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Seasonality and circadian preference in adult attention-deficit/hyperactivity disorder: clinical and neuropsychological correlates

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Abstract

Objective: The objective of the study was to measure both seasonal mood change and circadian preference, and their clinical and neuropsychological correlates, in adults with ADHD during the fall/winter months.

Method: Twenty-nine adults with attention-deficit/hyperactivity disorder (ADHD) were assessed in the fall/winter season using self-report measures of ADHD, mood, seasonality, and circadian preference. Neuropsychological tests were also completed. Correlations between chronobiologic variables and clinical/neuropsychological measures were performed.

Results: Consistent with prior work in adult ADHD, high rates of seasonal depression were reported in this sample. Based on the morningness-eveningness questionnaire, which assesses circadian preference 11 (40.7%, N = 27) subjects were designated as evening types and only 5 (18.5%) as morning types, a distribution highly discrepant with general population studies. Later circadian preference, independent of seasonality, was strongly correlated with both self-reported symptoms of ADHD and neuropsychological deficits, including impulsive responding and poor target discrimination. None of these findings was attributable to state depression.

Conclusions: In the fall/winter period, a mood-independent delay in circadian phase may contribute significantly to core pathology in many adults with ADHD. These findings establish a potential target for chronobiologic treatments such as light therapy in this complex population.

1. Introduction

It is now well established that most children with attention-deficit/hyperactivity disorder (ADHD) go on to have residual symptoms into late adolescence and adulthood [1]. Whereas the core symptoms of inattention and hyperactivity are the primary reasons for seeking psychiatric help in childhood, in adulthood, it is often the affective disturbances and deficits in arousal and executive functioning that lead patients to seek treatment. The mainstay of current treatment for adult ADHD is thus some combination of antidepressants and/or psychostimulants.

Emerging evidence suggests that chronobiologic disturbances may also contribute to the pathophysiology and disability associated with ADHD in various age groups. For example, many patients with ADHD have marked difficulties with falling asleep, morning awakening, and/or maintaining daytime alertness [2]. This alteration in daily activity rhythms can cause significant dysfunction in a society where a 9-to-5 schedule is the norm, contributing to truancy in teenagers and deficits in work attendance and performance in adults. In many cases, it may lead to job loss. Another chronobiologic factor that may compound this problem is winter seasonal affective disorder (SAD), a mood disorder characterized by hypersomnia and fatigue in most patients. Clinical, epidemiological, and pathophysiologic links between ADHD, SAD, and circadian rhythms have previously been described [3,4], including a possible genetic relationship related to the dopamine 4 receptor gene [5].

Although clinically, chronobiologic factors appear to contribute significantly to the disability associated with ADHD, few studies to date have focused on this area. The goals of the current study were to (1) quantify seasonal mood change and circadian preference in a heterogeneous sample of adults with ADHD in the fall/winter months and (2) assess how these chronobiologic factors relate to subjective and neuropsychological functioning. A 3-week trial of morning bright light therapy to reverse chronobiologic deficits was also administered, with results summarized in a separate article [6]. We report here results of our descriptive study in a sample of 29 adults with ADHD.

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2. Method

2.1. Subject recruitment and diagnostic assessment procedure

Recruitment was conducted via notices referring to a "novel nonpharmacologic treatment study of adult ADHD" posted on local internet sites and via posters and pamphlets distributed at local clinics and organizations working with adult clients with ADHD. To limit a possible recruitment bias favoring patients with seasonal fluctuations in mood and/or ADHD symptoms, there was no mention of seasonality or light therapy. At the time of consent, no potential study participants dropped out once it was established that light therapy would be used.

Given the ultimate treatment focus on light therapy, recruitment was done in the late summer through late winter months. All potential participants underwent an initial telephone screen to confirm a history of ADHD in childhood and whether symptoms were ongoing.

Prospective study subjects were next invited to come to the Centre for Addiction and Mental Health (CAMH), Toronto, Ontario, Canada, for a more detailed assessment interview. All were given a consent form with a summary of the purposes, procedures, and potential risks of the study, and provided informed written consent. The protocol was approved by the CAMH research ethics board.

On the day of the structured assessment at CAMH, potential study subjects were administered 3 self-report ADHD scales, including the Wender Utah Rating Scale (WURS) [7] for childhood ADHD symptoms and both the Brown Adult ADD (attention deficit disorder) Scale [8] and the Conners Adult ADHD Rating Scale (CAARS) [9]. To delineate comorbidity, subjects were also administered a semistructured clinical interview by a trained research assistant who was blind to the results of the ADHD self-report scales. This interview included the modules from the Structured Clinical Interview for the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (*DSM-IV*) (SCID) [10] that assessed mood, anxiety, substance abuse, and eating disorders. The Structured Interview Guide for the Hamilton Depression Rating Scale, Seasonal Affective Disorders Version (SIGH-SAD) [11], was administered by a research fellow blinded to the SCID results to assess current mood symptoms. A detailed summary of the clinical rating scales used in this assessment process is included in the Appendix A.

