A Randomized, Double-Blind, Placebo-Controlled, Parallel Group Study to Determine the Efficacy and Safety of Topiramate in the Treatment of Sleep-Related Eating Disorder (SRED)

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Background and Significance

Sleep-Related Eating Disorder (SRED) is a parasomnia characterized by arousals from sleep, compulsive consumption of food, poor sleep quality, and morning anorexia. SRED is generally more prevalent in females, with onset in early adulthood. SRED is thought to be closely related to Night Eating Syndrome (NES), another night-time eating disorder. It is thought that SRED and NES are related processes in which night-time eating occurs along a variable spectrum of arousal; individuals with NES are fully conscious during their night-eating episodes, whereas individuals with SRED are only partially conscious during their night-eating episodes[1]. This nosology is reflected in the most recent diagnostic criteria for SRED in the International Classification of Sleep Disorders, Second Edition (ICSD-2) in which the level of consciousness is not a diagnostic criteria, stressing rather, that the sleep-related eating behavior is involuntary in nature.

Night Eating Syndrome was first reported in 1955[2], however the syndrome was not further investigated and defined until almost 30 years later, and still lacks standard diagnostic criteria. Its prevalence in the general population is uncommon, estimated at 1.5%, but more common in the severely obese population, with estimates ranging from 9 to 43%[3]. Onset of the syndrome has been linked to stressful life experiences. Individuals with NES experience morning anorexia, consume over half of their daily caloric intake after 6 PM and suffer from insomnia[4]. NES patients have full awareness of their night-eating episodes; however, the binge eating is compulsive and difficult to suppress[5].

Sleep-Related Eating Disorder has only been reported in the last decade. It has been estimated that approximately 1% of young adults have exhibited this behavior, which usually occurs nightly, sometimes several times a night. Patients with SRED may have variable level of awareness during an episode of night eating, often describing their eating occurring while they are “half awake” or “half asleep”. Amnesia may be present the morning after an episode, and thus the occurrence of such an episode must be inferred from evidence observed in the morning. Individuals tend to eat high calorie foods, and some consume inappropriate foods (e.g. frozen foods, non-nutritive substances) during episodes. Weight gain is often associated with this behavior. Sleep disorders such as Restless Legs Syndrome and somnambulism are common among these patients.

Current treatments for SRED have been directed towards treating any underlying sleep disorder, eating or psychiatric disorder. Selective serotonin reuptake inhibitors (SSRIs), dopaminergic agonists, benzodiazepines, anorectics, hypnotics and opioids have been used, but success in treatment has varied.

Preliminary Reports with Topiramate

Preliminary reports of topiramate in individuals with NES or SRED indicate that topiramate may be a beneficial in the treatment of these syndromes. In an open-label study of four subjects (two with NES, two with SRED), one subject had complete elimination of night eating (NES subject), two had a 75-<100% reduction in night eating, and one had a 50-<75% reduction in night eating[5]. The dose of topiramate ranged from 100 mg-400 mg daily, with an average dose of 216 mg. Subjects also experienced weight loss ranging from 15-33 pounds. Topiramate was well tolerated. In addition to this study, a case study of a patient with NES and co-morbid Post-traumatic Stress Disorder reported improvement of NES with topiramate treatment[7]. More recently, there have been two larger case series published examining the use of topiramate in SRED[8,9]. In the case series of 17 patients conducted by Schenck and Mahowald, topiramate fully/substantially controlled in all 11 subjects who were able to continue with topiramate therapy [6 subjects discontinued the medication; 4 due to lack of efficacy and 2 due to side effects (purtiris, weight gain)][8]. In the retrospective case series conducted by Winkelman, over two-thirds (17/35) patients treated with topiramate were considered responders[9]. These reports suggest that further investigation of topiramate as a potential treatment for SRED is warranted.

Topiramate Background

Topiramate is a sulfamate-substituted monosaccharide derived from fructose. It is structurally distinct from any other anti-epileptic medication[10]. Topiramate is a structurally novel compound that is an effective anticonvulsant with a good safety profile after oral administration in animals and humans. Topiramate has been approved for marketing in the United States and most European Union countries for adjunctive treatment of pediatric and adult patients with partial onset seizures, Lennox-Gastaut syndrome, or primary generalized tonic-clonic seizures. It has also been approved as monotherapy in some countries. Topiramate is currently under investigation for a number of other disorders including migraine, bipolar disorder, and essential tremor. For a complete profile, see the package insert[11].

Nonclinical Studies

Pharmacologic Profile[11]

Topiramate has multiple mechanisms of action that may contribute to its anti-convulsant properties, as well as its potential therapeutic effect in other Central Nervous System (CNS) disorders. First, the drug inhibits voltage gated sodium channels and thus suppresses action potentials associated with sustained repetitive cell firing. Second, topiramate augments the inhibitory chloride ion influx mediated by γ-aminobutyrate (GABA). This is not blocked by flumazenil suggesting that the mechanism is different from that of benzodiazepines. Third, topiramate antagonizes the (α-amino-3-hydroxy-5-methylisoxazole-4-propionic acid) AMPA/kainate subtype of the glutamate receptor. It has no effect on the N-methyl-D-aspartate (NMDA) subtype. Fourth, topiramate reduces the firing of high voltage-activated (L-type) calcium channels. It is also a weak inhibitor of some isoenzymes of carbonic anhydrase.

