of morning but goes back to sleep 2 = unable to fall asleep again if gets out of bed
A6.	Have you been sleeping more than usual this past week? IF YES: How much more? IF NO: What about weekends? (What time have you been falling asleep? Have you been taking naps? That means you've been sleeping about ___ hours a day altogether? How much time do you usually sleep when you feel well?)	*HYPERSOMNIA (Compare sleep length to euthymic and NOT to hypomanic sleep length. (If this cannot be established, use 8 hours): 0 = no increase in sleep length 1 = at least 1 hour increase in sleep length 2 = 2+ hour increase 3 = 3+ hour increase 4 = 4+ hour increase Sleep length used (circle one): euthymic (___ hrs) 8-hour

H9. How has your energy been this past week? IF LOW ENERGY: Have you felt tired? (How much of the time? How bad has it been?) This week, have you had any aches or pains? (What about backaches, headaches, or muscle aches? Have you felt any heaviness in your limbs, back or head?	SOMATIC SYMPTOMS GENERAL: 0 = none 1 = heaviness in limbs, back or head. Backaches, headaches, muscle aches. Loss of energy and fatigability. 2 = any clear-cut symptom
A7. IF ACKNOWLEDGED FEELING TIRED ON PREVIOUS ITEM: How much of the time have you felt tired? (Every day? How much of each day?) Very tired, or just a little?	*FATIGABILITY (or low energy, or feelings of being heavy, leaden, weighed down); 0 = does not feel more fatigued than usual 1 = feels more fatigued than usual but this has not impaired function significantly; less frequent than in (2) 2 = more fatigued than usual; at least one hour a day; at least three days a week 3 = fatigued much of the time most days 4 = fatigued almost all the time
H10. Have you been putting yourself down, this past week, feeling you've done things wrong, or let others down? If Yes: What have your thoughts been? Have you been feeling guilty about anything that you've done or not done? What about things that happened a long time ago? Have you thought that you've brought (THIS DEPRESSION) on yourself in some way? Do you feel your being sick is a punishment?	FEELINGS OF GUILT: 0 = absent 1 = self-reproach, feels he/she has let people down 2 = ideas of guilt or rumination over past errors or sinful deeds 3 = present illness is a punishment: delusions of guilt 4 = hears accusatory or denunciatory voices and/or experiences threatening visual hallucinations
H11. This past week, have you had any thoughts that life is not worth living? IF YES: What about thinking you'd be better off dead? Have you had thoughts of hurting or killing yourself? IF YES: What have you thought about? Have you actually done anything to hurt yourself?	SUICIDE: 0 = absent 1 = feels life is not worth living 2 = wishes he were dead or any thoughts of possible death to self 3 = suicidal ideas or gesture 4 = attempts at suicide

H12. Have you been feeling especially tense or irritable this past week? IF YES: Is this more than when you are not depressed or down?

Have you been unusually argumentative or impatient?

Have you been worrying a lot about little things, things you don't ordinarily worry about? IF YES: Like what, for example?

ANXIETY PSYCHIC:

0 = no difficulty
1 = subjective tension and irritability
2 = worrying about minor matters
3 = apprehensive attitude apparent in face or speech
4 = fears expressed without questioning

H13. In this past week, have you had any of the following physical symptoms? (READ LIST, PAUSING AFTER EACH SX FOR REPLY. CIRCLE POSITIVE SXS.)

Have you had these only while you've been feeling depressed or down? IF YES: How much have these things been bothering you this past week? (How bad have they gotten? How much of the time, or how often, have you had them?)

Do you have any physical illness or are you taking any medication that could be causing these symptoms? (IF YES, RECORD PHYSICAL ILLNESS OR MEDICATION, BUT RATE SYMPTOMS ANYWAY:_____)

ANXIETY SOMATIC (physiologic Concomitants of anxiety, such as GI – dry mouth, indigestion, gas, diarrhea, stomach cramps,belching C-V – heart palpitations, headaches Resp – hyperventilating, sighing, having to urinate frequently, sweating:

0 = absent
1 = mild
2 = moderate
3 = severe
4 = incapacitating

H14. In the last week, how much have your thoughts been focused on your physical health or how your body is working (compared to your normal thinking)? (Have you worried a lot about being or becoming physically ill? Have you really been preoccupied with this?)

Do you complain much about how you feel physically? Have you found yourself asking for help with things you could really do yourself? IF YES: Like what, for example? How often has that happened?

HYPOCHONDRIASIS:

0 = not present
1 = self-absorption (bodily)
2 = preoccupation with health
3 = frequent complaints, requests for help, etc.
4 = hypochondriacal delusions

H15. RATING BASED ON OBSERVATION DURING INTERVIEW.

INSIGHT:

0 = acknowledges being depressed and ill OR not currently depressed
1 = acknowledges illness but attributes cause to bad food, overwork, virus, need for rest, etc.
2 = denies being ill at all

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H16. RATING BASED ON OBSERVATION DURING INTERVIEW

IF TELEPHONE INTERVIEW: Do you feel that your speech or physical movements are sluggish? Has anyone actually commented on this?

RETARDATION (slowness of thought and speech; impaired ability to concentrate; decreased motor activity):

0 = normal speech and thought
1 = slight retardation at interview
2 = obvious retardation at interview
3 = interview difficult
4 = complete stupor

H17. RATING BASED ON OBSERVATION INTERVIEW.

IF TELEPHONE INTERVIEW: As we talk, are you fidgeting at all, or having trouble sitting still? For instance, are you doing anything like playing with your hands or your hair, or tapping your foot? Do others notice that you are restless?

AGITATION:

0 = none
1 = fidgetiness
2 = playing with hands, hair, etc.
3 = moving about, can't sit still
4 = hand- wringing, nail biting, hair-pulling, biting of lips

17-ITEM TOTAL SCORE HAMILTON DEPRESSION   _____   _____

Over the past week, in the first few hours after waking up have you been feeling better or worse or no different from before you go to sleep?

DIURNAL VARIATION TYPE A:

A. Note whether symptoms are worse After awakening or before sleeping. If NO diurnal variation, mark none:
0 = no variation OR not currently depressed
1 = worse after awakening
2 = worse before going to sleep

RATER NOTE: DO NOT COUNT ABOVE SCORE IN SCALE TOTALS.

H18. IF VARIATION: How much worse do you feel in the (MORNING OR EVENING)?
IF UNSURE: A little bit worse or a lot worse?

B. When present, mark the severity of the variation:
0 = none
1 = mild
2 = severe

A8. This week, have you regularly had a slump in your mood or energy in the afternoon or evening?

IF YES: Is it mostly in your mood or your energy? Does it occur every day? At what time has the slump usually begun? (_____o'clock). When has it ended? Has that been at least an hour before you go to sleep? How big a slump do you have – would you say it's generally mild, moderate, or severe?

*DIURNAL VARIATION TYPE B:

0 = no
1 = yes, of mild intensity
2 = yes, of moderate intensity
3 = yes, of severe intensity

CIRCLE ONE   Mood   Energy
OR BOTH: Slump   Slump

NOTE: RATE ONLY SLUMPS THAT ARE FOLLOWED BY AT LEAST AN HOUR OF RECOVERED MOOD OR ENERGY BEFORE SLEEP.

H19.	In the past week, have you ever suddenly	DEPERSONALIZATION AND

H19.   In the past week, have you ever suddenly had the sensation that everything is unreal, or you're in a dream, or cut off from other people in some strange way? Any spacey feelings?

DEPERSONALIZATION AND DEREALIZATION (such as feelings of unreality and from Nihilistic ideas):

IF YES: Tell me about it. How bad has that been? How often this week has that happened?

0 = absent
1 = mild
2 = moderate
3 = severe
4 = incapacitating

H20.   This past week, have you thought that anyone was trying to give you a hard time or hurt you?

PARANOID SYMPTOMS:

0 = none
1 = suspicious
2 = ideas of reference
3 = delusions of reference and persecution

What about talking about you behind your back?

IF YES: Tell me about that.

H21.   In the past week, have there been things you've had to do over and over again, like checking the locks on the doors several times, or washing your hands? IF YES: Can you give me an example?

OBSESSIONAL AND COMPULSIVE SYMPTOMS:

0 = absent
1 = mild
2 = severe

Have you had any thoughts that don't make any sense to you, but that keep running over and over in your mind?
IF YES: Can you give me an example?

21-ITEM TOTAL SCORE HAMILTON DEPRESSION (without starred items):   _____ _____

TOTAL 8-ITEM ATYPICAL SCORE (starred items only):   _____ _____

TOTAL 29-ITEM SIGH-SAD SCORE   _____ _____

ATYPICAL BALANCE SCORE (total 8-item atypical score divided by total 29-item SIGH-SAD score, multiplied by 100):   _____ _____ **.** _____

NOTE: If patient is not depressed and score is derived primarily from symptoms of hypomania (e.g., items H4, H5, H6, H7, H8, H12, H17), administer HIGH-SAD and report both scores.

APPENDIX G

SEASONAL PATTERN ASSESSMENT QUESTIONNAIRE

1. Name _____   **2. Age** _____

3. Place of birth - City / Province (State) / Country _____

4. Today's date   _____   _____   _____
                        Month   Day   Year

5. Current weight (in lbs.)   _____

<table>
<tr><td>6. Years of education</td><td>Less than four years of high school</td><td>1</td></tr>
<tr><td></td><td>High school only</td><td>2</td></tr>
<tr><td></td><td>1-3 years post high school</td><td>3</td></tr>
<tr><td></td><td>4 or more years post high school</td><td>4</td></tr>
</table>

INSTRUCTIONS

* Please circle the number beside your choice.

Example:
Sex Male 1   Female 2

7. Sex -   Male 1   Female 2

<table>
<tr><td>8. Marital Status -</td><td>Single</td><td>1</td></tr>
<tr><td></td><td>Married</td><td>2</td></tr>
<tr><td></td><td>Sep./Divorced</td><td>3</td></tr>
<tr><td></td><td>Widowed</td><td>4</td></tr>
</table>

9. Occupation _____

10. How many years have you lived in this climatic area? _____

The purpose of this form is to find out how your mood and behaviour change over time. Please fill in all the relevant circles. Note: We are interested in your experience; **not others** you may have observed.

---

11. To what degree do the following change with the seasons?

	No Change	Slight Change	Moderate Change	Marked Change	Extremely Marked Change
A. Sleep length	0	1	2	3	4
B. Social activity	0	1	2	3	4
C. Mood (overall feeling of well being)	0	1	2	3	4
D. Weight	0	1	2	3	4
E. Appetite	0	1	2	3	4
F. Energy level	0	1	2	3	4

12. In the following questions, fill in circles for all applicable months. This may be a single month O, a cluster of months, e.g. O O O , or any other grouping.

At what time of year do you....

	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	**OR**	No particular month(s) stand out as extreme on a regular basis
A. Feel best	O	O	O	O	O	O	O	O	O	O	O	O		O
B. Gain most weight	O	O	O	O	O	O	O	O	O	O	O	O		O
C. Socialize most	O	O	O	O	O	O	O	O	O	O	O	O		O
D. Sleep least	O	O	O	O	O	O	O	O	O	O	O	O		O
E. Eat most	O	O	O	O	O	O	O	O	O	O	O	O	**OR**	O
F. Lose most weight	O	O	O	O	O	O	O	O	O	O	O	O		O
G. Socialize least	O	O	O	O	O	O	O	O	O	O	O	O		O
H. Feel worst	O	O	O	O	O	O	O	O	O	O	O	O		O
I. Eat least	O	O	O	O	O	O	O	O	O	O	O	O		O
J. Sleep most	O	O	O	O	O	O	O	O	O	O	O	O		O

14. How much does your weight fluctuate during the course of the year?

0-3 lbs	1		12-15 lbs	4
4-7 lbs	2		16-20 lbs	5
8-11 lbs	3		Over 20 lbs	6

15. Approximately how many hours of each 24-hour day do you sleep during each season? (Include naps)

Winter   0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 Over18

Spring   0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 Over18

Summer   0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 Over18

Fall   0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 Over18

16. Do you notice a change in food preference during the different seasons?

No   1   Yes   2   If yes, please specify :

17. If you experience changes with the seasons, do you feel that these are a problems for you?

No   1   Yes   2   If yes, is this problem -   mild   1

moderate   2

marked   3

severe   4

disabling   5

Thank you for completing this questionnaire.

---

* Raymond W. Lam 1998 (modified from Rosenthal, Bradt and Wehr 1987).

The Morningness-Eveningness Questionnaire

Instructions: There will be 19 questions about your daily sleep-wake habits and the times of day you prefer certain activities. Answering should take only about 5-10 minutes. For each question, circle the answer choice that best describes you. Base your judgments on how you have felt in recent weeks.