Final inclusion criteria included the following. (1) Subjects should have had a clinical diagnosis of childhood ADHD established by a specialist in the field and/or a WURS score above established cutoffs on a validated 25-item subscale of the WURS [7], that is, higher than 46 for patients with a history of major depression and higher than 36 for subjects without major depression. (2) Subjects should have had a chronic course of ADHD symptoms from childhood to adulthood, with functional impairment attributed to those symptoms. (3) Subjects not taking psychostimulants had to meet current *DSM-IV* criteria for ADHD based on the CAARS as described. Consistent with prior research [12], subjects receiving psychostimulants who endorsed 3 to 5 of 9 possible *DSM-IV* items for the inattentive and/or hyperactive/impulsive categories were designated as having "ADHD in partial (therapeutic) remission." These individuals were included in the final sample if they met other study criteria. (4) Subjects should have an IQ within the normal range and (5) be able and willing to provide informed consent. Subjects were excluded if they had 1 or more of the following: (1) a North American Adult Reading Test (NAART) [13] estimated IQ below 85, (2) a significant neurologic disorder that would confound neuropsychological testing, (3) acute suicidal ideation, (4) current substance dependence, (5) an inability or unwillingness to provide informed consent, (6) previous exposure to light therapy, (7) current use of a photosensitizing drug such as lithium or the phenothiazines, and (8) retinal disorders.

To assess both seasonal mood change and circadian preference, individuals who continued to meet study criteria at the end of the structured assessment day were given a package of self-report questionnaires for completion at home. The primary instrument used to assess seasonality was the Seasonal Pattern Assessment Questionnaire (SPAQ) [14]. The SPAQ asks about seasonal changes in 6 core symptoms of SAD, each rated from 0 to 4 (none to severe), with a maximum "global seasonality score" or GSS of 24. The SPAQ also assesses to what extent seasonality is a problem and the months of the year during which symptoms are most severe. Full-syndrome SAD was also assessed during the SCID interview based on standard *DSM-IV* criteria.

Circadian preference was assessed using a brief self-report, the Horne-Ostberg Morningness-Eveningness Questionnaire (MEQ) [15], which asks about the timing of sleep/wake cycles and other activities. It correlates highly with objectively measured circadian rhythms [16] and has been used as a proxy for these rhythms in prior research [17].

Subjects were also asked to complete a self-report sleep/wake diary to be filled out daily for 1 week before and during a 3-week trial of light therapy; however, compliance was poor for this particular measure.

2.2. Neuropsychological tests

Neuropsychological testing was completed on a separate visit within 2 weeks of the first hospital-based assessment. A standard set of neuropsychological instruments was selected to gain a measure of general intellectual ability as well as domains implicated in ADHD. These tests are listed in Table 4 (for detailed descriptions of these tests, see Lezak et al [18]). The primary objective measure of attention was the Conners Continuous Performance Test (CPT-II) [19]. The Conners CPT-II is a computerized sustained-attention test that consists of a series of trials in which letter stimuli appear in rapid succession on a computer monitor. Participants are

Table 1
Sociodemographic characteristics and medications in 29 adults with ADHD

Variable	N	%
Age (y)		
20-29	4	13.8
30-39	12	41.4
40-49	7	24.1
50-60	6	20.7
Sex		
Male	15	51.7
Female	14	48.3
Marital status		
Married	11	37.9
Divorced or separated	1	3.5
Never married	17	58.6
Education		
High school	4	13.8
College/part-graduate professional school	23	79.3
Completed graduate school	2	6.9
Employment (current)		
Employed full-/part-time and students	21	72.4
Unemployed/retired	8	27.6
Medications (current)		
Stimulants only	7	24.1
Antidepressants only	4	13.8
Both antidepressants and stimulants	4	13.8
No medications	14	48.3

required to press the space bar for each letter that appears, except the letter X. Thus, a prepotent behavioral response must be withheld or inhibited on X trials. Increased errors of omission in which the bar press is not made when appropriate indicate that participants are not orienting to the task or that responses are overly slow and occur after the stimulus has offset. Errors of commission occur when participants hit the button on X trials, when they have been instructed to withhold responding. A high level of commission errors reflects impulsivity and poor response inhibition. Hit reaction time is the mean response time over trials in which a space bar press is appropriately made. High T-scores on this dimension reflect slow responding, whereas low T-scores indicate fast or impulsive responding. A measure of detectability (d′ or d prime) is also obtained from CPT-II responses. This measures how well the participant discriminates between target and nontarget stimuli, or the signal-to-noise ratio required for accurate responding. The greater the difference between signal and noise, the better ability to detect X and non-X stimuli [19]. Although d′ is often reported as a difference score, the CPT-II output provides d′ in a T-score format, with high scores reflecting below-par d′ [19]. According to Conners, CPT-II T-scores ranging from 55 to 59 indicate mildly atypical performance, whereas those above 60 indicate moderately to markedly atypical performance [19].

2.3. Circadian timing of neuropsychological testing

The time of day at which neuropsychological testing was done was based solely on patient availability and convenience. All testing was done between 10 AM and 6 PM, with the research assistant blinded to a given subject's circadian preference data. As described, basic post hoc analyses were done retrospectively to assess whether matching of chronotype to the timing of neuropsychological testing had a major effect on performance.

