



## Controlled trial evaluation of exposure duration to negative air ions for the treatment of seasonal affective disorder



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### ARTICLE INFO

#### Keywords:

Seasonal depression  
Negative ionization  
Treatment efficacy  
Treatment safety  
Chronotypes

### ABSTRACT

This study evaluated the effectiveness of 30 or 60 min of daily exposure to high-density or to zero-density (placebo condition) negative air ions over 18 days on the symptoms of seasonal affective disorder (SAD) in 40 participants under controlled laboratory conditions. Exposure to high-density negative air ions was superior to zero-density negative air ions in alleviating depression and the atypical symptoms of SAD. Also, more subjects in the high-density negative air ions groups met two different clinical response criteria than did those in the zero-density groups. Within the high density treatment group, both the short and long daily exposure reduced SAD symptoms. Exposure to negative air ions produced no negative side effects, and no ozone was produced by the ion generators. In both the high-density negative air ions and zero-density negative air ions groups, a significant placebo effect was found for most clinical measures. Finally, for the high-density negative air ion groups, subjects with a morningness chronotype responded better to treatment with high-density negative air ions than did those with an eveningness chronotype.

### 1. Introduction

Seasonal affective disorder (SAD) is a recurrent mood disorder with a characteristic pattern of onset and remission that has been classified as a variant of major depressive disorder (American Psychiatric Association, 1994). Episodes of SAD occur predominantly in fall and winter and are characterized by symptoms of depression as well as atypical symptoms including excessive sleep, craving for carbohydrates, irritability, social withdrawal, daytime fatigue, and loss of concentration (Rosenthal et al., 1984). In addition to antidepressant medications (Lam et al., 2006) and exposure to bright light SAD (Terman and Terman, 2005), exposure to high-density negative air ions has been found effective for treating SAD (Flory et al., 2010; Perez et al., 2013; Terman and Terman, 1995, 2006; Terman et al., 1998).

Although high levels of negative ionization are superior to low levels for treating seasonal or chronic depression (Perez et al., 2013), no studies have systematically compared the antidepressant effects of long versus short daily exposures to negative air ions on the symptoms of SAD. For the major non-pharmacological treatment for SAD, morning bright light exposure, longer treatment duration has been associated with greater improvement in symptoms (Checkley et al., 1986; Terman et al., 1989a, 1989b; but see Wehr et al., 1986). Light therapy both

improves the depressive and atypical symptoms of SAD and acts to phase advance circadian rhythms (Wirz-Justice, 2009). The physiological mechanism of action of negative ions is unknown (Kinne, 1997; Terman et al., 1998), and it is unclear if longer daily exposure would influence treatment response. In a meta-analysis of several experiments, Perez et al. (2013) reported no dose-response effect between total exposure time to negative air ions over entire treatment time (in hours) and posttreatment depression severity in subjects with SAD.

The present study utilized a parallel-group design to evaluate the efficacy of two daily exposure durations (30 min and 60 min) of high-density negative air ions (HDNI) compared to the same two daily durations of zero-density negative ions (PLCB, the placebo) for treating SAD. As in the investigation of the effects of light, negative air ions, and auditory stimuli on mood changes (Goel and Etwaroo, 2006), all participants in this study received daily treatments in a controlled laboratory setting; unlike previous studies, we were able to directly measure both air ionization and ozone levels in treatment rooms during and after daily exposure sessions.

Based on previous research (Flory et al., 2010; Perez et al., 2013; Terman and Terman, 1995, 2006; Terman et al., 1998), we predicted that both the 30-min and the 60-min active treatment with HDNI would result in greater alleviation of SAD symptoms than would either PLCB

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group. We predicted that the 60-min HDNI treatment would have greater efficacy in alleviating SAD symptoms than would the 30-min HDNI treatment. Finally, we assessed the relationship between chronotype, e.g., morningness and eveningness, and levels of depression and SAD symptoms, because an eveningness chronotype has been associated with various mental disorders (Fares et al., 2015).

## 2. Methods

### 2.1. Subjects

A total of 41 female students and staff at Hollins University in Roanoke, an all-women's university in Virginia (latitude 37° 16', North; average sunrise time approximately 0732 during January) and one male staff relative participated in this study that was conducted during the months of January 2009 and 2010. Of these original 42 participants, two voluntarily withdrew from the January 2010 study. The final group, none of whom had prior experience with negative air ion therapy, included 37 white and 3 black subjects ranging in age from 18 to 55 years ( $M = 24.8$  years;  $S.D. = 10.5$  years). A request for subjects was communicated in a campus-wide media announcement prior to each study. Respondents to this announcement completed the Seasonal Pattern Assessment Questionnaire (SPAQ; Rosenthal et al., 1987), a retrospective self-report rating of pattern and degree of seasonal variation in sleep, social activity, mood, body weight, appetite, and energy level. The global seasonality score (GSS), derived from categorical scales of mood and behavior, ranges from 0 to 24. To meet the initial screening criteria for inclusion in this study, a respondent was required to score the following on the SPAQ: a GSS of at least 12, a winter pattern (feels worse, eats more, socializes less, and sleeps more in winter months than in summer months), and a rating of at least “moderate” personal discomfort [a score of 2 on a scale that ranges from 1 (*mild*) to 5 (*debilitating*)] as a result of these seasonal changes.