1	*Approximately* what time would you get up if you were entirely free to plan your day? 1) 5:00-6:30 a.m. 2) 6:30-7:45 a.m. 3) 7:45-9:45 a.m. 4) 9:45-11:00 a.m. 5) 11:00 a.m. - 12:00 noon 6) 12:00 noon – 5:00 a.m.
2	*Approximately* what time would you go to bed if you were entirely free to plan your evening? 1) 8:00-9:00 p.m. 2) 9:00-10:15 p.m. 3) 10:15-12:30 a.m. 4) 12:30-1:45 a.m. 5) 1:45-3:00 a.m. 6) 3:00 a.m. – 8:00 p.m.
3	If you usually have to get up at a specific time in the morning, how much do you depend on an alarm clock? 1) Not at all 2) Slightly 3) Somewhat 4) Very much
4	How easy do you find it to get up in the morning (when you are not awakened unexpectedly)? 1) Very difficult 2) Somewhat difficult 3) Fairly easy 4) Very easy

5	How alert do you feel during the first half hour after you wake up in the morning? 1) Not at all alert 2) Slightly alert 3) Fairly alert 4) Very alert
6	How hungry do you feel during the first half hour after you wake up? 1) Not at all hungry 2) Slightly hungry 3) Fairly hungry 4) Very hungry
7	During the first half hour after you wake up in the morning, how do you feel? 1) Very tired 2) Fairly tired 3) Fairly refreshed 4) Very refreshed
8	If you had no commitments the next day, what time would you go to bed compared to your usual bedtime? 1) Seldom or never later 2) Less than 1 hour later 3) 1-2 hours later 4) More than 2 hours later
9	You have decided to do physical exercise. A friend suggests that you do this for one hour twice a week, and the best time for him is between 7-8 a.m. Bearing in mind nothing but your own internal "clock," how do you think you would perform? 1) Would be in good form 2) Would be in reasonable form 3) Would find it difficult 4) Would find it very difficult

10	At *approximately* what time in the evening do you feel tired, and, as a result, in need of sleep? 1) 8-9 p.m. 2) 9-10:15 p.m. 3) 10:15 p.m. – 12:45 a.m. 4) 12:45-2:00 a.m. 5) 2-3 a.m.
11	You want to be at your peak performance for a test that you know is going to be mentally exhausting and will last two hours. You are entirely free to plan your day. Considering only your internal "clock," which one of the four testing times would you choose? 1) 8-10 a.m. 2) 11a.m. – 1 p.m. 3) 3-5 p.m. 4) 7-9 p.m.
12	If you got into bed at 11 p.m., how tired would you be? 1) Not at all tired 2) A little tired 3) Fairly tired 4) Very tired
13	For some reason you have gone to bed several hours later than usual, but there is no need to get up at any particular time the next morning. Which one of the following are you most likely to do? 1) Will wake up at usual time, but will not fall back asleep 2) Will wake up at usual time and will doze thereafter 3) Will wake up at usual time, but will fall asleep again 4) Will not wake up until later than usual
14	One night you have to remain awake between 4-6 a.m. in order to carry out a night watch. You have no time commitments the next day. Which one of the alternatives would suit you best? 1) Would not go to bed until the watch was over 2) Would take a nap before and sleep after 3) Would take a good sleep before and nap after 4) Would sleep only before the watch

15	You have to do two hours of hard physical work. You are entirely free to plan your day. Considering only your internal "clock," which one of the following times would you choose? 1) 8-10 a.m. 2) 11 a.m.- 1 p.m. 3) 3-5 p.m. 4) 7-9 p.m.
16	You have decided to do physical exercise. A friend suggests that you do this for one hour twice a week. The best time for her is between 10-11 p.m. Bearing in mind only your own internal "clock," how well do think you would perform? 1) Would be in good form 2) Would be in reasonable form 3) Would find it difficult 4) Would find it very difficult
17	Suppose you can choose your own work hours. Assume that you work a five-hour day (including breaks), your job is interesting and you are paid based on your performance. At *approximately* what time would you choose to begin? 1) 5 hours starting between 4 a.m. and 8 a.m. 2) 5 hours starting between 8 a.m. and 9 a.m. 3) 5 hours starting between 9 a.m. and 2 p.m. 4) 5 hours starting between 2 p.m. and 5 p.m. 5) 5 hours starting between 5 p.m. and 4 a.m.
18	At *approximately* what time of day do you usually feel your best? 1) 5-8 a.m. 2) 8-10 a.m. 3) 10 a.m. – 5 p.m. 4) 5-10 p.m. 5) 10 p.m. – 5 a.m.
19	One hears about "morning types" and "evening types." Which one of these types do you consider yourself to be? 1) Definitely a morning type 2) Rather more a morning type than an evening type 3) Rather more an evening type than a morning type 4) Definitely an evening type

Figure 1

Rohan's Integrative Cognitive-Behavioral Model of SAD

```
┌─────────────────────────┐         ┌─────────────────────────┐
│     Psychological        │         │   Environmental Cues    │
│ Appraisal/Expectation    │         │    (light, season,      │
│   s (anticipation of     │         │       weather)          │
│        winter)           │         │                         │
└────────────┬────────────┘         └────────────┬────────────┘
             │                                    │
             ▼                                    ▼
┌─────────────────────────┐         ┌─────────────────────────┐
│ Psychological Vulnerability│      │ Physiological Vulnerability│
│ • Cognitive              │         │ • Chronobiological       │
│   Brooding rumination;   │         │   Circadian misalignment;│
│   Dysfunctional attitudes;│       │ • Expanded melatonin     │
│   Negative cognitions    │  ◄────► │   release duration       │
│   regarding seasons and light│    │ • Retinal sub-sensitivity│
│ • Behavioral             │         │                          │
│   behavioral disengagement,│       │                          │
│   reactivity to light and│         │                          │
│   seasonal cues          │         │                          │
└────────────┬────────────┘         └────────────┬────────────┘
             │                                    │
             ▼                                    ▼
┌──────────────────────────────────────────────────────────────┐
│                      SAD Episode                              │
│                (winter depression severity)                   │
└──────────────────────────────────────────────────────────────┘
```

Figure 1. An illustration of the effects tested by this project, adapted from Rohan's integrative cognitive-behavioral model of SAD.

Figure 2

Temporal Relation between DLMO and Sleep
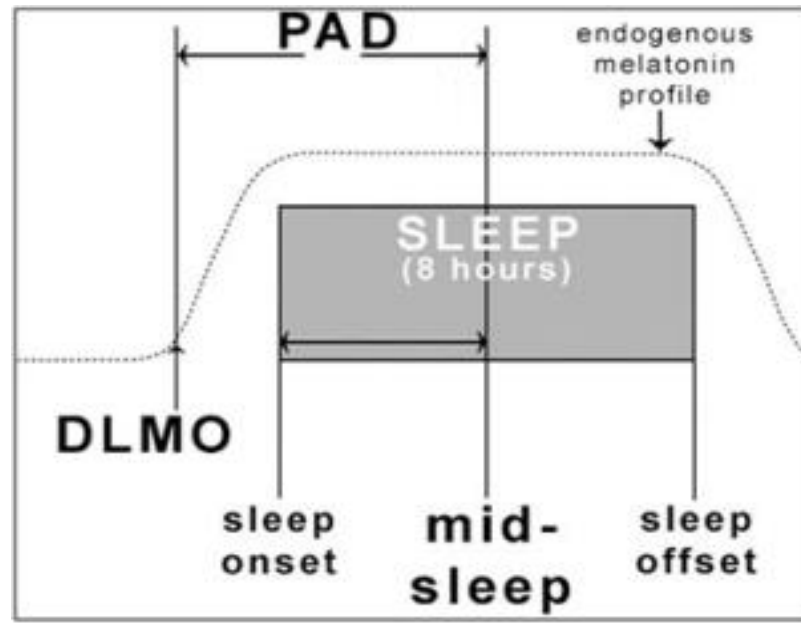
Figure 2. *PAD* = Phase Angle Difference (Hr); *DLMO* = Dim Light Melatonin Onset.
Illustration of the temporal relation between sleep/wake and circadian oscillators
during stable phase entrainment. Adapted from Lewy etl al., 2006.

Figure 3

Average Midsleep Clock Time by Patient Status and Season
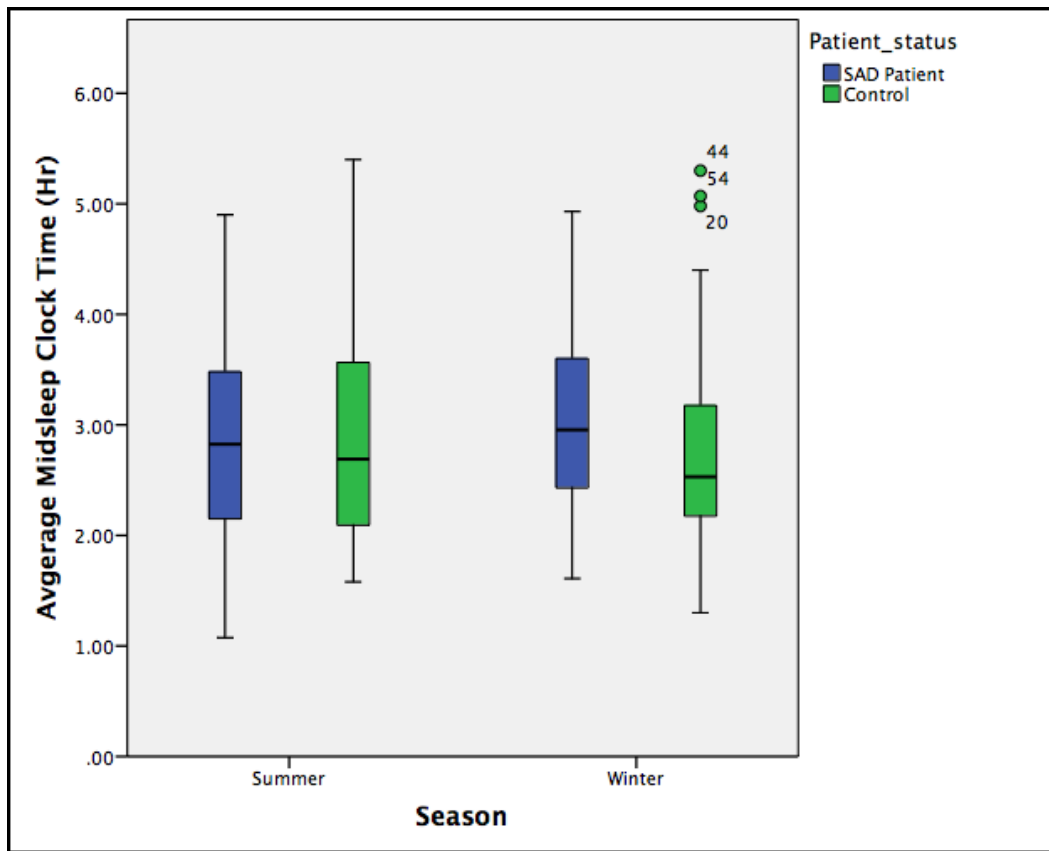
Figure 3. *Midsleep* = Midpoint of sleep episode. Midsleep clock times by patients and controls across season. No significant differences were found between SAD patients and controls, or as across summer or winter. Error bars represent standard errors.

Figure 4

DLMO Clock Time by Patient Status and Season
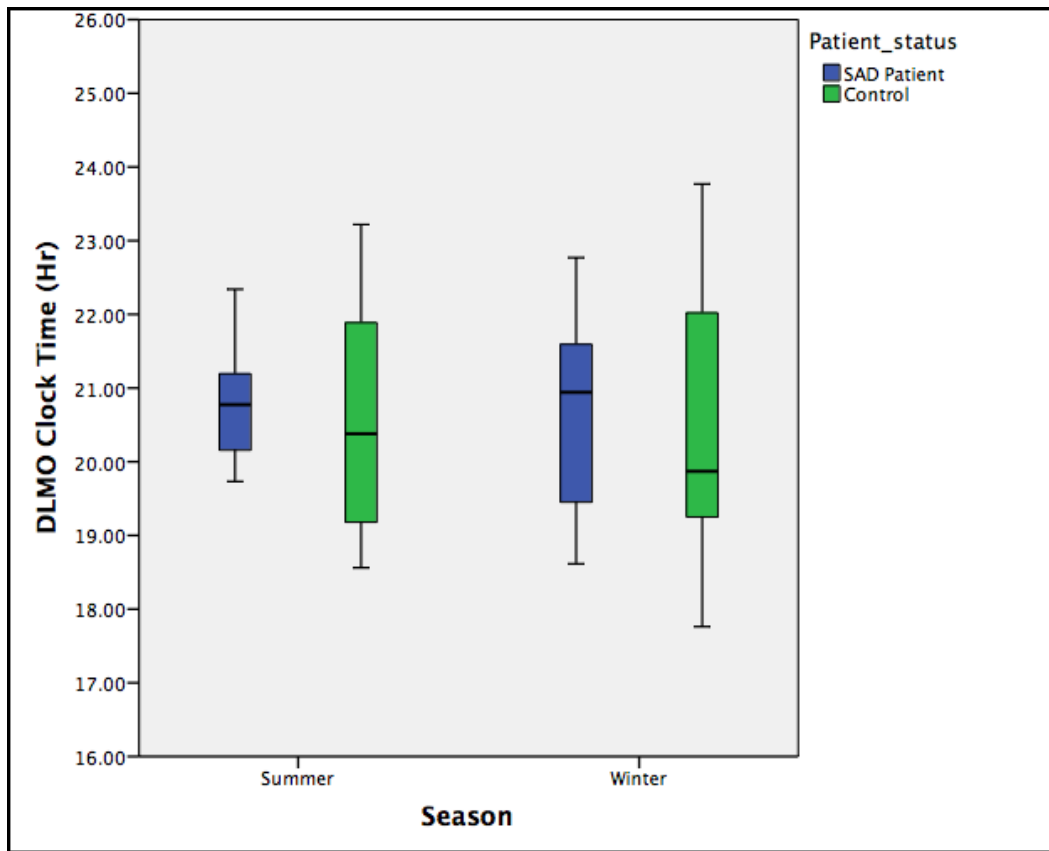
Figure 4. *DLMO* = Dim Light Melatonin Onset. Salivary DLMO (3 pg/ml) means depicted by patient status and season exhibit no significant differences were found in the timing of DLMO between patients and controls, or across summer or winter. Error bars represent standard errors.