3. Statistics

3.1. Descriptive analyses

The first step in our analysis was to describe our sample using simple means or proportions for well-established demographic and clinical variables including adult ADHD rating scales, the 29-item Hamilton Depression Rating Scale (SIGH-SAD), SCID-defined comorbidities, and neuropsychological measures. For the SPAQ data, we first calculated a standard total GSS of 0 to 24 for each subject as has been done in prior epidemiological studies [20]. To be designated as having full-syndrome SAD, subjects had to (1) meet full SCID criteria for SAD, (2) have an SPAQ GSS above the cutoff of 16.7 established in prior research [21], and (3) report that seasonality was at least a "marked problem" on the SPAQ. Subsyndromal SAD was assessed based on the criteria of Kasper et al [22]. Circadian preference was calculated from the MEQ by generating a total score using previously established scoring procedures [15], with higher scores reflecting greater "morningness." These total scores were also used to establish a categorical assessment of chronotype (strong morning, moderate morning, neutral, moderate evening, strong evening).

3.2. Clinical correlates of seasonality and circadian preference

We next explored which clinical characteristics of adult ADHD were associated with seasonality and/or morning-evening preference. For clinical rating scale variables that were continuous, simple univariate Pearson correlations were calculated using the GSS as the core measure of seasonality and the MEQ total score as the measure of circadian preference. Given the large number of correlation coefficients calculated, a relatively stringent significance level of $P < .01$ was used. However, given the novel and hypothesis-generating nature of this study and relatively modest sample size, correlations significant at $P < .05$ were also reported (as trends). For clinical variables that were categorical, analyses of variance were performed using the seasonality scores and MEQ scores as dependent measures and the clinical variables as predictors.

4. Results

4.1. Subjects

The sample consisted of 29 adult patients (15 male, 14 female) with ADHD with a mean age of 40.4 ± 10.2 years

Table 2
Psychiatric comorbidity in 29 adults with ADHD

Variable	Lifetime		Current	
	n	%	n	%
Mood disorders	21	72.4	15	51.7
Anxiety disorders	10	34.5	16	55.2
Substance abuse disorders	8	27.6	2	6.9
Eating disorders	6	20.7	5	17.2

(range, 20-60 years). Subtype designations based on *DSM-IV* criteria were inattentive, n = 14; hyperactive-impulsive, n = 2; and combined, n = 11. Two other subjects were designated as in partial therapeutic remission as defined in the "Method" section. Tables 1 and 2 summarize the demographic features, medication status, and psychiatric comorbidity of this sample. As shown, most study subjects were never married, most were educated beyond high school, and most were currently employed or enrolled in postsecondary education. This sample would be considered relatively highly educated and employed relative to prior samples of adult ADHD [23]. As shown in Table 1, just more than half of the study subjects were on stimulants and/or antidepressants.

Table 2 shows that mood, anxiety, and substance abuse disorders were common comorbid conditions in our sample, consistent with prior studies [23-25]. Rates of current and lifetime major depression were on the higher end of what has previously been reported in adult ADHD [24-26]. Four (13.8%) patients met criteria for full-syndrome SAD, whereas 6 (20.7%) others met criteria for subsyndromal SAD [22]. Three other patients had dysthymic disorder, which continued throughout the year, but with a fall/winter worsening reported during SCID interviewing. The 13.8% rate of full-syndrome SAD is considerably higher than the 2.9% rate estimated in the general population of Toronto [27] but highly consistent with a prior study of adult ADHD in Toronto [4].

Table 3
Baseline depression rating, seasonality, and morningness-eveningness scale scores of 29 adults with ADHD

Variable	Mean	SD
Brown ADD total score	84.7	20.4
Subscales		
Activation	20.1	5.7
Attention	20.0	5.0
Effort	19.6	5.5
Affect	12.3	5.0
Memory	12.6	3.8
CAARS total score	577.9	62.5
Subscales		
Inattention/memory	77.6	10.5
Hyperactivity/restlessness	63.4	9.8
Impulsivity/lability	66.8	11.4
Self-concept problems	66.0	11.1
HDRS–29-item (total SIGH-SAD)	14.5	11.3
HDRS-17	8.0	6.4
GSS (SPAQ)	12.4	5.1
Morningness-eveningness score (MEQ)[a]	46.2	10.3

HDRS indicates Hamilton Depression Rating Scale.

[a] The MEQ asks about the timing of sleep/wake cycles and other activities. Scores range from 16 to 86, with higher scores reflecting more morningness.

Table 4
Baseline neuropsychological results of 29 adults with ADHD

Measure	Mean (SD)	Relative Score
Full-scale IQ (FSIQ)		
NAART estimated FSIQ	115.4 (3.7)	High average
Attention		
Trails A	39.79 (14.03)	Below average to mildly impaired
Trails A time (s)	34.48 (14.0)	Below average to mildly impaired
Digit span	52.74 (8.71)	Average
CPT omission errors	48.36 (10.70)	Average
CPT commission errors	55.80 (10.90)	Above-average no. of errors
CPT d′	55.36 (9.60)	Above-average no. of errors
Processing speed		
CPT hit reaction time	35.72 (7.37)	Atypically fast
Executive function		
Trails B	53.52 (17.04)	Average
Trails B time (s)	61.03 (20.10)	Average
COWAT (*z* score)	0.63 (0.99)	Average
WCST total errors	46.32 (9.89)	Average
WCST perseverative responses	45.50 (7.93)	Average
WCST perseverative errors	43.93 (9.56)	Average
WCST conceptual-level responses	46.15 (7.64)	Average
Memory		
HVLT trial 1 (*z* score)	−0.77 (0.85)	Low average
HVLT total recall (*z* score)	−0.85 (1.20)	Low average
HVLT delayed recall (*z* score)	−0.47 (1.21)	Low average
Visual perception		
JLO	26.07 (3.40)	Average