Toxicology

The data for preclinical toxicology studies were obtained for dosage levels up to the maximum tolerated doses. Female rats and male and female dogs have received higher systemic exposure to topiramate than the highest anticipated clinical exposure in humans. It is notable that the female rat appears to provide the best animal model for human metabolism of topiramate.

In general, acute and long-term oral exposure of mice, rats, dogs, and rabbits to topiramate was well tolerated. Hyperplasia of the gastric and urothelial cells seen in shorter term studies did not progress to neoplasia after lifetime exposure in rats or mice and has not been reported during clinical studies. Smooth muscle tumors of the urinary bladder in mice appear to be unique to the species. There is no known clinical counterpart; therefore, these tumors were not considered to be of relevance to man. As with many other anticonvulsants, topiramate is teratogenic in mice, rats and rabbits. The teratologic effects of topiramate seen in rats and rabbits appear to be related to carbonic anhydrase inhibition. Reductions in weight of progeny were also indicated by reproductive studies in these species, but no effects on fertility were observed for male or female rats. Based on results of in vitro and in vivo mutagenicity assays, topiramate does not show genotoxic potential. For further background on the toxicology of topiramate, see the Investigator's Brochure.[10]

Pharmacokinetic Profile

Studies in humans show that topiramate is rapidly absorbed, with peak concentrations occurring at approximately 2 hours following an oral dose. The bioavailability of topiramate from tablet formulation is approximately 80% compared to a solution. Bioavailability is not affected by food. Topiramate exhibits linear pharmacokinetics with dose proportional increases in plasma concentration over the 100-400 mg b.i.d. (200-800 mg/day) dose range studied. Topiramate is poorly bound to plasma proteins, 13-17% (over the concentration range of 1-250 mcg/ml), but there is a low-capacity erythrocyte binding site for the drug. The mean plasma elimination half-life is 21 hours after single or multiple doses. Steady state is reached in approximately 4 days in subjects with normal renal functioning. The major route of elimination is via the kidneys.

Topiramate is not extensively metabolized and is primarily eliminated unchanged in the urine (approximately 70% of an administered dose). Six metabolites have been identified, none of which constitutes more than 5% of an administered dose. The metabolites are formed via hydroxylation, hydrolysis, and glucuronidation. Overall, plasma clearance is approximately 20 to 30 mL/min in humans following oral administration. Evidence of renal tubular reabsorption of topiramate was demonstrated in rats given probenecid to inhibit tubular reabsorption along with topiramate, where a significant increase in renal clearance of topiramate was observed.

OBJECTIVE

The primary objective of this study is to investigate the efficacy and safety of topiramate compared to placebo in the treatment of Sleep-Related Eating Disorder.

OVERVIEW OF STUDY DESIGN

This is a single center, 13-week, outpatient, randomized, double-blind, placebo-controlled, parallel group, pilot study of topiramate in subjects with Sleep-Related Eating Disorder.

After giving informed consent, subjects who meet all the inclusion and exclusion criteria may be enrolled. The study will consist of two phases:

- pre-randomization phase (up to 56 days prior to randomization), consisting of a screening/washout period (up to 42 days) and a prospective baseline period (14 days);
- treatment phase, consisting of titration period: up to 9 weeks; maintenance period: 4 weeks; taper period: 2 weeks.

The study medication will be titrated to 300 mg/day or the subject's minimum effective dose. Subjects must reach a minimum dose of 25 mg/day after the second week of titration. The taper period will last approximately two weeks during which subjects will gradually reduce their medication until they are no longer taking the study medication.

SUBJECT POPULATION

General Considerations

This study will enroll up to 240 subjects with the goal of randomizing 40 subjects with Sleep-Related Eating Disorder. The specific inclusion and exclusion criteria for enrolling subjects in this protocol are outlined below. Our estimated completion date for the study is January 2015.

Inclusion Criteria

Subjects must satisfy the following criteria before entering the study:

1. Subjects must have a diagnosis of the following for at least 6 months:

   Sleep-Related Eating Disorder, defined as (according to ISCD-2 criteria):

   A. Recurrent episodes of involuntary eating and drinking occur during the main sleep period.
   B. One or more of the following must be present with the recurrent episodes of involuntary eating and drinking:
      i. Consumption of peculiar forms or combinations of food or inedible or toxic substances
      ii. Insomnia related to sleep disruption from repeated episodes of eating, with a complaint of nonrestorative sleep, daytime fatigue, or somnolence
      iii. Sleep related injury
      iv. Dangerous behaviors performed while in pursuit of food or while cooking food
      v. Morning anorexia
      vi. Adverse health consequences from recurrent binge eating of high-caloric foods
   C. The disturbance is not better explained by another sleep disorder, medical or neurologic disorder, mental disorder, medication use, or substance use disorder

2. Subjects must experience 3 nights per week of nocturnal eating during the 14-day prospective baseline period prior to Visit 2.