Figure 5

PAD by Patient Status and Season
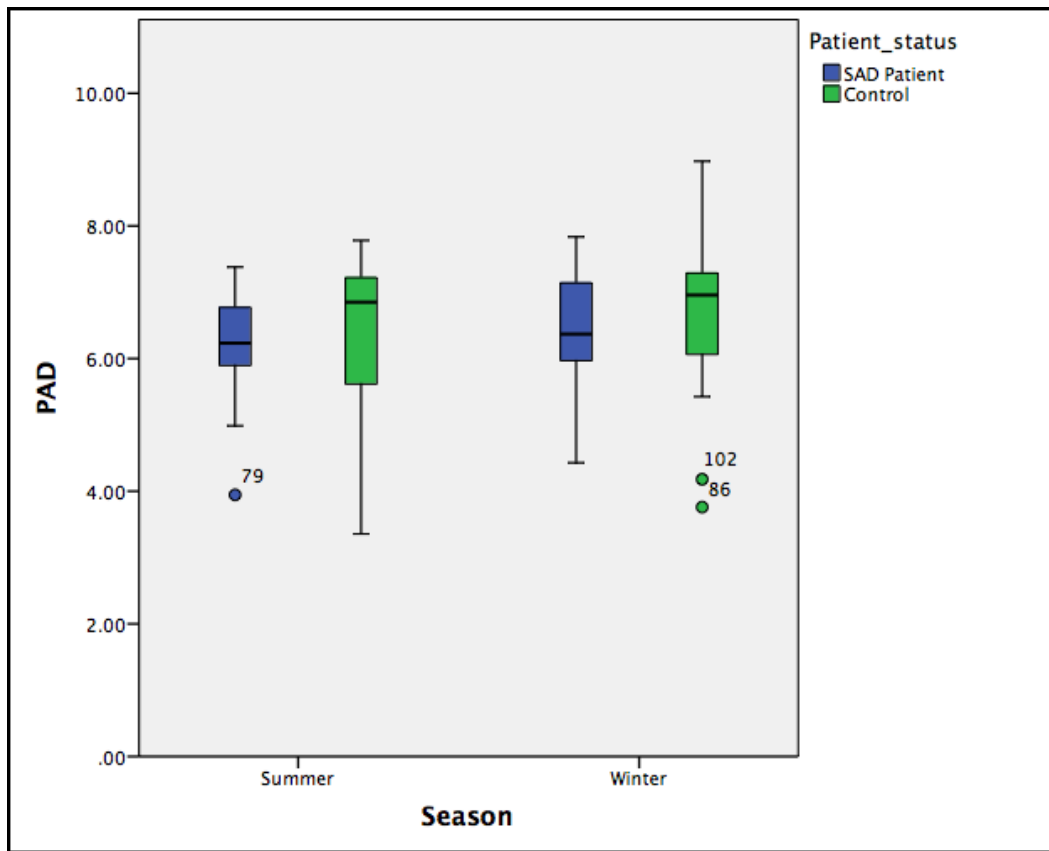
Figure 5. *PAD* = Phase Angle Difference (hr). There was a main effect of season, whereby PAD was longer in winter, collapsing across patients and control status. Error bars represent standard errors.

Figure 6

PAD-6 (SQRT) by Patient Status and Season
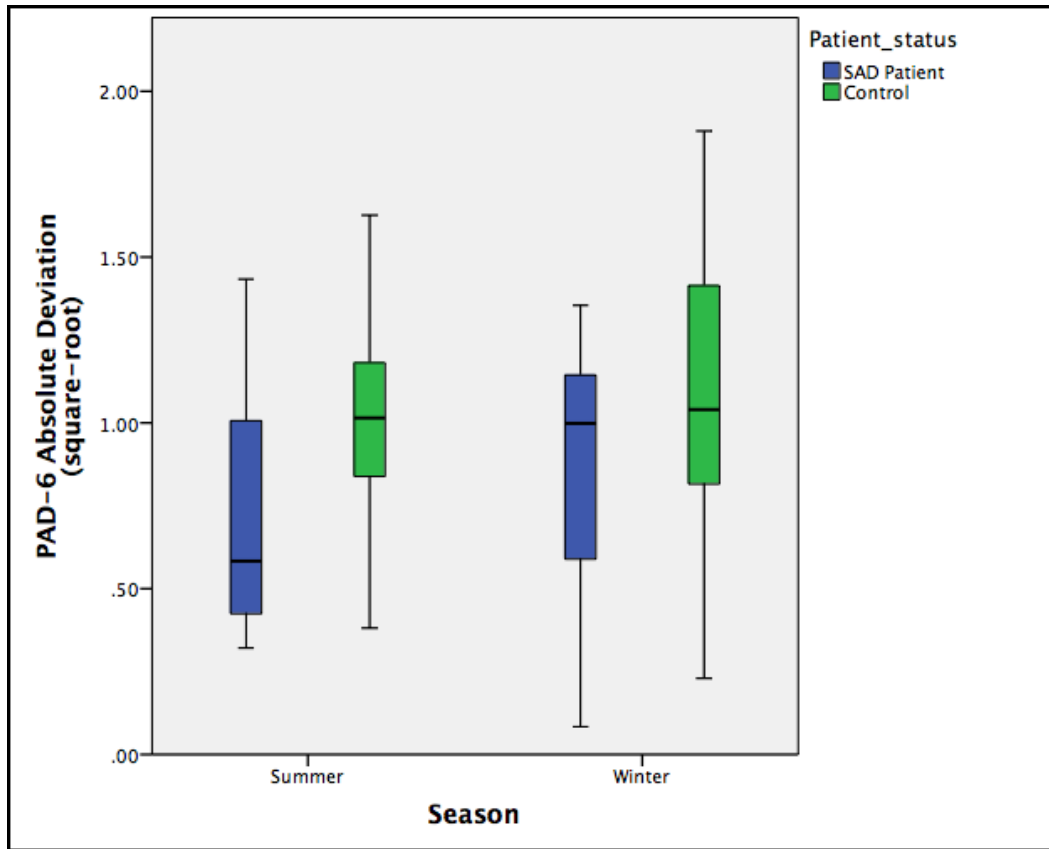
Figure 6. *PAD-6* = Absolute Deviation in Phase Angle Difference from 6 (hr). The linear model revealed that controls exhibited greater deviation from PAD-6, than patients, collapsing across seasons.. Morningness was a significant covariate, whereby greater morningness predicted greater deviation from PAD-6, collapsing across patient status and season. Error bars represented standard errors.

Figure 7

Brooding Rumination by Patient Status and Season
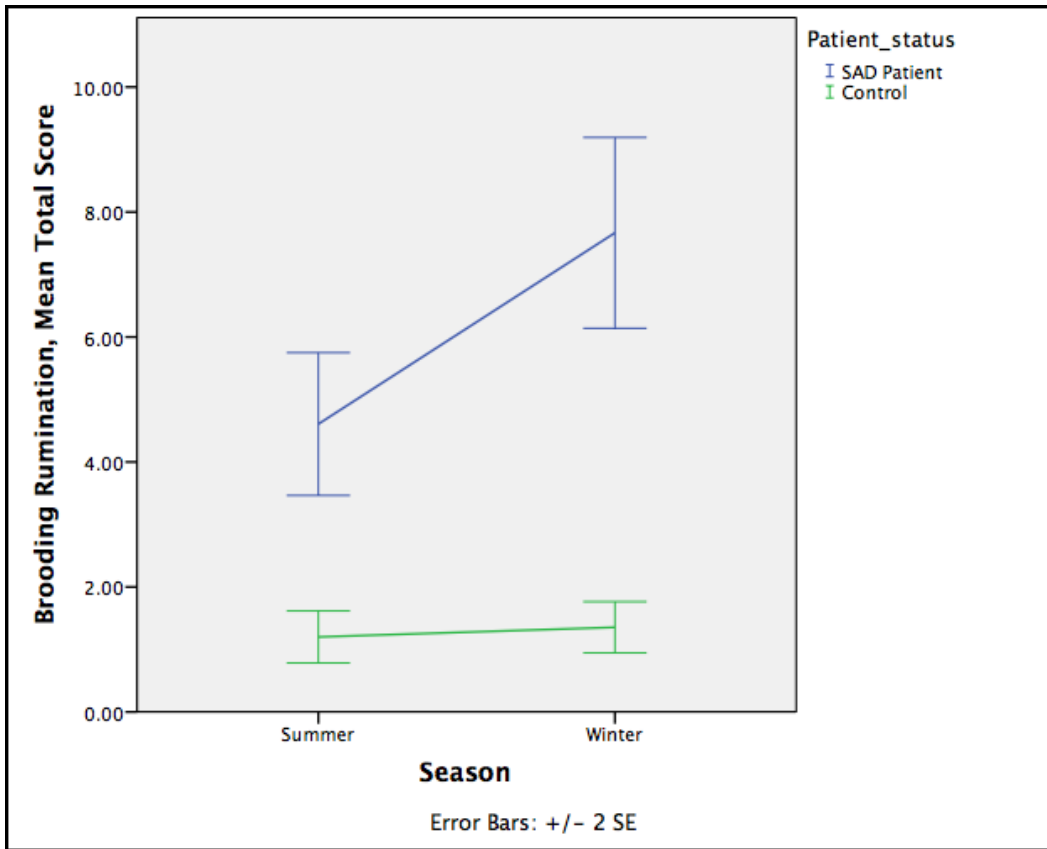
Figure 7. Brooding subscale of Ruminative Response Scale (Treynor et al., 2003). Brooding rumination total subscale score estimated marginal means depicted by patient status and group. SAD patients exhibited a unique seasonal variation in brooding rumination, endorsing a significantly greater tendency to brood in response to sad mood when depressed. As expected, SAD patients endorsed significantly greater tendency to brood than controls, across seasons.

Figure 8

Ruminative Response Scale by Patient Status and Season
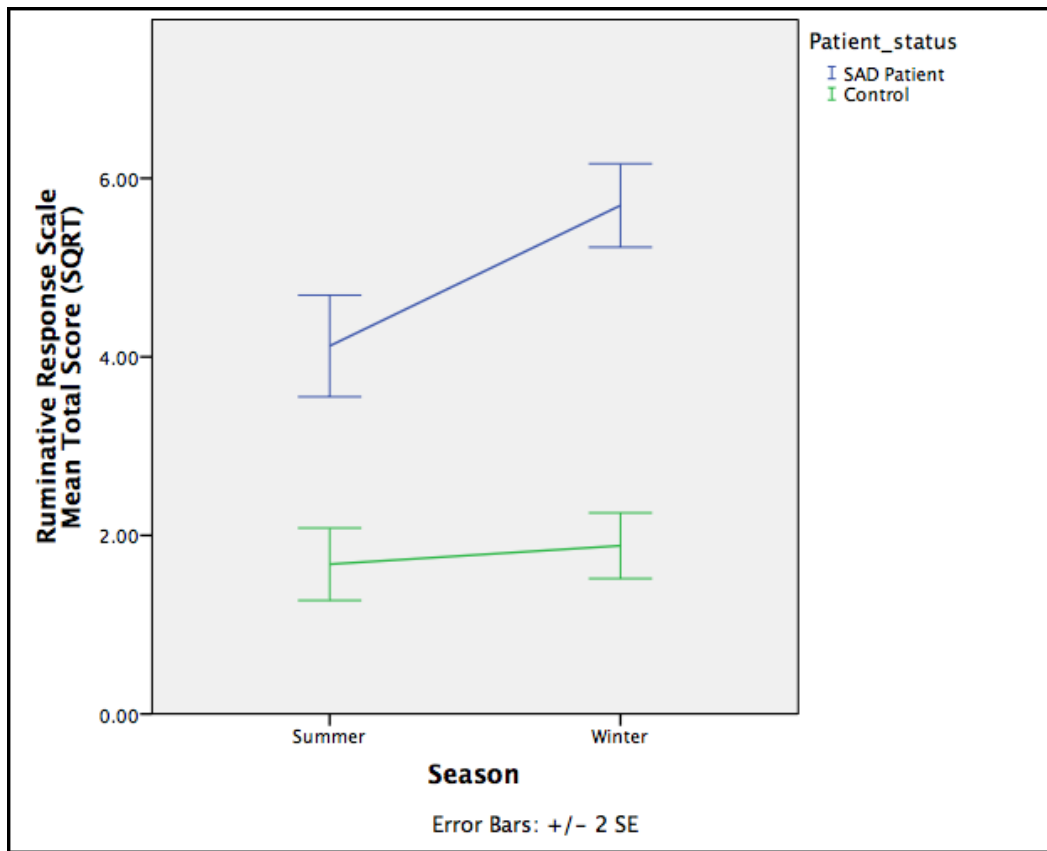
Figure 8. *RRS* = Ruminative Response Scale Total Score SQRT (Nolen-Hoeksema & Morrow, 1991). Estimated marginal means by patient status and season. SAD patients exhibited significant seasonal variation, endorsing greater RRS in winter relative to summer, and greater RRS than controls at both time points.