Unless otherwise noted, results are shown as T-scores correcting for age, sex, and education where appropriate. Negative values denote impaired performance for memory tasks. COWAT indicates Controlled Oral Word Association Test; WCST, Wisconsin Card Sorting Test; HVLT, Hopkins Verbal Learning Test; JLO, Benton Judgment of Line Orientation Test.

Eight (27.6%) subjects had a history of substance abuse disorders, lower than in prior studies [28]. The relatively high rate of depression and low rate of substance abuse in the current sample likely reflects the greater proportion of female subjects than in prior adult ADHD samples.

4.2. Clinical rating scale scores

Table 3 summarizes the scores on the ADHD rating scales, SIGH-SAD, SPAQ, and MEQ. As expected, the mean Brown ADD and CAARS scores were well above established cutoffs for probable adult ADHD [8,29]. The distribution of Brown subscale scores was very similar to that reported in prior research in the adult population with ADHD [30], whereas the mean SIGH-SAD scores were well below established cutoffs for major depression [31]. The SPAQ and MEQ results are discussed in more detail.

4.3. Neuropsychological variables

As noted, this sample was found to be relatively highly educated and employed relative to other ADHD samples [23]. Similarly, the overall sample was found to be functioning at a relatively high level intellectually, with NAART [13] estimated IQ in the high-average range (115.4 ± 3.7). The profile of baseline neuropsychological results showed a pattern of intact functioning and specific deficits or relative deficits that is consistent with previous findings in the ADHD neuropsychological literature [32]. Whereas some deficits fell in the clinically impaired range (eg, Trails A), others fell in the "below" or "low average" range. However, given that this is a high-functioning ADHD sample, with mean IQ estimated in the high-average range, neuropsychological performance in the below-average range could be considered significantly impaired on a relative basis. Thus, we considered relative strengths and weaknesses to characterize our sample as opposed to using the psychometric data in absolute terms [33] (Table 4).

Overall, the greatest difficulties were noted on tests of attention and response inhibition, with lesser relative deficits seen on measures of verbal memory and executive functioning. The Conner CPT-II is one of the most widely used measures of attention functioning in ADHD. In this sample, impaired performance in the mildly atypical range was noted across virtually all dimensions on the CPT-II, with the exception of mean number of omission errors (mean T-score = 48.4 ± 10.7), indicating that participants were oriented to the task. In contrast, evidence for attention impairment was noted on other aspects of performance. Participants demonstrated an above-average level of commission errors (mean T-score = 55.8 ± 10.9); an above-average d′ (mean T = 55.4 ± 9.6), indicating difficulty discriminating between targets and nontargets; as well as atypically fast responding across all trials of the CPT (mean hit reaction time, T = 35.7 ± 7.4). Together, these results indicate mild impulsivity and poor inhibition of behavior in this sample. Mild memory impairment was also noted on a verbal list-learning task (Hopkins Verbal Learning Test) [18].

Although overall memory performance fell within the low-average range compared with normative data, this is somewhat below what would be expected for a group of individuals with high-average intellectual ability and suggests a relative deficit in verbal memory. A similar argument for deficits relative to IQ can be made for the Wisconsin Card Sorting Test.

4.4. Chronobiologic variables

4.4.1. Global seasonality score

The mean GSS across all subjects was 12.4 ± 5.1. The highest individual-item SPAQ scores were for seasonality of mood, physical activity, and energy, whereas the lowest was for seasonality of body weight. The overall results were highly consistent with those from an earlier, independent sample of adults with ADHD who were recruited across all 4 seasons [4]. The most endorsed months for "feeling best" and "feeling worst" were June (n = 21) and February (n = 22), respectively.

4.4.2. Horne-Ostberg MEQ

The MEQ was available for 27 subjects, who had a mean total score of 46.2 ± 10.3, which is in the low-neutral range and close to the 41 cutoff score of 41, which distinguishes a moderate-evening chronotype. Higher MEQ scores indicate a morning preference. Regarding categorically defined chronotypes at baseline, 11 (40.7%) subjects were designated as moderate-evening types, 11 (40.7%) as neutral types, and only 5 (18.5%) as moderate-morning types. By comparison, a large community study in France with more than 2000 participants (mean age, 35 ± 11 years) found that just 10.8% of individuals were evening types [34], whereas 40.2% were morning types. This suggests that the current sample of adults with ADHD had a much greater tendency to report a late circadian preference than a general population sample, although more direct comparisons with matched Canadian controls, during the fall/winter months, would be needed to confirm this.