3. Subjects must be between 18 and 75 years of age.

4. Subjects must be able to take oral medication in capsule form, adhere to medication regimens and be willing to return for regular visits.

5. Subjects must have observed the designated washout periods for prohibited medications outlined under the Concomitant Therapy section of this protocol.

6. Female subjects must be:
   - postmenopausal for at least one year, surgically sterile, or
   - practicing an effective method of birth control (e.g., contraceptive injections, intrauterine device, double-barrier method, contraceptive patch, male partner sterilization, abstinence

and agree to continue abstinence or to use an acceptable method of contraception, as listed above, should sexual activity commence) before entry and throughout the study
- If taking prescription oral contraceptives, must agree to also use a barrier method of birth control throughout the study since topiramate may affect the metabolism of prescription oral contraceptives.
- Have a negative urine pregnancy test at Visit 2 (Day 1).

7. Subjects must be able to read and comprehend written instructions, and be willing and able to comply with protocol requirements.

8. Subjects must have signed an informed consent document indicating that they understand the purpose of and procedures required for the study and are willing to participate in the study

Exclusion Criteria
Subjects will be excluded from the study if they meet any of the following criteria:

1. Subjects with evidence of untreated primary sleep disorders (e.g.,Obstructive Sleep Apnea, Restless Legs Syndrome, Periodic Leg Movements of Sleep) as determined in the sleep screening questionnaire and clinical history.

2. Subjects who have a DSM-IV diagnosis of substance dependence or abuse (with the exception of nicotine) that has been active within the past 6 months.

3. Subjects taking exclusionary medications, such as benzodiazepines/benzodiazepine receptor agonists, tricyclic antidepressant medications or antipsychotics as these medications have been reported to cause SRED[12-15], who are unable or unwilling to complete the required washout of these medications.

4. Subjects with an active or unstable major psychiatric disorder requiring further treatment (e.g., major depressive disorder). Subjects with clinically significant depression defined by a HAM-D >20 or who, in the investigator's judgment might require intervention with either pharmacological or non-pharmacological therapy over the course of the study, will also be excluded.

5. Subjects with an active daytime DSM-IV-TR™ diagnosis of Anorexia Nervosa or Bulimia Nervosa within the 3 months prior to screening.

6. Subjects judged clinically to be at serious suicidal or homicidal risk.

7. Subjects with a body mass index (BMI) $\geq$50 kg/m^2.

8. Subjects who have positive urine drug screening (phencyclidine, cocaine, amphetamines, tetrahydrocannabinol, and opiates) at Visit 1 (Day -14).

9. Subjects who report consumption of more than 2 alcoholic beverages daily, 14 or more alcoholic beverages weekly

10. Subjects who report consumption of more than 4 beverages containing caffeine daily.

11. Subjects who are rotating or third shift workers.

12. Subjects who are pregnant or lactating.

13. Subjects with a history of recurrent nephrolithiasis or on another carbonic anhydrase inhibitor.

14. Subjects with progressive or degenerative neurological disorders or a structural disorder of the brain from birth, trauma or past infection.

15. Subjects who have recently had or are planning to have surgery.

16. Subjects who have previously been treated with topiramate and discontinued treatment due to an adverse event or subjects with a known hypersensitivity to topiramate.

17. Subjects who have previously taken Topiramate.

18. Subjects known to have clinically significant, unstable medical conditions as determined by careful clinical interview and review of medical records, including but not limited to:

    - Symptomatic coronary artery disease or peripheral vascular disease
    - Malignancy or history of malignancy within the past 5 years (except basal cell carcinoma)
    - Clinically significant renal disease including creatinine >1.5 or creatinine clearance (calculated by standard method) <60
    - Clinically significant diseases of the gastrointestinal system including active liver disease with a history of LFTs >3x ULN as determined by review of medical history or records
    - Any disease or condition that compromises the function of those body systems that could result in altered absorption, excess accumulation, or impaired metabolism or excretion of topiramate

19. Subjects who have participated in an investigational drug or device trial within the 4 weeks prior to enrollment.

20. Subjects who in the opinion of the investigator should not be enrolled in the study because of the Precautions, Warnings or Contraindications sections of the topiramate package insert.

21. Subjects with glaucoma.

STUDY MEDICATION AND SUPPLIES

Study Treatments

The study medication will consist of 25 mg or 100 mg of topiramate tablets, or matching placebo, prepared in identically appearing capsules by the MGH IDS. The medication will be titrated over a 9-week period according to the following suggested schedule:

Titration Schedule *

Double-Blind Topiramate / Placebo Dosing				
Days	**Study Medication 25 mg Tablets**	**100 mg Tablets**	**Total Daily Dose Topiramate**	**Placebo**
1-7	1 capsule		25 mg	Matching capsules
8-14	2 capsules		50 mg	
15-21	3 capsules		75 mg	
22-28	4 capsules		100 mg	
29-35	5 capsules		125 mg	
36-42	6 capsules		150mg	
43-49		2 capsules	200mg	
50-56	2 capsules	2 capsules	250 mg	
57+		3 capsules	300 mg	

Subjects will be instructed to take the study medication one hour prior to bedtime (h.s.). Subjects will be informed during the consent process that they may be asked to take up to six pills at different points during the titration period. The study medication will be titrated to 300 mg/day or the subject's minimum effective dose (MED).