Figure 9

Cognitive Reactivity by Patient Status across a Negative Mood Induction
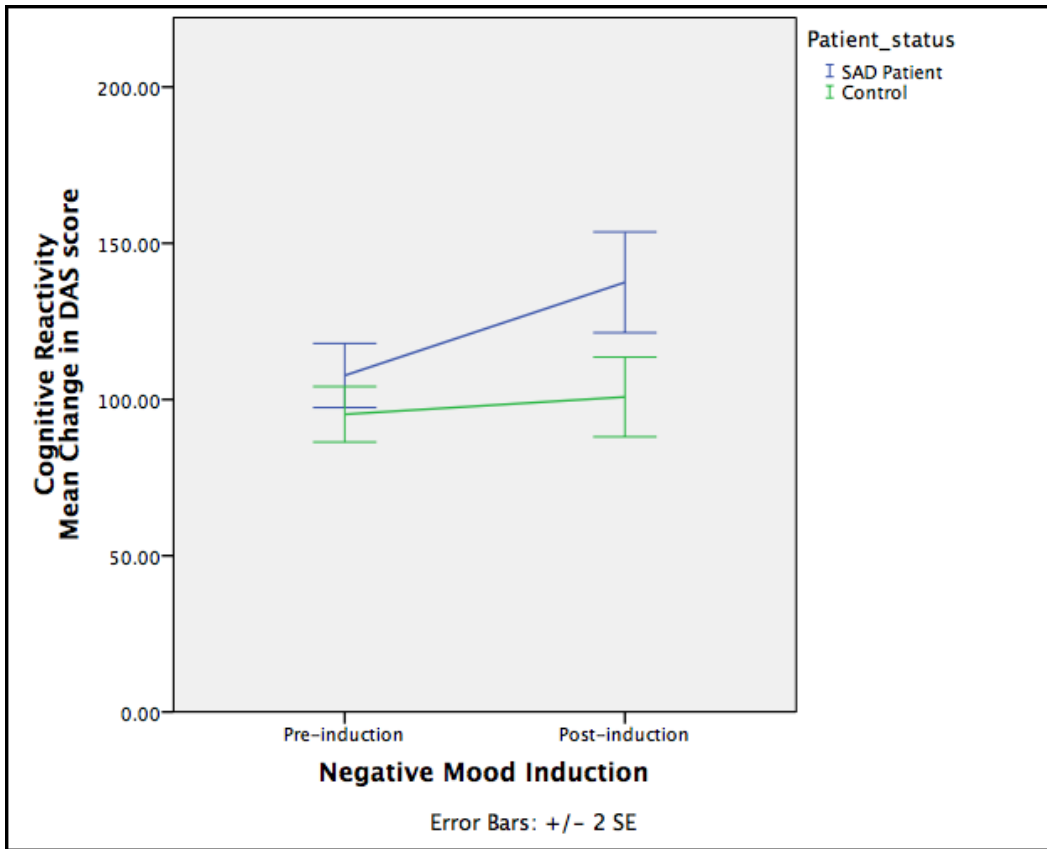
Figure 9. *Cognitive Reactivity* = DAS change from pre- to post- negative mood induction. *DAS* = Dysfunctional Attitudes Scale, Form A (Weissman & Beck, 1978). Cognitive reactivity in response to a negative mood induction, as illustrated by patient status. SAD patients exhibited a unique increase in dysfunctional attitudes (i.e., cognitive reactivity) from pre- to post- negative mood induction. SAD patients also endorsed a significantly greater mean level of cognitive reactivity at post-induction only, relative to controls.

Figure 10

Dysfunctional Attitudes Scale by Patient Status and Season
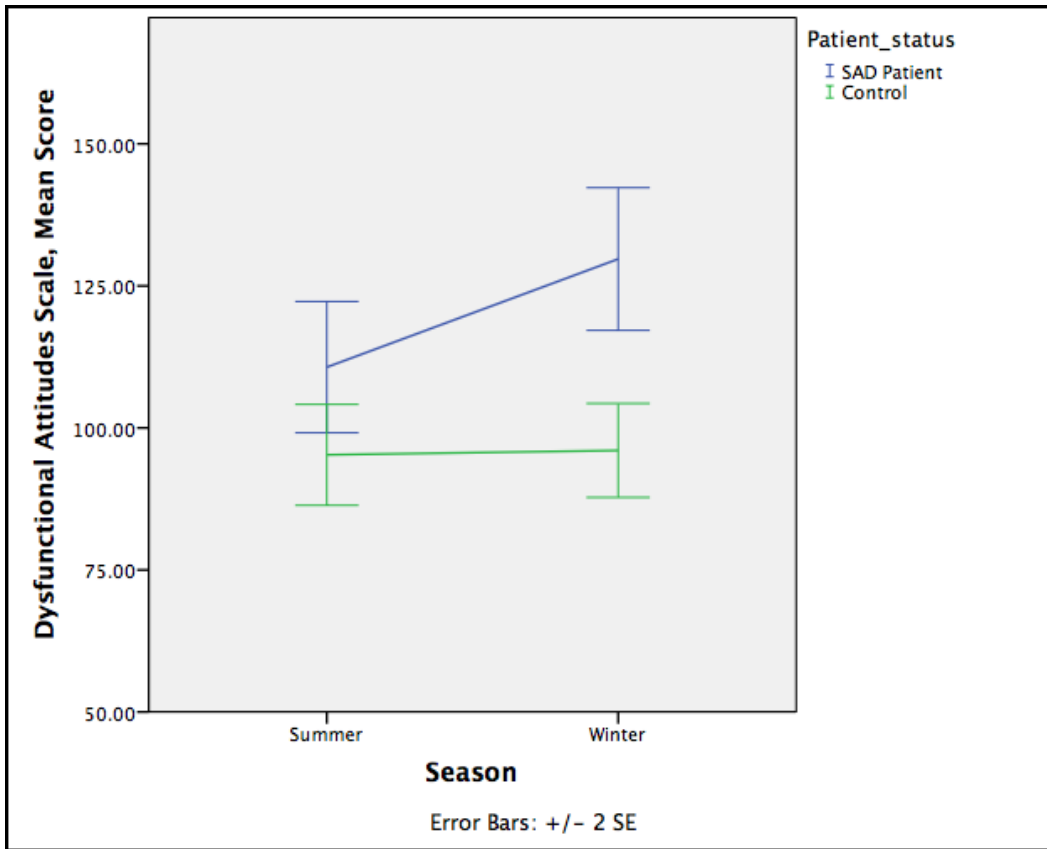
Figure 10. *DAS* = Dysfunctional Attitude Scale (Weissman & Beck,1978). Estimated marginal mean DAS scores by patient status and season, indicating that SAD patients exhibit unique seasonal variation in dysfunctional attitudes. Winter scores were significantly different from summer scores for patients only. Patients endorsed significantly greater levels than controls in both summer and winter, with a greater between-group difference in winter.

Figure 11

Seasonal Beliefs Questionnaire by Patient Status and Season
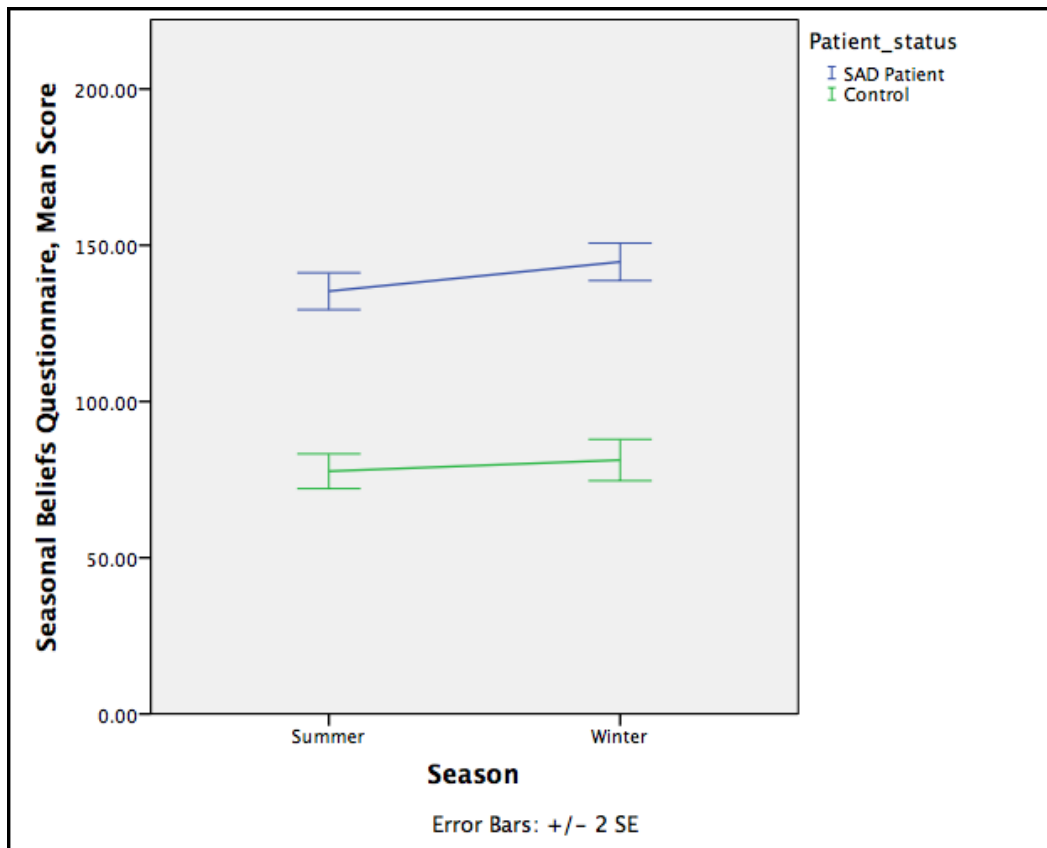
Figure 11. *SBQ* = Seasonal Beliefs Questionnaire (Rohan, Nillni, Lippy, Roecklein, & Hillhouse, 2007) estimated marginal means by patient status and season, depicting that SAD patients endorse greater seasonal beliefs than controls, collapsing across seasons. Additionally, there was significant seasonal variation, as both patients and controls endorsed greater SBQ scores in winter, relative to summer.

Figure 12

SIGH-SAD (SQRT) Estimated Marginal Means by Patient Status and Season

Figure 12. *SIGH-SAD* = Structured Interview Guide for the Hamilton Depression Rating Scale, Seasonal Affective Disorder Version (Williams et al., 1992). Square-root transformed SIGH-SAD estimated marginal means depicting unique seasonal variation by SAD patient relative to controls, with averaged patient scores significantly greater in winter, yet comparable in summer, as characteristic of SAD. Error bars represent standard errors.

Figure 13

BDI-II (SQRT) Estimated Marginal Means by Patient Status and Season
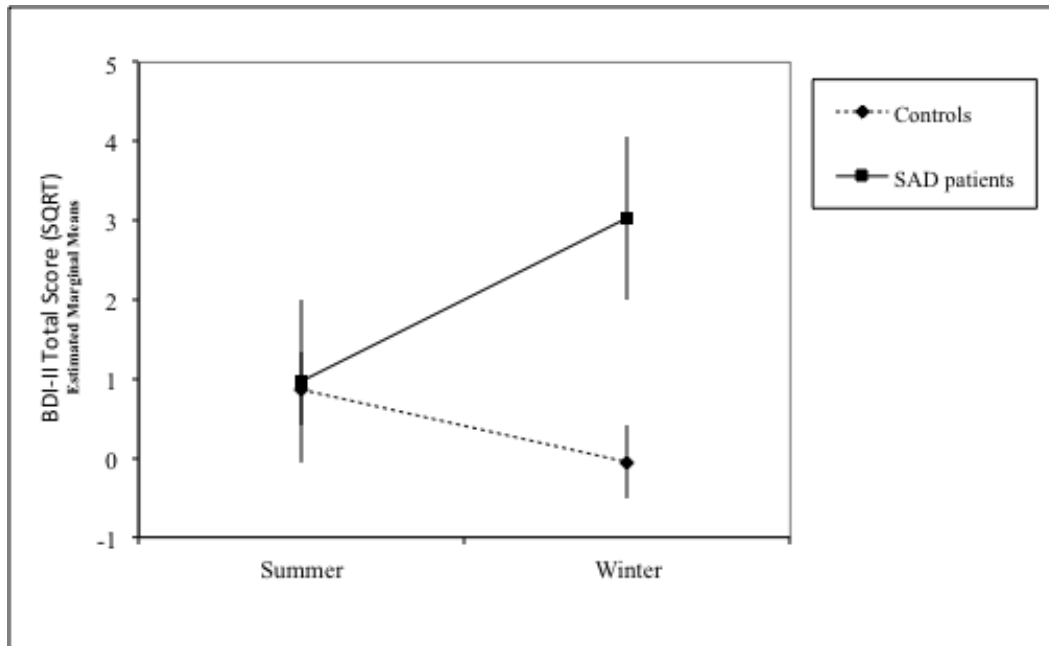
Figure 13. *BDI-II* = Beck Depression Inventory – II (Beck, Steer, & Brown, 1996).
BDI-II square root transformed estimated marginal means display a unique seasonal
variation in BDI-II core by SAD patients, with significant greater depression in winter,
as characteristic of SAD. Error bars represent standard errors.