Subjects were instructed to maintain pre-established prescription medication regimens, if any, throughout the 18 consecutive treatment sessions and during the week prior to the study and to also document that these regimens were unchanged in a posttreatment questionnaire. None of the subjects changed medications or dosages during the study. Of the 40 subjects, 12 remained on prescribed medications other than psychotropic drugs, and 11 remained on a psychotropic medication regimen of one or more of the following: a selective serotonin reuptake inhibitor, a norepinephrine/dopamine reuptake inhibitor, a serotonin modulator, an anxiolytic, or a combination of two or more of these psychotropic medications. During both January studies, each participant received a monetary incentive stipend of \$150 for remaining in the 18-consecutive day study, and one of these subjects received an additional \$100 in a random lottery drawing. The two participants who withdrew from the study were each provided a pro-rated stipend. Subjects read and signed a written informed consent form after the document was fully discussed with them. The study received institutional approval from the Hollins University Human Research Review Committee.

### 2.2. Apparatus

#### 2.2.1. Negative air ion generators and treatment rooms

Six negative ion generators (Model VI-2500, SphereOne, Inc., Silver Plume, CO, USA), each measuring 19.7 cm by 7.6 cm, were located in six similar treatment rooms with dimensions of approximately 2.0 m by 3.0 m by 2.5 m. Each generator was placed on a 76.0-cm high table and was positioned ~ 46.0 cm to one side of a portable DVD player screen in front of the participant. The ion output of each of the six generators was measured using AlphaLab Air Ion Counters (AlphaLab, Inc., Salt Lake City, UT, USA) by a physicist (JA). Three generators that emitted  $\sim 2.0 \times 10^6$  ions/cm<sup>3</sup> at the subject's sitting distance of ~ 60 cm from the generator served as the high-density negative air ion (HDNI)

treatment devices. The remaining three generators, modified to emit a zero level of negative air ions, served as the placebo (PLCB) treatment devices. A grounded wrist strap on each generator maximized ion flow toward the subject's body, and doors to the treatment rooms were closed during daily sessions. The ambient level of negative air ions in each of the six treatment rooms was  $\sim 2.0 \times 10^3$  ions/cm<sup>3</sup>. A warning sign was placed on each generator to decrease the possibility that participants would touch the generator's corona emitter wand and, thereby, receive feedback as to their treatment condition. During periodic observation of subjects during treatment sessions, there was no indication that any of them touched the emitter wand.

#### 2.2.2. Ozone measuring device

Prompted by recent safety concerns associated with the use of high-density negative ion generators (Waring and Siegel, 2011), ozone levels were measured with an ECO ozone meter (Model EZ-1X, Eco Sensors, Inc., Santa Fe, NM, USA) at various locations within each treatment room during negative air ion generator operation. Measurements of different areas within the treatment rooms were necessary because ozone levels can vary greatly within a closed space.

### 2.3. Treatment assessment inventories

#### 2.3.1. Systematic Assessment for Treatment Emergent Effects (SAFTEE)-self-rating version

The self-rating version of the SAFTEE, an adaptation of the original comprehensive interview (National Institute of Mental Health, 1986), incorporates a 5-point checklist format for each of 132 questions to detect and assess the strength of adverse physical and psychological side-effects of clinical treatments.

#### 2.3.2. Treatment Expectation Questionnaire (TEQ)

This self-report scale, modeled on the concepts of Borkovec and Nau (1972), provides a rating, ranging from 0 to 4, of the subject's belief of benefit from completing the assigned treatment, the expectation that the treatment would make symptoms worse (reverse scored), the belief that the treatment was logical, and the degree of comfort in recommending the treatment to a friend with SAD. Data from all four questions on the TEQ were used for analysis, with total scores ranging from 0 to 16 and higher scores corresponding to greater expectation of treatment benefits.

#### 2.3.3. Structured Interview Guide for the Hamilton Depression Rating Scale–Seasonal Affective Disorder Version–Self Rating (SIGH-SAD-SR)

The SIGH-SAD-SR consists of two scales: a structured interview for the 21-item Hamilton Depression Rating Scale (HAM-D) and an 8-item scale that assesses the atypical characteristics of SAD (ATYP8) (Williams et al., 1998) including hypersomnia, hyperphagia with associated weight gain, and daytime fatigue. Previous studies (Terman and Terman, 1995; Terman et al., 1998) reported that both scales of the SIGH-SAD-SR were of value in determining treatment response to bright light as well as to negative air ions. The self-rating version of the SIGH-SAD (SIGH-SAD-SR) has been shown to produce results consistent with the interview-administered version (Terman and Williams, 1994; Terman et al., 2001) and has been used as a primary measure of seasonal depression (Partonen et al., 1993, 1998; Wileman et al., 2001) and nonseasonal depression (Ando et al., 1999; Loving et al., 2002; Leppämäki et al., 2004).

#### 2.3.4. Beck Depression Inventory (BDI)

The BDI (Beck et al., 1961) is designed to assess the severity of depression in adolescents and adults and has been validated in college populations (Bumberry et al., 1978; Goel and Grasso, 2004). Each of the 21 multiple-choice questions on the BDI consists of a 4-point scale ranging in symptom severity from 0 to 3. Total scores of 0–9 are within the minimal range, scores of 10–16 indicate mild depression, scores of

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