4.5. Clinical and neuropsychological correlates of seasonality and circadian preference

The clinical variables that were used as predictor variables for this analysis included the various demographic variables, adult ADD scales and subscale scores, and the HDRS (SIGH-SAD) scores summarized in Tables 1 and 2.

4.5.1. Clinical correlates of the SPAQ GSS

Sex was associated with mean GSS (males, 10.5 ± 4.4; females, 14.5 ± 5.0; $t = -2.3$; df = 27; $P = .029$). This was expected based on the well-documented association of seasonality with female sex [35]. There was also a correlation between GSS and SIGH-SAD depression scores ($r = .41$, N = 29, $P = .029$). None of the ADHD variables significantly correlated with the GSS.

4.5.2. Clinical correlates of MEQ scores

As expected, there was a positive correlation between age and total MEQ scores ($r = .40$, N = 27, $P = .039$), reflecting increased morningness in older subjects. There was a trend for a negative correlation between MEQ scores and Brown total scores ($r = -.40$, N = 27, $P = .039$) and a strong negative correlation between MEQ scores and the sustaining energy and effort (EFFORT) subscale of the Brown ADD Scale ($r = -.59$, N=27, $P = .001$; see Fig. 1). This suggests that an evening circadian preference was strongly associated with difficulty sustaining EFFORT in this sample. Other Brown ADD subscales did not show a significant relationship with the MEQ. There was no significant correlation between MEQ scores and either SIGH-SAD depression scores or SPAQ scores. Similarly, Terman et al [36] reported no significant correlation between baseline melatonin onset and SIGH-SAD scores in patients with SAD. Thus,

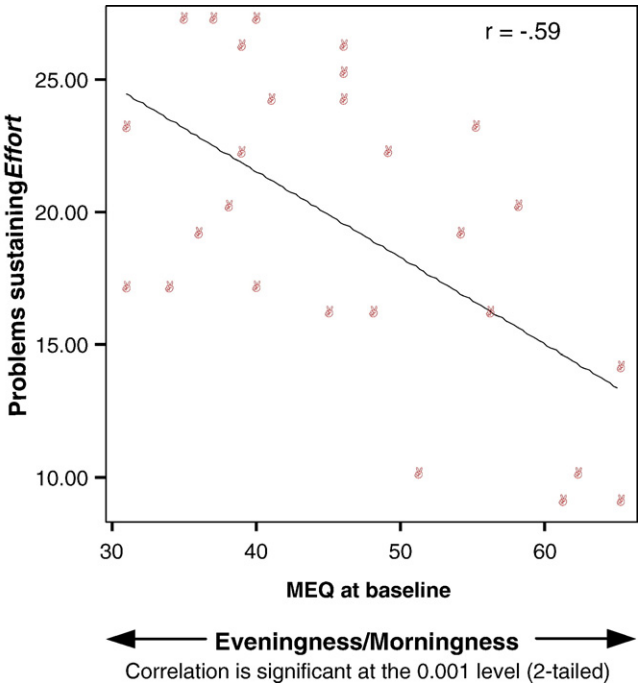

Fig. 1. Correlation between baseline MEQ and Brown EFFORT subscale in 29 adults with ADHD.

seasonality and state depression were not strongly contributing to the late circadian preference in this sample.

4.5.3. Is the relationship between eveningness and ADHD symptoms mediated by seasonality and/or mood?

To further clarify the relative strength of the associations between GSS, MEQ, and state depression scores with the

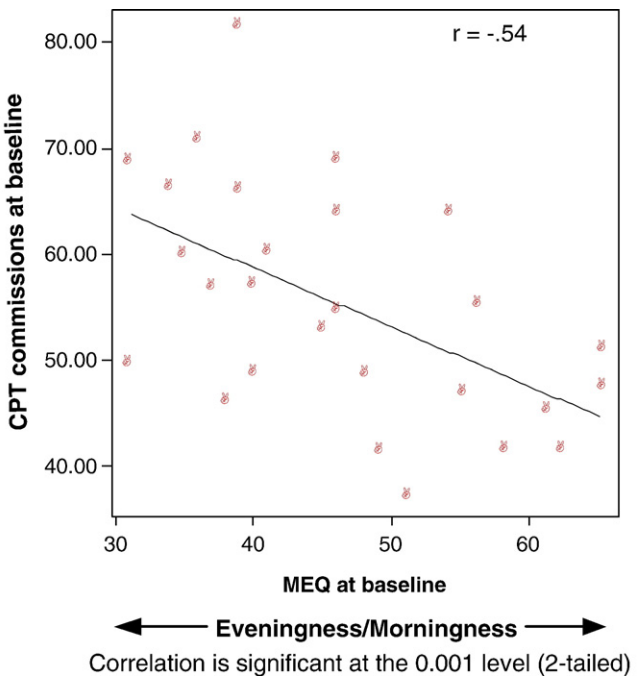

Fig. 2. Correlation between baseline MEQ and CPT commission errors in 29 adults with ADHD.