Figure 14

BDI-II (SQRT) by State Brooding Rumination and Patient status
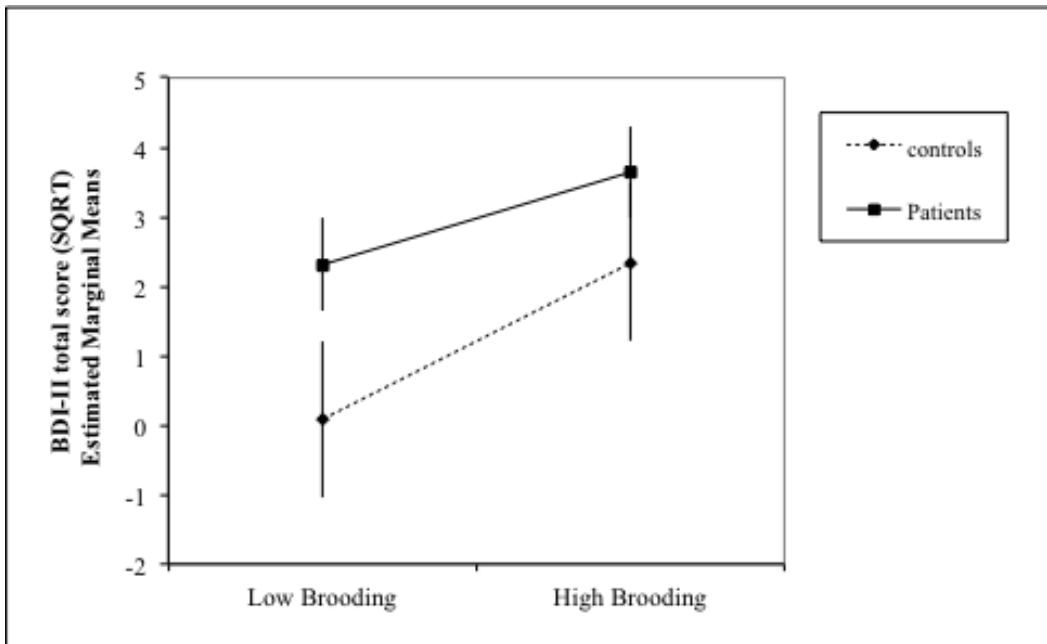
Figure 14. *BDI-II* = Beck Depression Inventory – II (Beck, Steer, & Brown, 1996); Brooding subscale of Ruminative Response Scale (Treynor et al., 2003). BDI-II square root transformed estimated marginal means display variation in BDI-II (SQRT) score by state brooding rumination, whereby higher levels of brooding were significantly associated with greater levels of rumination, for both patients and controls. Contrary to the hypothesized effects, state brooding rumination was more strongly associated with depression severity within controls. Error bars represent standard errors.

Figure 15

BDI-II (SQRT) by State Rumination and Patient Status
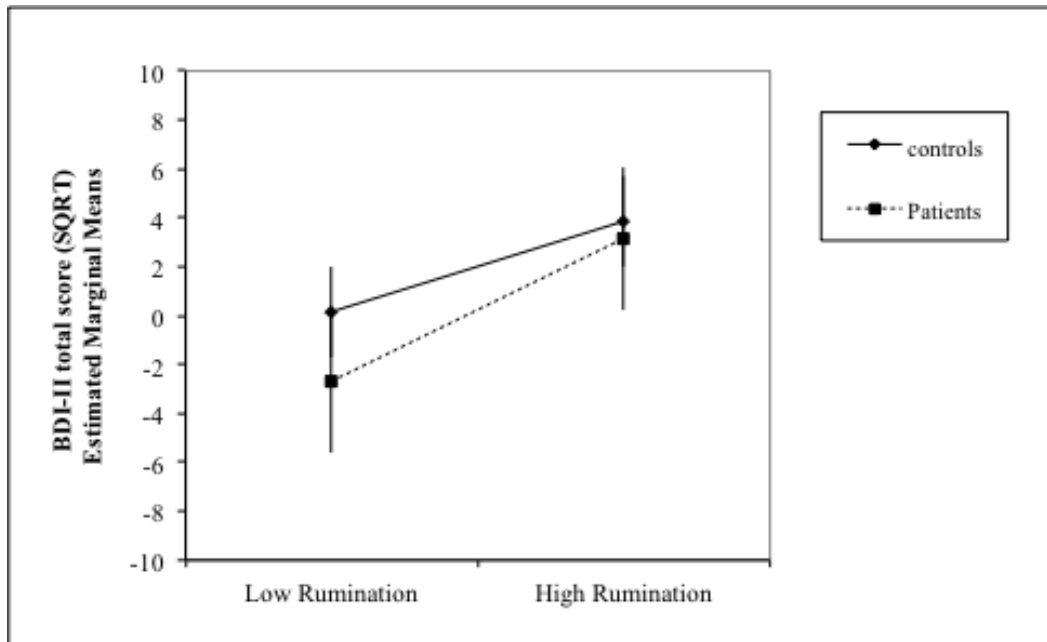
Figure 15. *BDI-II* = Beck Depression Inventory – II (Beck, Steer, & Brown, 1996); Ruminative Response Scale Total Score (Nolen-Hoeksema & Morrow, 1991). BDI-II square root transformed estimated marginal means display variation in BDI-II (SQRT) score by state rumination, whereby higher levels of brooding were significantly associated with greater levels of rumination, for both patients and controls, with a stronger effect within the patient group.

Figure 16

BDI-II (SQRT) by State Rumination and Season
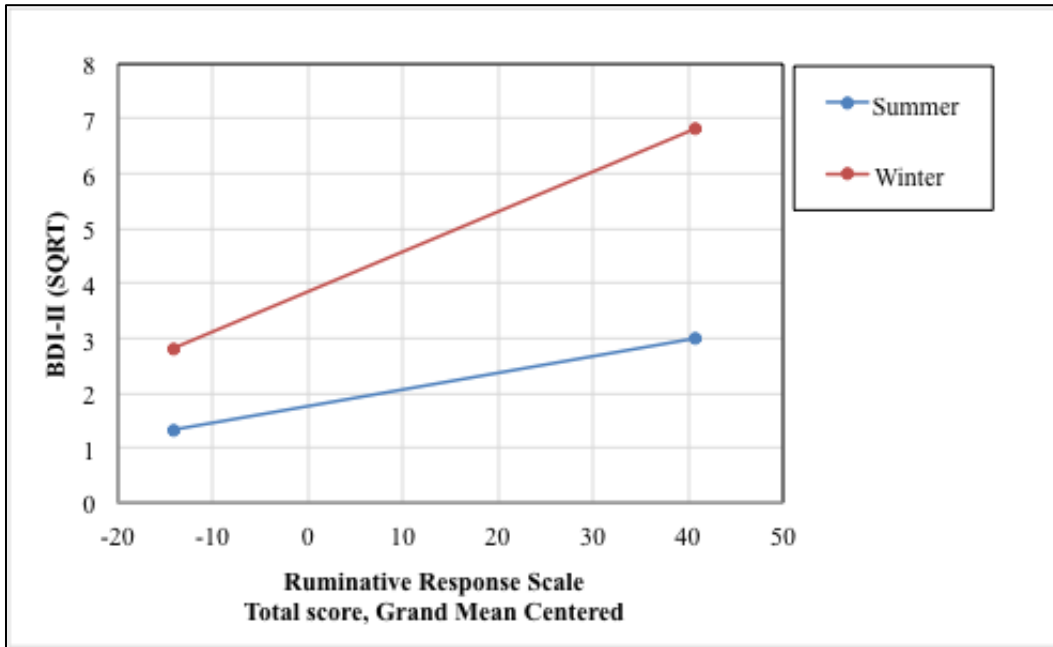
Figure 16. *BDI-II* = Beck Depression Inventory – II (Beck, Steer, & Brown, 1996); Ruminative Response Scale Total Score SQRT (Nolen-Hoeksema & Morrow, 1991). A 2-way interaction of state rumination by season on BDI-II (SQRT) revealed that rumination significantly predicted greater depression scores in winter only, with a trend toward significance in summer.

Figure 17

BDI-II (SQRT) by Dysfunctional Attitudes, Patient Status, and Season
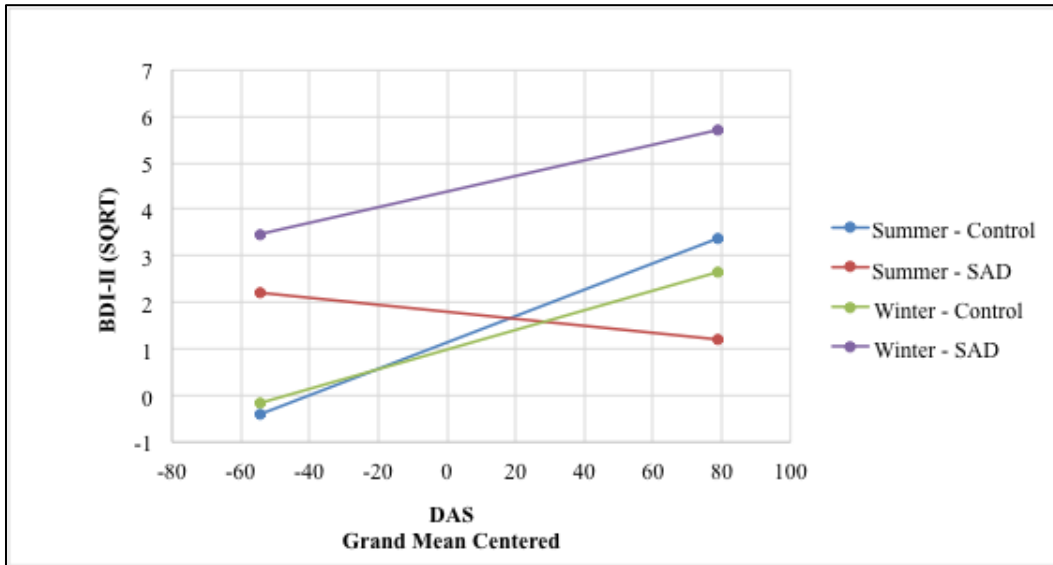
Figure 17. *BDI-II* = Beck Depression Inventory – II (Beck, Steer, & Brown, 1996); *DAS* = Dysfunctional Attitudes Scale (Weissman & Beck, 1978). BDI-II square root transformed estimated marginal means display a 3-way interaction, whereby the effect of DAS on BDI-II varied by patient status and season. DAS significantly predicts BDI-II severity for patients in winter, but not summer, whereas DAS predicts minimal BDI-II severity in controls year-round.