At the investigator's discretion the titration rate may be adjusted. However, after the second week of titration, subjects must take at least 25 mg/day of topiramate or matching placebo for the duration of the double-blind phase. During the maintenance period, subjects should remain at the dose attained at the end of the titration period, however dose adjustments will be permitted at the discretion of the investigators.

Subjects will taper their study medication by decreasing the dose by approximately 30% every three days over approximately a 14-day period until they are no longer taking study medication.

*Subjects with an estimated creatinine clearance <70 but >60 will be included in the study, but will follow a modified titration schedule. Dose increases for these subjects will be take place no less than every 14 days rather than every 7 days, and at the end of the titration period they will reach a maximum dose of 125mg. During the maintenance period, subjects should remain at the dose attained at the end of the titration period, however dose adjustments will be permitted at the discretion of the investigators up to a maximum dose of 150mg.

Study Medication Packaging

Medication will be prepared and packaged by the MGH IDS Pharmacy. For the first 6 weeks of the titration period the investigator will dispense bottles with sufficient 25mg capsules for 7+3 days of the necessary dose. After the subject reaches a dose of 150 mg the medications will be packaged in bottles as prescribed by the investigator depending on the dose and number of tablets needed. All study medication will be dispensed in child-resistant packaging. Bottles will be labeled with the patient name and ID and the dosing information. Bottles will be clearly labeled as containing either 25 mg or 100 mg matching placebo or topiramate tablets.

Subjects will be dispensed the appropriate number of tablets needed until they return for their next office visit. Study medication should be stored at room temperature 15-30°C (59-86°F), be protected from moisture, and be maintained in a secure area.

Study Medication Accountability and Compliance
Starting at Visit 2 (Day 1), study medication will be dispensed to each subject with instructions to return all unused medication and packaging (including empty bottles) at the next study visit in order to assess compliance. Returned study medication bottles may be redispensed to the same subject if appropriate. Additional bottles will be dispensed to each subject as needed.

All study medication dispensed by the investigator or designee will be accounted for throughout the study. Information about subject dosing and compliance will be recorded in the subject's study records.

Subjects who are noncompliant with medications (according to pill counts and diaries) may be removed from the study at the discretion of the investigators.

The investigator agrees not to allow access to the study medication to any person except those named as sub-investigator(s) or clinical care staff, and dispense only to qualified subjects participating in the study.

Randomization
Randomization will be used to avoid bias in the assignment of subjects to treatment, to increase the likelihood that known and unknown subject attributes (e.g., demographics and baseline characteristics) are evenly balanced across treatment groups, and to enhance the validity of statistical comparisons across treatment groups. Blinded treatment will be used to reduce potential bias during data collection and evaluation of clinical endpoints.

At the time of Screening (Visit 1A), subjects will be assigned a three-digit subject number, in ascending sequential order beginning with 001. The subject number will be retained by the subject for the duration of the study. The MGH IDS Pharmacy will provide and maintain randomization and blinding. Subjects will be randomized to receive either topiramate or placebo in a 1:1 ratio. The randomization will be balanced by using permuted blocks of 4. Subject and investigator will be blinded to treatment assignment. Subjects will be randomized sequentially as they qualify for the study.

Blinding
The randomization code will be maintained by the MGH IDS Pharmacy and will not be revealed to study subjects, investigators or clinical staff until all subjects have completed and the database has been finalized.

To maintain the blind, sealed envelopes containing the study drug identification (e.g., active or placebo) will be provided to the investigator. These sealed envelopes will be kept together, in a limited access area that is accessible 24 hours per day. The study drugs will be identical in appearance and will be packaged in identical containers.

Under normal circumstances, the blind should not be broken. The blind should be broken only if specific treatment would be dictated by knowing the treatment status of the subject.. Individual code breaks by the investigator will normally result in withdrawal of the subject from the trial. The date, time and reason for the unblinding must be documented in the study files.

After the termination of the double-blind portion of the study, subjects can be made aware of the study medication they were given at their request.

Medication Side Effects
The package insert for Topamax includes warnings and precautions related to the following side effects or adverse events: acute myopia and secondary angle closure glaucoma, oligohidrosis, psychomotor slowing, difficulty with concentration, speech or language problems (word-finding difficulties in particular), somnolence, fatigue, kidney stones, paresthesia, dizziness, ataxia, difficulty with memory, and diplopia. Dose-related adverse events at doses greater than 200mg per day also include nervousness, confusion, depression, anxiety, anorexia, and weight loss.