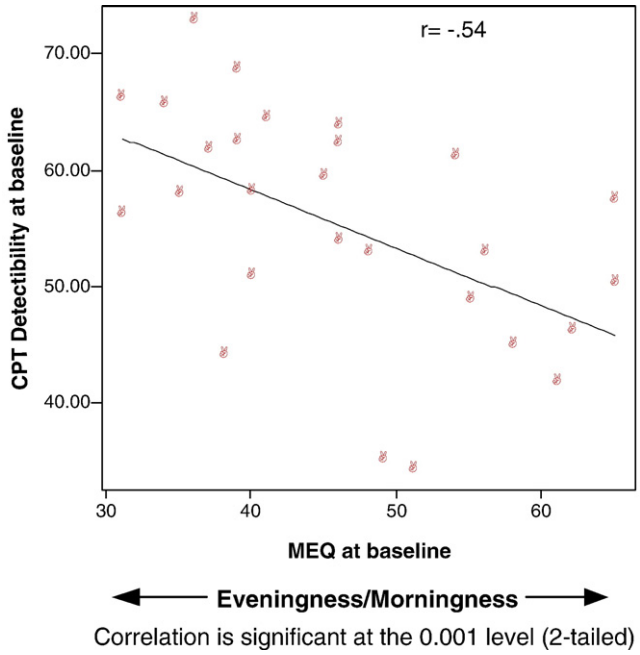

Fig. 3. Correlation between baseline MEQ and CPT d′ errors in 29 adults with ADHD.

Brown ADD Scale, 2 separate multiple regressions were performed using these 3 former measures as predictor variables and the Brown ADD total score and Brown EFFORT scores as dependent variables. The first model predicting Brown ADD total scores was moderately significant ($F_{3,23}$ = 2.87, P = .059; model r^2 = .27), with none of the individual predictor variables being significant on its own. The model predicting Brown EFFORT scores was highly significant ($F_{3,23}$ = 6.0, P = .003; model r^2 = .44), with the MEQ score being the only significant individual predictor in this model (β = −.29, t = -3.21, P = .004). These data confirm that having a later chronotype was the strongest predictor of self-reported Brown ADHD symptoms in this sample (particularly for problems sustaining EFFORT). Furthermore, multiple regression analysis suggests that this association was independent of seasonality and/or state depression.

4.5.4. Medication effects

There was no significant effect of taking either stimulants and/or antidepressants on the GSS or MEQ.

4.5.5. Neuropsychological correlates of seasonality and circadian preference

There was a strong negative correlation between MEQ scores and both commission errors (r = −.54, P = .004) and d′ errors (r = −.54, P = .004) on the CPT-II (see Figs. 2 and 3). In contrast, GSS based on the SPAQ did not correlate significantly with key neuropsychological measures. These findings suggest that later circadian preference, but not seasonality, is associated with poor sustained and careful attention. Those with a greater degree of eveningness demonstrated a higher level of impulsive, erroneous

Table 5
Correlations between neuropsychological and clinical measures in 29 adults with ADHD

Measure	Brown total	Connors total	SIGH-SAD (total, 29-item)
Full-scale IQ			
NAART estimated FSIQ	−.45 [a]	−.17 [b]	−.09
Attention			
Trails A	.17 [b]	.06	−.23 [b]
Trails A time (s)	−.12 [b]	.06	.18 [b]
Digit span	.16 [b]	.38	.04
CPT omission errors	.16 [b]	.05	.58 [c]
CPT commission errors	.51 [c]	.29	.28 [c]
CPT d′	.48 [c]	.29	.12 [b]
Processing speed			
CPT hit reaction time	−.14 [b]	−.19 [b]	.04
Executive function			
Trails B	−.11 [b]	−.01	.17 [b]
Trails B time (s)	−.14 [b]	−.07	.04
COWAT (*z* score)	.01	.004	−.15 [b]
WCST total errors	−.06	−.05	.03
WCST perseverative responses	.17 [b]	.11 [b]	−.09
WCST perseverative errors	−.01	−.08	.01
WCST conceptual level responses	.09	.11 [b]	−.04
Memory			
HVLT trial 1 (*z* score)	−.02	.37 [a]	−.21 [b]
HVLT total recall (*z* score)	−.06	.27 [a]	−.07
HVLT delayed recall (*z* score)	−.12 [b]	.14 [b]	−.11 [b]
Visual perception			
JLO	−.16 [b]	−.10 [b]	−.48 [c]

[a] Medium effect size.
[b] Small effect size.
[c] Large effect size.

responding and more difficulty discriminating between target and nontarget stimuli when attempting to sustain attention.

4.6. Other clinical correlates of neuropsychological measures

Table 5 summarizes the correlations between neuropsychological measures and traditional clinical measures of adult ADHD. Brown total scores (and Connors total scores, to a lesser extent) were negatively correlated with NAART estimated IQ, such that those endorsing higher levels of ADHD symptomatology tended to have a lower estimated intellectual ability. Brown ADD total scores were also significantly positively correlated with CPT-II commission errors and d′, demonstrating a confluence between subjective complaints and objective measures of neuropsychological dysfunction. Further analyses revealed that the Brown ADD subscale measuring difficulties sustaining EFFORT was the most highly correlated with these neuropsychological deficits (r = .54 and r = .46, respectively). In effect, those who reported that they felt they needed to expend more effort in their daily actions also demonstrated a higher degree of impulsivity, difficulty inhibiting an overlearned motor response, and difficulty discriminating between target and nontarget stimuli on the CPT-II. Positive correlations of medium effect size were found between CAARS total scores and verbal memory scores, that is, those endorsing higher levels of ADHD symptoms on the CAARS recalled a greater number of list words after a single learning trial and in total across 3 successive learning trials.