Figure 18

SIGH-SAD (SQRT) by Seasonal Beliefs, Patient Status, and Season
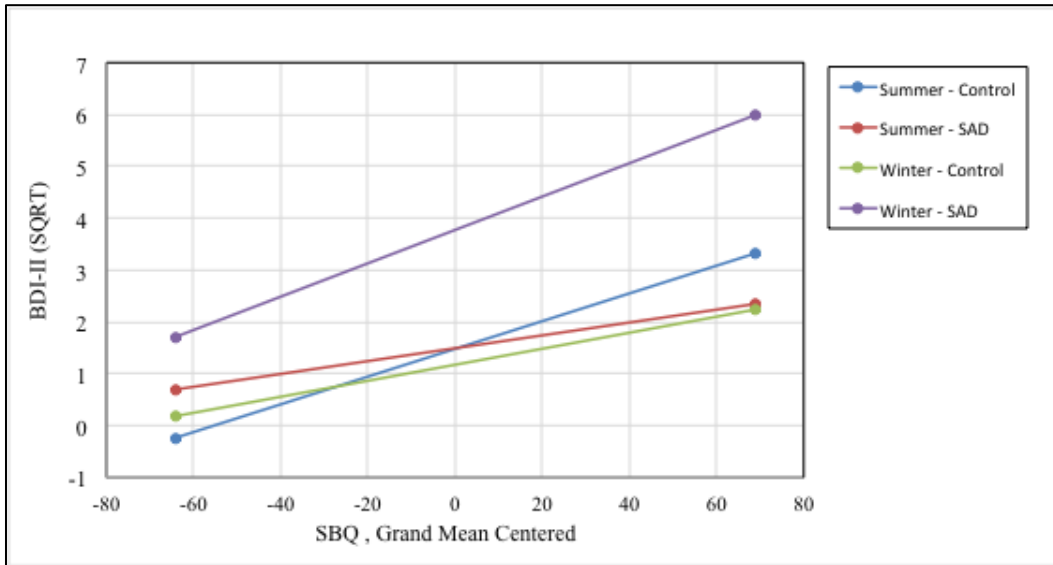
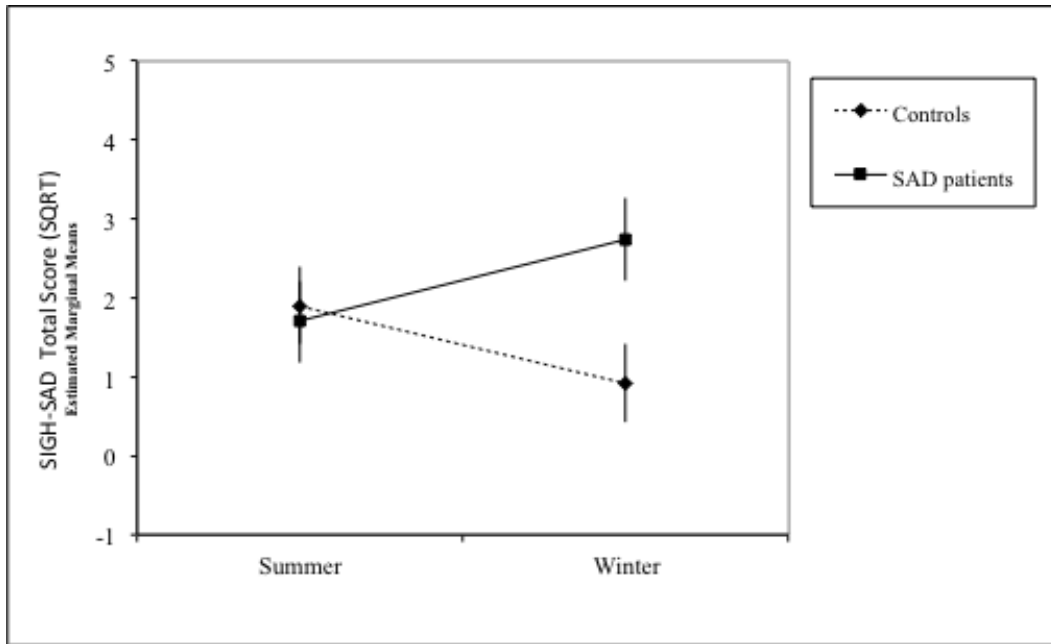Figure 18. *SIGH-SAD*: Structured Interview Guide for the Hamilton Depression Rating Scale, Seasonal Affective Disorder Version (Williams et al., 1992); *SBQ* = Seasonal Beliefs Questionnaire (Rohan, Nillni, Lippy, Roecklein, & Hillhouse, 2007). SIGH-SAD (SQRT) as predicted by SBQ by patient and season. SBQ was a significant predictor of depression for patients in winter, but not summer.

Table 1

Sample Characteristics

Characteristic	Total Sample (N = 64)	SAD (n = 31)	Controls (n = 33)	t/c^2	df	p
Age, Mean (SD)	45.5 (13.0)	49.0 (11.2)	42.2 (13.9)	2.2	61	.034
Sex, Number (%)				2.0	1	.161
Female	52 (81.3)	23 (74.2)	29 (87.9)			
Male	12 (18.8)	8 (25.8)	4 (12.1)			
Race, Number (%)				4.2*	1	.041
Caucasian	52 (81.3)	22 (71.0)	30 (90.9)			
African American	5 (7.8)	3 (9.7)	2 (6.1)			
American Indian	4 (6.3)	4 (12.9)				
Asian	2 (3.1)	1 (3.2)	1 (3.0)			
Hispanic	1 (1.6)	1 (3.2)				
SPAQ, Mean (SD)	9.1 (7.2)	5.8 (4.7)	3.3 (2.4)	12.9	40	.000
MEQ, Mean (SD)	53.9 (9.0)	51.6 (8.3)	56.1 (9.2)	-2.0	62	.044

Note. *The Chi square statistic reflects comparison of Caucasian vs. other between patients and controls. *SPAQ* = Seasonal Pattern Assessment Questionnaire (Rosenthal et al., 1987); *MEQ* = Morningness-Eveningness Questionnaire (Horne & Östberg, 1976).

Table 2

Patterns of Included Data (N = 64)

	Summer		Winter	
	SAD (*n* = 28)	Controls (*n* = 25)	SAD (*n* = 23)	Controls (*n* = 31)
BDI-II, Number (%)	28 (90.3)	25 (75.8)	23 (74.2)	31 (93.9)
SIGH-SAD, Number (%)	27 (87.1)	25 (75.8)	23 (74.2)	31 (93.9)
RRS, Number (%)	28 (90.3)	25 (75.8)	22 (71.0)	31 (93.9)
DAS, Number (%)	26 (83.9)	23 (69.7)	22 (71.0)	29 (87.9)
Cognitive Reactivity, Number (%)	24 (77.4)	11 (33.3)	-	-
SBQ, Number (%)	28 (90.3)	25 (75.8)	23 (74.2)	31 (93.9)
MEQ, Number (%)	28 (90.3)	25 (75.8)	23 (74.2)	31 (93.9)
Midsleep, Number (%)	22 (71.0)	19 (57.6)	22 (71.0)	25 (75.8)
DLMO, Number (%)	19 (61.3)	17 (51.5)	19 (61.3)	21 (63.6)

PAD, Number (%)*	17 (54.8)	16 (48.5)	19 (61.3)	21 (63.6)

Note. *BDI-II* = Beck Depression Inventory – II (Beck, Steer, & Brown, 1996), *SIGH-SAD* = Structured Interview Guide for the Hamilton Depression Rating Scale, Seasonal Affective Disorder Version (Williams et al., 1992); *RRS* = Ruminative Response Scale (Nolen-Hoeksema & Morrow, 1991); *DAS* = Dysfunctional Attitudes Scale Form A (Weissman & Beck,1978); *SBQ* = Seasonal Beliefs Questionnaire (Rohan, Nillni, Lippy, Roecklein, & Hillhouse, 2007); *MEQ* = Morningness – Eveningness Questionnaire (Horne & Östberg, 1972); *Midsleep* = Midpoint of Sleep; *DLMO* = Dim Light Melatonin Onset; *PAD* = Phase Angle Difference. *PAD-6 calculations were derived from PAD data, therefore missing data patterns for PAD and PAD-6 are identical.

Table 3

Depression Outcome Variable Descriptives (N = 64)

	Summer		Winter	
	SAD (*n* = 28)	Controls (*n* = 25)	SAD (*n* = 23)	Controls (*n* = 31)
BDI-II				
Original Data				
Raw Mean (SD)	4.7 (4.2)	1.3 (2.1)	26.5 (8.7)	1.1 (1.9)
SQRT Mean (SD)	1.8 (1.2)	0.7 (1.0)	5.1 (0.8)	0.6 (0.9)
Imputed Data (*N* = 64)				
Raw Mean (SD)	4.5 (4.1)	1.7 (2.1)	22.8 (10.0)	1.8 (3.2)
SQRT Mean (SD)	1.8 (1.2)	0.9 (1.0)	4.7 (1.0)	0.8 (1.1)
SIGH-SAD				
Original Data				
Raw Mean (SD)	9.1 (4.1)	4.2 (3.8)	30.9 (6.8)	4.6 (3.4)
SQRT Mean (SD)	2.9 (0.8)	1.7 (1.3)	5.5 (0.6)	2.0 (0.8)
Imputed Data (*N* = 64)				
Raw Mean (SD)	8.8 (4.0)	4.7 (3.6)	26.9 (9.1)	5.3 (4.5)
SQRT Mean (SD)	2.8 (0.7)	1.9 (1.1)	5.1 (0.9)	2.1 (1.0)

Note: *BDI-II* = Beck Depression Inventory − II (Beck, Steer, & Brown, 1996); *SIGH-SAD* = Structured Interview Guide for the Hamilton Depression Rating Scale, Seasonal Affective Disorder Version (Williams et al., 1992); *SQRT* = Square root transformed Mean. Descriptive means of depression severity are presented by patient status and controls in summer and winter, with raw and transformed outcomes. Imputed data means reflect grand means across 20 imputations.

Table 4

Aim 1 Chronobiological Vulnerability Results, Estimated Marginal Means

	Summer		Winter	
	SAD (*n* = 22)	Controls (*n* = 19)	SAD (*n* = 22)	Controls (*n* = 25)
Midsleep, Mean (SE)	2.9 (0.1)	2.9 (0.2)	3.0 (0.2)	2.9 (0.2)
DLMO, Mean (SE)	20.9 (0.3)	20.4 (0.3)	20.8 (0.3)	20.1 (0.3)
PAD, Mean (SE)	6.0 (0.2)	6.5 (0.2)	6.3 (0.2)	6.9 (0.3)
PAD-6				
Raw Mean (SE)	0.6 (0.1)	1.1 (0.1)	1.1 (0.2)	1.2 (0.2)
SQRT, Mean (SE)	0.7 (0.1)	1.0 (0.1)	0.9 (0.1)	1.0 (0.1)

Note. Estimated marginal means of chronobiological vulnerabilities adjusted for significant influence by season and patient status in Aim 1 analyses. *Midsleep* = Midpoint of sleep; *DLMO* = Dim Light Melatonin Onset (3 pg/ml); *PAD* = Phase Angle Difference; *PAD-6* = Absolute deviation from PAD - 6 hr; *PAD-6 SQRT* = square root transformation of PAD-6.

Table 5

Aim 1 Cognitive Vulnerability Results, Estimated Marginal Means

	Summer		Winter	
	SAD (*n* = 28)	Controls (*n* = 25)	SAD (*n* = 23)	Controls (*n* = 31)
Brooding Rumination, Mean (SD)	4.8 (0.6)	1.2 (0.5)	7.3 (0.6)	1.1 (0.5)
RRS, Mean (SD)				
Raw	17.9 (1.6)	4.6 (1.6)	33.4 (1.6)	5.0 (1.4)
SQRT	4.0 (0.2)	1.8 (0.2)	5.6 (0.2)	1.9 (0.2)
SBQ, Mean (SD)	134.7 (3.1)	75.8 (3.0)	142.8 (3.5)	81.1 (3.2)
DAS, Mean (SD)	109.1 (4.9)	96.9 (5.0)	127.5 (4.9)	96.7 (4.5)
Cognitive Reactivity, Mean (SD)	27.6 (5.7)	6.3 (7.9)	-	-

Note. Estimated Marginal Means of cognitive vulnerabilities adjusted for significant influence by season and patient status in Aim 1 analyses. *Brooding Rumination* = Brooding subscale of the Ruminative Response Scale (Treynor et al., 2003); *RRS* = Ruminative Response Scale (Nolen-Hoeksema & Morrow, 1991); *SBQ* = Seasonal Beliefs Questionnaire (Rohan, Nillni, Lippy, Roecklein, & Hillhouse, 2007); *Cognitive Reactivity* = DAS change from pre- to post- negative mood induction. *DAS* = Dysfunctional Attitudes Scale, Form A (Weissman & Beck,1978).

Table 6

Zero-order Correlations between Depression Severity and Sample Variability

Variable	1	2	3	4	5	6	7	8	9	10
1. BDI-II, raw	1	.90**	.94**	.83**	-.16	.01	-.04	-.15	.16	-.17
2. SIGH-SAD, raw		1	.87**	.96**	-.16	.02	.00	-.11	.15	-.18*
3. BDI-II, SQRT			1	.85**	-.18*	.01	-.11	-.20*	.19*	-.17
4. SIGH-SAD, SQRT				1	-.13	.03	-.07	-.11	.17	-.18*
5. Study Site					1	.35**	-.33**	.28**	-.18*	-.07
6. Season Order						1	-.02	-.05	.12	-.21*
7. Completer Status							1	-.01	.06	.13
8. Sex								1	.34**	.52**
9. Age									1	.43**
10. MEQ										1

Note. *p* < .05; ***p* < .01. *BDI-II* = Beck Depression Inventory – II raw total score mean (Beck, Steer, & Brown, 1996); *SIGH-SAD* = Structured Interview Guide for the Hamilton Depression Rating Scale raw total score mean, Seasonal Affective Disorder Version (Williams et al., 1992); *BDI-II (SQRT)* = Square-root transformation of BDI-II total score mean; *SIGH-SAD (SQRT)* = Square root transformation of SIGH-SAD total score mean; *MEQ* = Morningness- Eveningness Questionnaire (Horne & Östberg, 1976). Coefficients reflect averaged estimates from imputed data.

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Table 7

Zero-order Correlations of Chronobiological Vulnerability Measures and Depression Severity (SQRT)

Variable	1	2	3	4	5	6	7	8	9	10	11	12
1. SIGH-SAD, summer	1	.47**	.56**	.52*	-.13	-.08	-.07	-.14	-.13	.09	-.23	-.19
2. SIGH-SAD, winter		1	.34**	.91**	-.04	.08	.01	-.003	-.06	.04	-.16	-.28*
3. BDI-II, summer			1	.45**	-.02	-.06	-.11	-.14	.05	.11	-.31**	-.28
4. BDI-II, winter				1	-.01	.05	-.03	-.06	.02	.11	-.30*	-.29*
5. Midsleep, summer					1	.50**	.19	.24	.21	.06	-.07	-.08
6. Midsleep, winter						1	.11	.29	.13	.03	.03	-.17
7. DLMO, summer							1	.35**	-.36**	-.29	.10	.06
8. DLMO, winter								1	-.10	-.58**	.07	-.06
9. PAD, summer									1	.25	-.19	-.03
10. PAD, winter										1	-.07	-.08
11. PAD-6, summer											1	.04
12. PAD-6, winter												1

Note. *p < .05; **p < .01. *PAD* = Phase Angle Difference; *PAD-6* = Phase Angle Difference absolute deviation from 6 hr; *DLMO* = Dim Light Melatonin Onset; *Midsleep* = Midpoint of sleep episode; *BDI-II* = Beck Depression Inventory – II (Beck, Steer, & Brown, 1996),

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SIGH-SAD = Structured Interview Guide for the Hamilton Depression Rating Scale, Seasonal Affective Disorder Version (Williams et al., 1992). Correlations reflect imputed estimates. BDI-II and SIGH-SAD scores were square-root transformed outcomes for Aim 2 analyses.