STUDY EVALUATIONS

General Considerations
Starting at Visit 1, subjects will be required to keep a daily sleep and eating diary for the duration of the study. The following information will be collected: bedtime, time to fall asleep, whether the subject awoke during the night to eat, number of times the subject awoke to eat, duration and level of consciousness of each awakening, whether the subject remembers all of his/her night eating episodes, final wake time and time spent asleep. The diary will also capture the number of tablets of study medication taken. In addition, the diary includes an optional section for a bed partner or family member to provide information about witnessed night eating events.

Assessment scales included in this protocol will be administered/completed as outlined in the visit schedule. Evaluations for each phase of the study will be performed as described below.

Once a subject is randomized and is taking the study drug capsules, all visits must occur within a window of +/- 3 days of the schedule as given below.

Pre-randomization Phase
The Pre-randomization Phase may last up to 42 days based on washout requirements, not including a 14-day prospective baseline period. At Visit 1A (up to Day -42), the study will be explained and subjects will provide informed consent to participate in the study. Subjects will complete Visit 1 (Day -14) screening procedures following appropriate washout of prohibited medications.

Visit 1A* (Up to Day -56)
1. Obtain informed consent
2. Review inclusion/exclusion criteria
3. Assess previous and concomitant medications. Medication used for the past 42 days must be obtained.
4. Obtain detailed medical and psychiatric history and permission to contact primary care provider(s) for medical records
5. Perform physical examination
6. Perform neurological examination
7. Administer the eating disorders portion of the SCID
8. Obtain height and weight
9. Administer Hamilton Rating Scale for Depression (HAM-D)
10. Administer the Eating Attitudes Test
11. Schedule return visit

Visit 1* (Day -14)

1. Review inclusion/exclusion criteria
2. Assess concomitant medications
3. Obtain weight
4. Obtain non-fasting clinical laboratory tests as follows:
   - Urine Drug Screen [cocaine, amphetamines, methamphetamines, benzodiazepines, tetrahydrocannabinol (THC), and opiates].
   - Hemoglobin A1C
   - Creatinine (creatinine clearance will be calculated using standard formula)
5. Perform urine pregnancy test (subjects of childbearing potential only)
6. Administer the Three Factor Eating Questionnaire (TFEQ)
7. Administer the Sheehan Disability Scale
8. Dispense sleep and night eating diary
9. Record adverse events
10. Schedule return visit

*Visits 1A and 1 may be combined for subjects who do not require washout from prohibited medications.

Subjects who are eligible for study entry based on the results of the above will be instructed to return for Visit 2 (Day 1).

Double-Blind Phase

Subjects who continue to meet all entrance criteria will be randomized for study entry at Visit 2 (Day 1). The following procedures will be performed:

Visit 2 (Day 1)

1. Review inclusion/exclusion criteria
2. Assess concomitant medications
3. Administer the Medical Outcome Study (MOS) Sleep Scale
4. Administer the Epworth Sleepiness Scale
5. Collect and review sleep and night eating diary
6. Dispense sleep and night eating diary
7. Record adverse events
8. Dispense study medication
9. Schedule return visit in one week

Visit 3 (Day 7)

1. Assess concomitant medications
2. Obtain weight
3. Collect and review sleep and night eating diary
4. Dispense sleep and night eating diary
5. Collect study medication and perform drug accountability
6. Record adverse events
7. Dispense study medication
8. Schedule phone contact in one week and return visit in two weeks

Telephone contact (Day 14)

1. Assess concomitant medications
2. Discuss sleep and eating diary and remind subject to complete diary daily
3. Discuss medication compliance and remind subject to take medication daily
4. Record adverse events
5. Discuss medication dose and make adjustments if indicated
6. Offer option to come in to clinic for unscheduled visit in the event that subject wishes to discuss adverse events or issues with study protocol and compliance
7. Confirm scheduled return visit in one week

Visit 4 (Day 21)

1. Assess concomitant medications
2. Obtain weight
3. Collect and review sleep and night eating diary
4. Dispense sleep and night eating diary
5. Collect study medication and perform drug accountability
6. Record adverse events
7. Dispense study medication
8. Schedule phone contact in one week and return visit in two weeks

Telephone Contact (Day 28)

1. Assess concomitant medications
2. Discuss sleep and eating diary and remind subject to complete diary daily
3. Discuss medication compliance and remind subject to take medication daily
4. Record adverse events
5. Discuss medication dose and make adjustments if indicated
6. Offer option to come in to clinic for unscheduled visit in the event that subject wishes to discuss adverse events or issues with study protocol and compliance
7. Confirm scheduled return visit in one week

Visit 5 (Day 35)

1. Assess concomitant medications
2. Obtain weight
3. Perform urine pregnancy test (subjects of childbearing potential only)
4. Administer the Medical Outcome Study (MOS) Sleep Scale
5. Administer the Epworth Sleepiness Scale
6. Administer the HAM-D
7. Collect and review sleep and night eating diary
8. Dispense sleep and night eating diary
9. Collect study medication and perform drug accountability
10. Record adverse events
11. Dispense study medication
12. Schedule phone contact in one week and return visit in two weeks