4.6.1. Depression and anxiety

Unpaired t tests revealed no significant difference in neuropsychological test results in subjects with and without a *DSM-IV* diagnosis of either current or past major depression. However, SIGH-SAD depression scores were positively correlated with omission errors on the CPT-II, indicating that state depression was associated with inattention on this test. State depression was also negatively correlated with visual perceptual ability on the Benton Judgment of Line Orientation Test. Individual SIGH-SAD items measuring current insomnia or hypersomnia were not significantly correlated with neuropsychological performance.

Regarding anxiety disorders, unpaired t tests showed that a current diagnosis of any anxiety disorder was associated with greater CPT commission errors (P = .035) and poor CPT d′ (P = .048). Similar results were found when only lifetime anxiety disorders were considered. In addition, CPT hit reaction times were significantly faster, indicating hyperactive responding to target stimuli, for individuals who had any lifetime anxiety diagnosis (P = .027).

A more dimensional measure of current anxiety was created by summing the anxiety items (12, 13, and 17) of the 29-item SIGH-SAD. This score did not correlate with neuropsychological performance.

To better understand the relationship between lifetime anxiety, circadian preference, and neuropsychological performance, multiple regression analyses were completed. Results indicated that both circadian preference and lifetime anxiety disorders independently predicted both CPT commission errors (at P = .003 and P = .002, respectively; total model R^2 = .526) and CPT d′ errors (at P = .005 and P = .024, respectively; total model R^2 = .416). This suggests that circadian preference and lifetime anxiety disorders had independent associations with neuropsychological performance in this sample.

There was no relationship between any neuropsychological measure and either stimulant or antidepressant use.

4.6.2. Time of testing

The specific time of day at which neuropsychological testing was done was recorded for 23 of the 29 study subjects. A post hoc analysis revealed that 10 study subjects did neuropsychological testing during their feeling best time based on the MEQ, whereas 13 subjects did not. Unpaired t tests revealed that digit span was the only neuropsychological measure to differ in subjects who were and were not tested during their "feeling best" times; furthermore, the direction of change was for improved digit

span performance in individuals who were not tested at their preferred time. This suggests that time of testing was not a major factor in the current results.

5. Discussion

The goal of the current report was to measure both seasonal mood change and circadian preference, and their clinical and neuropsychological correlates, in adults with ADHD during the fall/winter months. Consistent with prior research [4], a high rate of seasonal mood change was reported in this adult ADHD sample. Independently of this, more than 40% of subjects were designated as evening chronotypes based on the MEQ, whereas only 18.5% reported a morning preference. Of great clinical interest, there was a very strong correlation between greater eveningness as measured by the MEQ and both subjective and objective deficits in functioning. More specifically, later circadian preference was highly correlated with problems sustaining EFFORT as measured on the Brown ADD Scale and both a higher level of impulsive responding and more difficulty discriminating between target and nontarget stimuli on the CPT-II. Although seasonality and/or state depression and/or anxiety disorders were reported by many subjects, the relationship between late circadian preference and ADHD pathology appeared to be independent of these comorbidities. These overall results point to a possible mood-independent circadian phase delay in a significant proportion of adults with ADHD, at least during the fall/winter period. This establishes a potential new target for chronobiologically based treatments in this population [6].

Our finding of a strong link between a later evening preference, difficulties maintaining effort, and objectively measured attentional difficulties is highly congruent with prior models of ADHD that focus on deficits in arousal mechanisms. Hypoarousal is highly prominent in many ADHD patients, and it may be that some individuals who report inattention are simply experiencing lowered arousal levels [2]. This may in turn reflect 1 or more primary sleep disturbances in patients with ADHD. Delayed onset of sleep, difficulties in awakening, and/or maintaining alertness during the day can all significantly exacerbate the cognitive and behavioral symptoms associated with ADHD in different age groups [37]. Failure to adjust circadian sleep and activity rhythms to the realities of social needs often leads to severe and persistent academic and work problems and is often reported to be the single most disruptive factor for families with ADHD [38]. Mirsky and Duncan [39] have suggested that the component of attention that is most affected by sleep disturbance is the ability to sustain it. Because the current data set showed that the greatest neuropsychological deficits were related to speeded visual attention, sustained visual attention and stimulus discrimination as measured by Trail Making test-A and by the CPT-II, respectively, this offers further indirect evidence that arousal mechanisms may have been involved.

A case report of a young girl with ADHD, featuring delayed sleep phase syndrome and SAD, has previously been described by Rosenthal [3]. In finding high rates of both SAD and a late circadian preference in the current sample, our data extend this general finding to an adult population with ADHD. In his case report, Rosenthal [3] speculated on whether this symptom triad was simply a coincidental onset of 3 common but separate (childhood) conditions or whether it might be a distinct syndrome with a unique underlying mechanism. Although more research in larger samples is needed to explore this question further, the current results suggest that seasonality and delayed circadian phase are at least partially independent contributors to ADHD pathology.