Table 8

Zero-order Correlations of Cognitive Vulnerability Measures and Depression Severity (SQRT)

Variable	1	2	3	4	5	6	7	8	9	10	11	12	13
1. SIGH-SAD, summer	1	.47**	.56**	.52**	.52**	.44*	.48**	.48**	.43**	.29*	.02	.23	.32*
2. SIGH-SAD, winter		1	.34	.91**	.47**	.71**	.49**	.83**	.71**	.86**	.16	.31*	.61**
3. BDI-II, summer			1	.45**	.34*	.27*	.34**	.33**	.45**	.27*	.17	.16	.24
4. BDI-II, winter				1	.49**	.76**	.51**	.87**	.67**	.87**	.18	.29*	.61**
5. BR, summer					1	.61**	.89**	.63**	.55**	.43**	-.03	.45**	.46*
6. BR, winter						1	.57**	.92**	.56**	.64**	.09	.44**	.60**
7. RRS, summer							1	.63**	.60**	.43**	-.03	.42**	.49**
8. RRS, winter								1	.65**	.75**	.16	.41*	.64**
9. SBQ, summer									1	.74**	.22	.29*	.51**
10. SBQ, winter										1	.17	.27*	.57**
11. Cognitive Reactivity											1	-.25*	.12
12. DAS A, summer												1	.62**
13. DAS A, winter													1

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Note. *p < .05; **p < .01. *SIGH-SAD* = Structured Interview Guide for the Hamilton Depression Rating Scale, Seasonal Affective Disorder Version (Williams et al., 1992); *BDI-II* = Beck Depression Inventory-II Beck, Steer, & Brown, 1996); *BR* = Brooding subscale of Ruminative Response Scale (Treynor et al., 2003); *RRS* = Ruminative Response Scale (Nolen-Hoeksema & Morrow, 1991); *SBQ* = Seasonal Beliefs Questionnaire (Rohan, Nillni, Lippy, Roecklein, & Hillhouse, 2007), *Cognitive Reactivity* (i.e., mood induction DAS change score); *DAS* = Dysfunctional Attitudes Scale (Weissman & Beck,1978). Correlations reflect imputed estimates. BDI-II and SIGH-SAD scores were square-root transformed outcomes for Aim 2 analyses.

Table 9

Aim 2 Linear Mixed Modeling Results for Trait Brooding Rumination on SIGH-SAD (SQRT)

	Model 1*				Model 2				Model 3				Model 4			
	b	*SE*	*t*	*p*	*b*	*SE*	*t*	*p*	*b*	*SE*	*t*	*p*	*b*	*SE*	*t*	*p*
BR	0.1	0.04	2.3	.033	0.1	0.04	1.9	.073	0.003	0.1	0.1	.787	0.03	0.1	0.6	.552
BR*Group	-	-	-	-	0.04	0.1	0.5	.607	0.04	0.1	0.5	.607	-0.1	0.1	-0.9	.425
BR*Season	-	-	-	-	-	-	-	-	0.1	0.1	2.0	.063	0.1	0.1	1.1	.294
BR*Group*Season	-	-	-	-	-	-	-	-	-	-	-	-	0.3	0.2	1.8	.126

Note. *Best fitting model. BR* = Brooding rumination subscale of the Ruminative Response Scale (Treynor et al., 2003); *SIGH-SAD* = Structured Interview Guide for the Hamilton Depression Rating Scale, Seasonal Affective Disorder Version (Williams et al., 1992). Aim 2 Linear Mixed Modeling analyses examining the covariate effect of trait brooding rumination (i.e., RRS brooding subscale summer score) on SIGH-SAD square root transformed mean total scores.

Table 10

Aim 2 Linear Mixed Modeling Results for Trait Brooding Rumination on BDI-II (SQRT)

	Model 1*				Model 2				Model 3				Model 4			
	b	*SE*	*t*	*p*	*b*	*SE*	*t*	*p*	*b*	*SE*	*t*	*p*	*b*	*SE*	*t*	*p*
BR	0.1	0.1	1.1	.276	0.02	0.1	0.4	.726	-0.01	0.1	-0.1	.761	0.03	0.1	0.4	.648
BR*Group	-	-	-	-	0.2	0.1	1.7	.128	0.2	0.1	1.7	.128	-0.003	0.2	-0.02	.753
BR*Season	-	-	-	-	-	-	-	-	0.1	0.1	0.7	.516	-0.02	0.1	-0.3	.745
BR*Group*Season	-	-	-	-	-	-	-	-	-	-	-	-	0.4	0.2	2.0	.091

Note. *Best fitting model*. *BR* = Brooding rumination subscale of the Ruminative Response Scale, summer score (Treynor et al., 2003); *BDI-II* = Beck Depression Inventory – II (Beck, Steer, & Brown, 1996). Aim 2 Linear Mixed Modeling analyses examining the covariate effect of trait brooding rumination (i.e., RRS brooding subscale, summer score) on BDI-II square root transformed mean total scores.

Table 11

Aim 2 Linear Mixed Modeling Results for State Brooding Rumination on SIGH-SAD (SQRT)

	Model 1*				Model 2				Model 3				Model 4			
	b	*SE*	*t*	*p*	*b*	*SE*	*t*	*p*	*b*	*SE*	*t*	*p*	*b*	*SE*	*t*	*p*
BR	0.1	0.03	4.4	.0001	0.1	0.03	3.4	.002	0.1	0.04	2.7	.016	0.1	0.04	2.7	.014
BR*Group	-	-	-	-	0.2	0.1	1.8	.116	0.1	0.1	1.7	.123	0.1	0.1	1.0	.421
BR*Season	-	-	-	-	-	-	-	-	.001	0.1	0.2	.797	0.001	0.1	0.01	.859
BR*Group*Season	-	-	-	-	-	-	-	-	-	-	-	-	0.1	0.2	0.5	.633

Note. *Best fitting model.* *BR* = Brooding rumination subscale score of the Ruminative Response Scale total score (Treynor et al., 2003); *SIGH-SAD* = Structured Interview Guide for the Hamilton Depression Rating Scale, Seasonal Affective Disorder Version (Williams et al., 1992). Aim 2 Linear Mixed Modeling analyses examining the covariate effect of state brooding rumination (i.e., RRS brooding subscale, summer and winter scores) on SIGH-SAD square root transformed mean total scores.

Table 12

Aim 2 Linear Mixed Modeling Results for State Brooding Rumination on BDI-II (SQRT)

	Model 1*				Model 2				Model 3				Model 4			
	b	*SE*	*t*	*p*	*b*	*SE*	*t*	*p*	*b*	*SE*	*t*	*p*	*b*	*SE*	*t*	*p*
BR	0.2	0.3	4.9	.0001	0.1	0.04	3.5	.003	0.2	0.04	4.0	.001	0.2	0.04	4.0	.001
BR*Group	-	-	-	-	0.3	0.1	3.1	.008	0.3	0.1	3.4	.003	0.3	0.1	2.3	.043
BR*Season	-	-	-	-	-	-	-	-	-0.1	0.1	-2.0	.066	-0.1	0.1	-2.0	.054
BR*Group*Season	-	-	-	-	-	-	-	-	-	-	-	-	0.1	0.2	0.5	.577

Note. *Best fitting model. BR* = Brooding rumination subscale of the Ruminative Response Scale (Treynor et al., 2003); *BDI-II* = Beck Depression Inventory – II (Beck, Steer, & Brown, 1996). Aim 2 Linear Mixed Modeling analyses examining the covariate effect of state brooding rumination (i.e., RRS brooding subscale, summer and winter scores) on BDI-II square root transformed mean total scores.

Table 13

Aim 2 Linear Mixed Modeling Results for Trait Rumination on SIGH-SAD (SQRT)

	Model 1*				Model 2				Model 3				Model 4			
	b	SE	t	p	b	SE	t	p	b	SE	t	p	b	SE	t	p
RRS	0.02	0.01	1.8	.089	0.2	0.01	1.6	.124	0.001	0.01	0.1	.790	0.01	0.01	0.5	.604
RRS*Group	-	-	-	-	<.001	0.02	0.01	.774	-0.003	0.02	-0.01	.774	-0.03	0.03	-1.0	.346
RRS*Season	-	-	-	-	-	-	-	-	0.03	0.02	1.9	.399	0.02	0.02	1.0	.352
RRS*Group*Season	-	-	-	-	-	-	-	-	-	-	-	-	0.1	0.04	1.5	.168

Note. *Best fitting model. RRS = Ruminative Response Scale total score (Nolen-Hoeksema & Morrow, 1991); *SIGH-SAD* = Structured Interview Guide for the Hamilton Depression Rating Scale, Seasonal Affective Disorder Version (Williams et al., 1992). Aim 2 Linear Mixed Modeling analyses examining the covariate effect of trait rumination (i.e., RRS summer score) on SIGH-SAD square root transformed mean total scores.

Table 14

Aim 2 Linear Mixed Modeling results for trait rumination on BDI-II (SQRT)

	Model 1*				Model 2				Model 3				Model 4			
	b	SE	t	p	b	SE	t	p	b	SE	t	p	b	SE	t	p
RRS	0.01	0.01	0.9	.406	0.01	0.01	0.4	.696	-0.003	0.02	-0.2	.739	0.01	0.02	0.4	.711
RRS*Group	-	-	-	-	0.03	0.03	1.0	.365	-0.03	0.03	1.0	.365	-0.02	0.04	-0.6	.563
RRS*Season	-	-	-	-	-	-	-	-	0.02	0.02	1.9	.399	0.001	0.02	1.0	.793
RRS*Group*Season	-	-	-	-	-	-	-	-	-	-	-	-	0.1	0.04	2.2	.052

Note. *Best fitting model. RRS = Ruminative Response Scale total score (Nolen-Hoeksema & Morrow, 1991); BDI-II = Beck Depression Inventory – II (Beck, Steer, & Brown, 1996). Aim 2 Linear Mixed Modeling analyses examining the covariate effect of trait rumination (i.e., RRS summer score) on BDI-II square root transformed mean total scores.

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Table 15

Aim 2 Linear Mixed Modeling Results for State Rumination on SIGH-SAD (SQRT)

	Model 1*				Model 2				Model 3				Model 4			
	b	SE	t	p	b	SE	t	p	b	SE	t	p	b	SE	t	p
RRS	0.04	0.01	5.1	.0001	0.04	0.01	4.1	.0001	0.04	0.01	4.1	.0001	0.04	0.01	3.9	.979
RRS*Group	-	-	-	-	0.03	0.02	1.6	.149	0.04	0.02	1.7	.122	0.04	0.03	1.3	.219
RRS*Season	-	-	-	-	-	-	-	-	-0.02	0.02	-1.2	.234	-0.02	0.02	-1.1	.300
RRS*Group*Season	-	-	-	-	-	-	-	-	-	-	-	-	-0.01	0.04	-0.2	.766

Note. *Best fitting model. RRS* = Ruminative Response Scale total score (Nolen-Hoeksema & Morrow, 1991); *SIGH-SAD* = Structured Interview Guide for the Hamilton Depression Rating Scale, Seasonal Affective Disorder Version (Williams et al., 1992). Aim 2 Linear Mixed Modeling analyses examining the covariate effect of state rumination (i.e., RRS summer and winter scores) on SIGH-SAD square root transformed mean total scores.

Table 16

Aim 2 Linear Mixed Modeling Results for State Rumination on BDI-II (SQRT)

	Model 1				Model 2				Model 3*				Model 4			
	b	*SE*	*t*	*p*	*b*	*SE*	*t*	*p*	*b*	*SE*	*t*	*p*	*b*	*SE*	*t*	*p*
RRS	0.1	0.01	6.5	.0001	0.1	0.01	5.2	.0001	0.1	0.01	5.9	.0001	0.1	0.1	5.9	.0001
RRS*Group	-	-	-	-	0.1	0.02	3.1	.006	0.1	0.02	3.4	.004	0.1	0.03	2.5	.036
RRS*Season	-	-	-	-	-	-	-	-	-0.04	0.02	-2.9	.006	-0.1	0.02	-2.9	.007
RRS*Group*Season	-	-	-	-	-	-	-	-	-	-	-	-	0.02	0.04	0.4	.572

Note. *Best fitting model*. *RRS* = Ruminative Response Scale total score (Nolen-Hoeksema & Morrow, 1991); *BDI-II* = Beck Depression Inventory – II (Beck, Steer, & Brown, 1996). Aim 2 Linear Mixed Modeling analyses examining the covariate effect of state rumination (i.e., RRS summer and winter scores) on BDI-II square root transformed mean total scores.