Telephone Contact (Day 42)

1. Assess concomitant medications
2. Discuss sleep and eating diary and remind subject to complete diary daily
3. Discuss medication compliance and remind subject to take medication daily
4. Record adverse events
5. Discuss medication dose and make adjustments if indicated

6. Offer option to come in to clinic for unscheduled visit in the event that subject wishes to discuss adverse events or issues with study protocol and compliance
7. Confirm scheduled return visit in one week

Visit 6 (Day 49)
1. Assess concomitant medications
2. Obtain weight
3. Collect and review sleep and night eating diary
4. Dispense sleep and night eating diary
5. Collect study medication and perform drug accountability
6. Record adverse events
7. Dispense study medication
8. Schedule phone contact in one week and return visit in two weeks

Telephone Contact (Day 56)
1. Assess concomitant medications
2. Discuss sleep and eating diary and remind subject to complete diary daily
3. Discuss medication compliance and remind subject to take medication daily
4. Record adverse events
5. Discuss medication dose and make adjustments if indicated
6. Offer option to come in to clinic for unscheduled visit in the event that subject wishes to discuss adverse events or issues with study protocol and compliance
7. Confirm scheduled return visit in one week

Visit 7 (Day 63)
1. Assess concomitant medications
2. Obtain vital signs (sitting blood pressure, pulse, and weight)
3. Perform urine pregnancy test (subjects of childbearing potential only)
4. Administer the Medical Outcome Study (MOS) Sleep Scale
5. Administer the Epworth Sleepiness Scale
6. Collect and review sleep and night eating diary
7. Dispense sleep and night eating diary
8. Collect study medication and perform drug accountability
9. Record adverse events
10. Dispense study medication
11. Schedule return visit in four weeks

Telephone Contact (Day 77)
1. Assess concomitant medications
2. Record adverse events
3. Confirm return visit in two weeks

Visit 8 (Day 91)
1. Assess concomitant medications
2. Perform physical examination
3. Obtain weight
4. Administer the Medical Outcome Study (MOS) Sleep Scale
5. Administer the Epworth Sleepiness Scale
6. Administer the HAM-D
7. Administer the TFEQ

8. Administer the SDS
9. Obtain blood sample for HbA1C
10. Collect and review sleep and night eating diary
11. Collect study medication and perform drug accountability
12. Record adverse events
13. Dispense medication and instruct the subject on tapering.
14. Schedule Post-Taper Visit 9 (Day 105) in approximately 2 weeks

Taper Period
After completion of the titration and maintenance periods (13 weeks), subjects will taper their study medication by decreasing their dose by approximately 30% every three days. Subjects will return for Visit 9 (Day 105) and the following procedures will be performed:

Visit 9 (Day 105)
1. Assess concomitant medications
2. Obtain weight
3. Record adverse events
4. Collect study medication and perform drug accountability

Early Withdrawal
Subject participation may be terminated based upon subject choice, protocol violation (e.g., non-compliance), adverse event, or if a subject is lost to follow-up. The primary reason for withdrawal should be clearly indicated in the subject's study file.

In the event that a subject discontinues prematurely, final visit procedures will be performed at the time of discontinuation, if possible. Subjects who discontinue prematurely should be scheduled promptly for final visit (Visit 8, Day 91) procedures, preferably within 24 hours of the last dose. Subjects should taper study medication as discussed under Study Treatments. All adverse events should be followed to resolution, if possible. All unused study medication must be returned to the investigator.

CONCOMITANT THERAPY

General
Subjects may have concurrent illnesses that require prescription or over-the-counter medication during the course of the study. All exclusionary medications taken within 4 weeks (28 days) prior to Visit 1 (Day-14), with the exception of flurazepam and protriptyline which should be recorded within 5 weeks (35 days) and 6 weeks (42 days), respectively, of Visit 1, as well as those continued at the start of the study or started during the study (other than study medication), including the drug name, dose, duration and indication for use, should be recorded in the subjects' study files.

If the patient is taking a prohibited medication, the investigator and patient will discuss the risk and benefits of a trial of tapering and discontinuation of the medication. Any potential medication discontinuation will also be discussed with the prescribing physician.

Modifications to a subject's pre-existing treatment and regimen are not to be made for the explicit purpose of entering this trial, but should be done only where deemed clinically appropriate by the investigator.