There are several limitations of this study that must be considered in interpreting the current findings. Although we tried to prevent a possible recruitment bias favoring patients with ADHD with high rates of seasonality, communication between patients regarding the treatment program (light therapy) and the general timing of the study in the fall/winter months may have attracted a highly seasonal subgroup. Arguing against this, the mean GSS in the current sample was almost identical to that of our previous study on adults with ADHD recruited across all 4 seasons [4]. Furthermore, the overall pattern of results suggests that seasonality and state depression could not account for either the high rates of a late circadian preference reported by this sample or the strong relationship between eveningness and both subjective and objective measures of core ADHD pathology. To more fully evaluate possible relationships between seasonality, circadian preference, and ADHD, further studies in the spring/summer period would be of great interest, as would inclusion of an age- and sex-matched control group.

Although this study sample reported a relatively high frequency of evening preference based on the MEQ self-report, full assessment of intrinsic circadian rhythmicity requires a more direct approach, such as dim light melatonin onset, which can be done using salivary sampling. In addition to a primary disturbance in circadian phase, several behavioral factors might contribute to an evening preference, including inadequate routines in preparation for sleep, anxiety and family strain contributing to high levels of arousal in the late evening, and/or a wish to perform important work away from a busy and distracting daytime environment [2]. Much more work is needed to tease out the specific biologic and behavioral factors contributing to a late circadian preference in this population.

Although the objective neuropsychological deficits were somewhat milder in the present sample than in previous studies of ADHD [23], the current sample was also more highly educated and employed and demonstrated above-average intellectual ability compared with earlier study subjects. Thus, the overall profile of cognitive functions in the current sample does suggest relative deficits in attention, impulsivity, d′, verbal memory, and, to a lesser extent, executive function.

The large amount of data and, thus, high number of analyses performed increase the possibility of false-positive results due to multiple testing. We attempted to address this by using more stringent levels of statistical significance. Moreover, the consistency of results across both subjective and objective measures of ADHD pathology further supports the validity of the main findings. However, replication of these findings in much larger samples is needed to confirm these initial results.

In sum, these overall data suggest that a mood-independent delay in circadian phase contributes significantly to core pathology in many adults with ADHD during the fall/winter period. These findings establish a potential target for chronologically based treatments such as light therapy in this complex population.

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Appendix A. The following details the clinical rating scales used in the assessment process described in the "Method" section

1. The WURS for Childhood ADHD [7]: *DSM-IV* currently specifies that ADHD symptoms must have been present before the age of 7 for a diagnosis of adult ADD. The WURS, which retrospectively assesses childhood ADHD, was thus used at the first stage of recruitment. We used a cutoff score of 36 on a subset of 25 core items from the WURS (WURS-25) that correctly classified 96% of individuals identified as meeting Wender Utah criteria for ADHD and 96% of the normal subjects on the retrospective reporting of childhood ADHD symptoms [7].

2. The Brown ADD Scale for Adults [8]: With its focus on disturbances of activation and arousal, the Brown ADD scale is particularly well suited for chronobiologic studies in this population. It consists of 40 self-reported items rated from 0 (never) to 3 (almost daily). There are 5 major clusters, which measure difficulties with (abbreviated cluster name in brackets) organization and activation to work (ACTIVATION), sustaining attention and concentration (ATTENTION), sustaining energy and effort (EFFORT), managing affective interference (AFFECT), and using working memory/recall (MEMORY). A cutoff score of 50 or higher suggests probable ADD [29].

3. Conners Adult ADHD Rating Scale [9]: This 66-item self-report instrument measures primary and secondary symptoms of ADHD according to 6 symptom scales: inattention/memory, hyperactivity/restlessness, impulsivity/emotional lability, *DSM-IV* inattention, *DSM-IV* hyperactive/impulsive symptoms, and an ADHD index scale that is designed to maximize the differentiation of individuals with ADHD from those without the disorder. We used data converted into standard T-scores, which consider age and sex. Cut-off T-score of higher than 65 suggests clinically elevated symptoms. Eighteen core items were used to assess *DSM-IV* criteria for ADHD, including 9 items each for the inattentive and hyperactive/impulsive categories. These 18 core items were each scored on a 4-point scale from 0 (not at all) to 3 (very much, very frequently). A given item was considered positive if it was endorsed at a level of 2 ("pretty much, often") or higher. As per the *DSM-IV*, subjects had to have 6 of 9 items positively endorsed to meet criteria for a respective category.

4. Structured Clinical Interview for *DSM-IV* [10]: The *DSM-IV*-based diagnostic assessment was completed by a trained research assistant blinded to the results of the other rating scales. The SCID was administered to assess comorbid *DSM-IV* (Axis 1) disorders and further confirm a diagnostic history of ADHD.

5. The Structured Interview Guide for the Hamilton Depression Rating Scale, Seasonal Affective Disorders Version [11]: The 29-item SIGH-SAD includes the classic 17-item HDRS, 4 miscellaneous symptoms, and an 8-item "atypical" addendum to measure characteristic symptoms of SAD. This is the standard assessment tool of mood in studies of SAD and seasonality [11]. The SIGH-SAD was administered by a research fellow blinded to the SCID results.

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