Table 17

Aim 2 Linear Mixed Modeling Results for Cognitive Reactivity on SIGH-SAD (SQRT)

	Model 1*				Model 2				Model 3				Model 4			
	b	*SE*	*t*	*p*	*b*	*SE*	*t*	*p*	*b*	*SE*	*t*	*p*	*b*	*SE*	*t*	*p*
CR	-0.001	0.00	-0.2	.749	0.00	0.003	0.02	.773	0.002	0.00	0.4	.644	0.001	0.00	0.4	.643
CR*Group	-	-	-	-	-0.01	0.01	-1.1	.295	-0.01	0.01	-1.1	.295	-0.01	0.01	-0.7	.492
CR*Season	-	-	-	-	-	-	-	-	-0.003	0.01	-0.6	.594	-0.003	0.01	-0.5	.635
CR*Group*Season	-	-	-	-	-	-	-	-	-	-	-	-	-0.003	0.02	-0.2	.734

Note. *Best fitting model. CR* = Cognitive reactivity (i.e., DAS change from pre- to post- negative mood induction); *SIGH-SAD* = Structured Interview Guide for the Hamilton Depression Rating Scale, Seasonal Affective Disorder Version (Williams et al., 1992). Aim 2 Linear Mixed Modeling analyses examining the covariate effect of cognitive reactivity on SIGH-SAD square root transformed mean total scores.

Table 18

Aim 2 Linear Mixed Modeling Results for Cognitive Reactivity on BDI-II (SQRT)

	Model 1*				Model 2				Model 3				Model 4			
	b	SE	t	p	b	SE	t	p	b	SE	t	p	b	SE	t	p
CR	0.003	0.003	0.9	.410	0.004	0.004	1.6	.260	0.003	0.01	0.7	.521	0.003	0.01	0.7	.501
CR*Group	-	-	-	-	-0.02	0.01	-1.3	.239	-0.02	0.01	-1.3	.239	-0.02	0.02	-1.1	.288
CR*Season	-	-	-	-	-	-	-	-	0.002	0.01	0.4	.674	0.002	0.01	0.3	.727
CR*Group*Season	-	-	-	-	-	-	-	-	-	-	-	-	0.004	0.02	0.2	.712

Note. *Best fitting model.* CR = Cognitive reactivity (i.e., DAS change from pre- to post- negative mood induction); *BDI-II* = Beck Depression Inventory – II (Beck, Steer, & Brown, 1996). Aim 2 Linear Mixed Modeling analyses examining the covariate effect of cognitive reactivity on BDI-II square root transformed mean total scores.

Table 19

Aim 2 Linear Mixed Modeling Results for Dysfunctional Attitudes on SIGH-SAD (SQRT)

	Model 1*				Model 2				Model 3				Model 4			
	b	*SE*	*t*	*p*	*b*	*SE*	*t*	*p*	*b*	*SE*	*t*	*p*	*b*	*SE*	*t*	*p*
DAS	0.01	0.00	3.4	.001	0.01	0.00	2.3	.025	0.02	0.01	2.9	.006	0.02	0.01	2.9	.006
DAS*Group	-	-	-	-	0.004	0.01	0.6	.554	0.003	0.01	0.5	.650	0.001	0.01	0.02	.904
DAS*Season	-	-	-	-	-	-	-	-	-0.01	0.01	-1.7	.094	-0.01	0.01	-1.7	.094
DAS*Group*Season	-	-	-	-	-	-	-	-	-	-	-	-	0.01	0.01	0.6	.585

Note. *Best fitting model. DAS* = Dysfunctional Attitudes Scale, total score (Weissman & Beck,1978); *SIGH-SAD* = Structured Interview Guide for the Hamilton Depression Rating Scale, Seasonal Affective Disorder Version (Williams et al., 1992). Aim 2 Linear Mixed Modeling analyses examining the covariate effect of DAS scores on SIGH-SAD square root transformed mean total scores.

Table 20

Aim 2 Linear Mixed Modeling results for dysfunctional attitudes on BDI-II (SQRT)

	Model 1*				Model 2				Model 3				Model 4			
	b	*SE*	*t*	*p*	*b*	*SE*	*t*	*p*	*b*	*SE*	*t*	*p*	*b*	*SE*	*t*	*p*
DAS	0.01	0.00	3.1	.002	0.02	0.01	1.0	.342	0.01	0.00	1.8	.074	0.02	0.01	2.6	.013
DAS*Group	-	-	-	-	0.02	0.01	2.5	.015	0.02	0.01	2.3	.029	0.004	0.01	0.4	.675
DAS*Season	-	-	-	-	-	-	-	-	-0.01	0.01	-1.9	.069	-0.02	0.01	-2.9	.006
DAS*Group*Season	-	-	-	-	-	-	-	-	-	-	-	-	0.03	.01	2.3	.028

Note. *Best fitting model. DAS = Dysfunctional Attitudes Scale, total score (Weissman & Beck,1978); *BDI-II* = Beck Depression Inventory – II (Beck, Steer, & Brown, 1996). Aim 2 Linear Mixed Modeling analyses examining the covariate effect of DAS scores on BDI-II square root transformed mean total scores.

Table 21

Aim 2 Linear Mixed Modeling results for seasonal beliefs on SIGH-SAD (SQRT)

	Model 1				Model 2				Model 3*				Model 4			
	b	*SE*	*t*	*p*	*b*	*SE*	*t*	*p*	*b*	*SE*	*t*	*p*	*b*	*SE*	*t*	*p*
SBQ	0.02	0.0	5.2	.0001	0.02	0.01	3.6	.0001	0.03	0.01	5.0	.0001	0.03	0.01	-4.8	.0001
SBQ*Group	-	-	-	-	0.00	0.01	-0.1	.951	0.00	0.01	-0.1	.757	-0.01	0.01	-1.3	.217
SBQ*Season	-	-	-	-	-	-	-	-	-0.02	0.3	-1.0	.363	-0.04	0.01	-4.1	.001
SBQ*Group*Season	-	-	-	-	-	-	-	-	-	-	-	-	0.03	0.01	2.2	.043

*Note. *Best fitting model*. SBQ* = Seasonal Beliefs Questionnaire, total score (Rohan, Nillni, Lippy, Roecklein, & Hillhouse, 2007); *SIGH-SAD* = Structured Interview Guide for the Hamilton Depression Rating Scale, Seasonal Affective Disorder Version (Williams et al., 1992). Aim 2 Linear Mixed Modeling analyses examining the covariate effect of seasonal beliefs on SIGH-SAD square root transformed mean total scores.

Table 22

Aim 2 Linear Mixed Modeling Results for Seasonal Beliefs on BDI-II (SQRT)

	Model 1*				Model 2				Model 3				Model 4			
	b	*SE*	*t*	*p*	*b*	*SE*	*t*	*p*	*b*	*SE*	*t*	*p*	*b*	*SE*	*t*	*p*
SBQ	0.02	0.0	4.7	.0001	0.02	0.01	3.1	.002	0.03	0.01	3.5	.001	0.03	0.01	4.1	.0001
SBQ*Group	-	-	-	-	0.02	0.01	-0.4	.662	-0.003	0.01	-0.4	.674	-0.02	0.01	-1.5	.164
SBQ*Season	-	-	-	-	-	-	-	-	-0.01	0.01	-0.9	.417	-0.02	0.01	-1.9	.073
SBQ*Group*Season	-	-	-	-	-	-	-	-	-	-	-	-	0.03	0.02	2.0	.710

Note. *Best fitting model. SBQ = Seasonal Beliefs Questionnaire, total score (Rohan, Nillni, Lippy, Roecklein, & Hillhouse, 2007); BDI-II = Beck Depression Inventory – II (Beck, Steer, & Brown, 1996). Aim 2 Linear Mixed Modeling analyses examining the covariate effect of seasonal beliefs on BDI-II square root transformed mean total scores.

Table 23

Aim 2 Linear Mixed Modeling Results for Phase Angle Difference on SIGH-SAD (SQRT)

	Model 1*				Model 2				Model 3				Model 4			
	b	*SE*	*t*	*p*	*b*	*SE*	*t*	*p*	*b*	*SE*	*t*	*p*	*b*	*SE*	*t*	*p*
PAD	-0.03	0.1	-0.5	.504	0.04	0.1	0.4	.589	0.1	0.1	0.9	.419	0.1	0.2	0.3	.512
PAD*Group	-	-	-	-	-0.1	0.2	-0.7	.515	-0.1	0.2	-0.8	.482	-0.01	0.2	-0.1	.568
PAD*Season	-	-	-	-	-	-	-	-	-0.2	0.1	-1.2	.309	-0.01	0.2	-0.1	.604
PAD*Group*Season	-	-	-	-	-	-	-	-	-	-	-	-	-0.2	0.3	0.7	.495

Note. *Best fitting model. PAD* = Phase Angle Difference (hr), DLMO (3 pg/ml) to Midsleep; *SIGH-SAD* = Structured Interview Guide for the Hamilton Depression Rating Scale, Seasonal Affective Disorder Version (Williams et al., 1992). Aim 2 Linear Mixed Modeling analyses examining the covariate effect of PAD on SIGH-SAD square root transformed mean total scores.

Table 24

Aim 2 Linear Mixed Modeling Results for Phase Angle Difference on BDI-II (SQRT)

	Model 1*				Model 2				Model 3				Model 4			
	b	SE	t	p	b	SE	t	p	b	SE	t	p	b	SE	t	p
PAD	0.7	0.1	1.1	.361	-0.04	0.1	-0.3	.757	0.2	0.2	1.3	.318	0.3	0.2	1.4	.262
PAD*Group	-	-	-	-	0.1	0.2	0.7	.464	-0.1	0.2	-0.6	.544	-0.2	0.2	-0.8	.512
PAD*Season	-	-	-	-	-	-	-	-	-0.1	0.2	-0.6	.517	-0.2	0.3	-0.8	.443
PAD*Group*Season	-	-	-	-	-	-	-	-	-	-	-	-	0.2	0.3	0.6	.536

Note. *Best fitting model. PAD* = Phase Angle Difference (hr), DLMO (3 pg/ml) to Midsleep; *BDI-II* = Beck Depression Inventory – II (Beck, Steer, & Brown, 1996). Aim 2 Linear Mixed Modeling analyses examining the covariate effect of PAD on BDI-II square root transformed mean total scores.

Table 25

Aim 2 Linear Mixed Modeling results for Deviation from Phase Angle Difference - 6 hr on SIGH-SAD (SQRT)

	Model 1*				Model 2				Model 3				Model 4			
	b	*SE*	*t*	*p*	*b*	*SE*	*t*	*p*	*b*	*SE*	*t*	*p*	*b*	*SE*	*t*	*p*
PAD-6	-0.2	0.1	-1.4	.230	-0.1	0.2	-0.3	.601	0.2	0.2	0.1	.624	0.2	0.3	0.5	.481
PAD-6*Group	-	-	-	-	-0.2	0.2	-0.7	.477	-0.2	0.2	-0.8	.444	-0.4	0.3	-1.1	.309
PAD-6*Season	-	-	-	-	-	-	-	-	-0.1	0.2	-0.6	.532	-0.4	0.4	-1.0	.373
PAD-6*Group*Season	-	-	-	-	-	-	-	-	-	-	-	-	0.4	0.5	0.8	.449

Note. *Best fitting model*. *PAD-6* = Absolute deviation from a Phase Angle Difference of 6 hr, DLMO to Midsleep; *SIGH-SAD* = Structured Interview Guide for the Hamilton Depression Rating Scale, Seasonal Affective Disorder Version (Williams et al., 1992). Aim 2 Linear Mixed Modeling analyses examining the covariate effect of PAD-6 on square root transformed SIGH-SAD mean total scores.

Table 26

Aim 2 Linear Mixed Modeling Results for Deviation from Phase Angle Difference - 6 hr on BDI-II (SQRT)

	Model 1*				Model 2				Model 3				Model 4			
	b	*SE*	*t*	*p*	*b*	*SE*	*t*	*p*	*b*	*SE*	*t*	*p*	*b*	*SE*	*t*	*p*
PAD-6	-0.2	0.1	-1.5	.226	-0.2	0.2	-0.9	.463	-0.1	0.3	-0.2	.679	0.2	0.3	0.5	.519
PAD-6*Group	-	-	-	-	-0.01	0.3	-0.04	.634	-0.03	0.3	-0.1	.626	-0.4	0.4	-1.0	.397
PAD-6*Season	-	-	-	-	-	-	-	-	-0.3	0.3	-1.0	.363	-0.7	0.4	-1.6	.195
PAD-6*Group*Season	-	-	-	-	-	-	-	-	-	-	-	-	0.7	0.6	1.2	.283

Note. *Best fitting model. PAD-6 = Absolute deviation from a Phase Angle Difference of 6 hr, DLMO to Midsleep; *BDI-II* = Beck Depression Inventory – II (Beck, Steer, & Brown, 1996). Aim 2 Linear Mixed Modeling analyses examining the covariate effect of PAD-6 on square root transformed BDI-II mean total scores.