The following medications are prohibited during the trial and subjects must observe the designated washout periods prior to Visit 1 (Day -14):

Prohibited Medications Prior to Visit 1 (Day –14) and During the Trial	Washout Period
Anorexigenic agents for obesity management, including, but not limited to: • Sibutramine (Meridia®) • Orlistat (Alli™, Xenical®) • Over-the-counter agents such as phentermine, hypericum • Herbal preparations, including but not limited to: • Mah Wang • Ephedra • Herbal-life • Tahitian Noni-Juice	4 weeks
Tricyclic Antidepressants • imipramine (Tofranil®) • reboxetine (Edronax®) • trimipramine (Surmontil®)	1 week
• desipramine (Norpramine®) • amoxapine (Asendin®) • maprotiline • nortriptyline (Pamelor®, Aventyl®) • clomipramine (Anafranil®) • amitriptyline (Elavil®) • doxepin (Sinequan®)	2 weeks
• protriptyline (Vivactil®)	6 weeks
Benzodiazepine Receptor Agonists • zolpidem (Ambien®, Ambien CR®) • eszopiclone (Lunesta®) • zopiclone (Imovane®, Zimovane®) • zaleplon (Sonata®)	2 weeks
Benzodiazepines • estazolam (Prosom®) • lorazepam (Ativan®) • temazepam (Restoril®) • triazolam (Halcion®)	1 week
• alprazolam (Xanax®)	2 weeks
• clonazepam (Klonopin®) • clorazepate (Tranxene®) • quazepam (Doral®)	3 weeks
• flurazepam (Dalmane®) • chlordiazepoxide (Librium)	5 weeks
Drugs with mixed actions • mirtazapine (Remeron®)	2 weeks

MAO Inhibitors • isocarboxazid (Marplan®) • phenelzine (Nardil®)	4 weeks
• tranylcypromine (Parnate®) • selegiline hydrochloride (Eldepryl®))	5 weeks
Antiepileptic agents • topiramate (Topamax®) • phenytoin sodium, phenytoin (Dilantin®) • phenytoin sodium (Phenytek™) • methsuximide (Celontin®) • valproate sodium (Depacon®) • valproic acid (Depakene®) • divalproex sodium, divalproex, valproic acid (Depakote®) • ethosuximide (Zarontin®) • carbamazepine (Tegretol®, Carbatrol®, Epitol®)	3 weeks
Dopamine antagonists • perphenazine (Trilfon®) • thioridazine (Mellaril®) • trifluoperazine (Stelazine®) • fluphenazine (Prolixin®, Permitil®)	3 weeks
• mesoridazine (Serenti®l) • chlorpromazine (Thorazine®) • haloperidol (Haldol®) • droperidol (Inapsine®) • thiothixene (Navane®)	3 weeks
Carbonic anhydrase inhibitors • acetazolamide (Diamox®) • triamterene (Dyazide®, Dyrenium®, Maxzide®) • zonisamide (Zonegran®)	4 weeks
Atypical Antipsychotics • risperidone (Risperdal®) • olanzapine (Zyprexa®, Zyprexa Zydis®)	4 weeks
Use of an investigational drug or device	4 weeks

*Chronic use of antacids and the use of calcium supplements greater than the recommended daily dose are prohibited during the trial.

ADVERSE EVENTS

This study follows Partners Health Care guidelines regarding the definitions and reporting policies of adverse events.

Definition: An adverse event is any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research

(modified from the definition of adverse events in the 1996 International Conference on Harmonization E-6 Guidelines for Good Clinical Practice).

This includes any occurrence that is new in onset or aggravated in severity or frequency from the baseline condition, or abnormal results of diagnostic procedures including laboratory test abnormalities. Any such event is considered an adverse event if it meets any of the following conditions:

- results in discontinuation from the study;
- requires treatment or any other therapeutic intervention;
- requires further diagnostic evaluation (excluding a repetition of the same procedure to confirm the abnormality); or
- is associated with clinical signs or symptoms judged by the investigator to have a significant clinical impact.

Adverse events may or not be related to the study medication or research procedures. Those that are considered related meet the criteria listed below and those that are unrelated are all others that do not. Adverse events may be serious or non-serious. Serious adverse events include those that meet the criteria listed below, and non-serious adverse events include all others. Adverse events may also be unexpected or expected. Unexpected adverse events meet the criteria listed below and expected adverse events are all others that do not.

Serious Adverse Event

A serious adverse event is any untoward medical occurrence that meets the above definition and any of the following conditions:

- results in death;
- is life threatening (places the subject at immediate risk of death from the event as it occurred);
- requires inpatient hospitalization or prolongation of existing hospitalization;
- results in a persistent or significant disability/incapacity;
- results in a congenital anomaly/birth defect; or
- any other adverse event that, based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the outcomes listed above (examples of such events include allergic bronchospasm requiring intensive treatment in the emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse).

Note: Medical and scientific judgment should be exercised in deciding whether expedited reporting is appropriate in other situations; for example, important medical events may not be immediately life-threatening or result in death or hospitalization, but may jeopardize the subject or may require intervention to prevent one of the outcomes listed in the definition above.

Unexpected (Unlisted) Adverse Event

- Any adverse event occurring in one or more subjects participating in a research protocol, the nature, severity, or frequency of which is not consistent with either:

- the known or foreseeable risk of adverse events associated with the procedures involved in the research that are described in (a) the protocol-related documents, such as the IRB-approved research protocol, any applicable investigator brochure,

and the current IRB-approved informed consent document, and (b) other relevant sources of information, such as product labeling and package inserts; or

- the expected natural progression of any underlying disease, disorder, or condition of the subject(s) experiencing the adverse event and the subject's predisposing risk factor profile for the adverse event.

Associated with the Use of the Drug
An adverse event is considered associated with the use of the drug if the attribution is possible, probable or very likely by the definitions listed below:

Attribution Definitions

- Not related An adverse event which is not related to the use of the drug.

- Doubtful An adverse event for which an alternative explanation is more likely, e.g., concomitant drug(s), concomitant disease(s), and/or the relationship in time suggests that a causal relationship is unlikely.

- Possible There is a reasonable possibility that the adverse event, incident, experience or outcome may have been caused by the procedures involved in the research (modified from the definition of associated with use of the drug in FDA regulations at 21 CFR 312.32(a)). A reasonable possibility is defined as more likely than not related to the research procedures or, in other words, there is a > 50% likelihood of the event having been caused by the procedures involved in the research.

- Probable An adverse event which might be due to the use of the drug. The relationship in time is suggestive (e.g., confirmed by dechallenge). An alternative explanation is less likely, e.g., concomitant drug(s), concomitant disease(s).

- Very likely An adverse event which is listed as a possible adverse reaction and cannot be reasonably explained by an alternative explanation, e.g., concomitant drug(s), concomitant disease(s). The relationship in time is very suggestive (e.g., it is confirmed by dechallenge and rechallenge).

All Adverse Events
All adverse events that occur between the first study-related procedure and within 30 days of the last dose of study medication will be reported. Adverse events will be reported to the PHRC according to their guidelines.

Subjects should report any adverse events voluntarily or in response to general, non-directed questioning (e.g., "How has your health been since the last visit?). For each adverse event reported by the subject, the investigator should obtain all the information required to complete documentation in the subject's research file.

All adverse events, regardless of seriousness, severity, or presumed relationship to study therapy, must be recorded using medical terminology in the subject's study documents. Whenever possible, diagnoses should be given when signs and symptoms are due to a common etiology (e.g., cough,

runny nose, sneezing, sore throat, and head congestion should be reported as “upper respiratory infection”). The investigator must document his/her opinion concerning the relationship of the adverse event to study therapy. All measures required for adverse event management must be recorded in the source document.

Pregnancies
Pregnancies occurring during the study will be reported by the investigational staff within one working day of their knowledge of the event. Any subject who becomes pregnant during participation in this study will be promptly withdrawn from the study. Follow-up information regarding the outcome of the pregnancy and any postnatal sequelae in the infant will be required.

Compensation
Subjects will be compensated $30.00 for each study visit, for a total of up to $300.00 for those who complete the entire study. Subjects will not be compensated for phone calls.

STATISTICAL METHODS

Sample Size Determination
The sample size for this pilot study was not based upon statistical considerations.

Efficacy Analyses
The efficacy analyses will be performed on an intent-to-treat (ITT) population defined as all randomized subjects who were dispensed study medication and for whom one post-baseline efficacy measurement is available.

Efficacy analyses will be conducted separately for subjects with night eating syndrome or sleep-related eating disorder, and across all subjects with either of these two diagnoses. The primary efficacy parameter will be the change in the number of nights per week of the specified nocturnal eating episode.

The primary efficacy parameter of number of nights per week with nocturnal episodes will be analyzed using ANCOVA with baseline frequency of nocturnal episodes as a co-variate. Diagnostic procedures will be conducted to determine whether the statistical assumptions are met.

The MOS, SDS, TFEQ, HAM-D, HbA1C, body weight and Epworth Sleepiness Scale will be analyzed using an ANCOVA with the baseline value as a covariate.

Information obtained from the sleep diaries will be summarized.

Safety Analyses

Adverse Events
The percent of subjects with specific treatment-emergent adverse events will be summarized by treatment group.

Additional tabulations will be conducted to summarize those subjects who have discontinued treatment due to an adverse event or who experienced a severe or a serious adverse event.

Clinical Laboratory Tests
Laboratory data will be summarized by treatment group by the type of laboratory test.

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TIME AND EVENTS SCHEDULE

	Visit 1A (Day -56)	Visit 1 (Day -14)	Visit 2 (Day 1)	Visit 3 (Day 7)	Phone Contact (Day 14)	Visit 4 (Day 21)	Phone Contact (Day 28)	Visit 5 (Day 35)	Phone Contact (Day 42)	Visit 6 (Day 49)	Phone Contact (Day 56)	Visit 7 (Day 63)	Phone Contact (Day 77)	Visit 8 (Day 91)	Visit 9 (Day 105)
Informed Consent	X														
Review Inclusion/Exclusion Criteria	X	X	X												
Concomitant Medication Review	X	X	X	X	X	X	X	X	X	X	X	X	x	X	X
Medical & Psychiatric History	X														
Physical Examination	X														
Neurologic Examination	X														
SCID Eating Disorders	X														
Weight	X	X	X	X		X		X		X		X		X	X
Urine Pregnancy Test		X						X				X			
Urine Drug Screen		X													
Blood HbA1C		X*												X	
MOS			X					X				X		X	
Epworth Sleepiness Scale			X					X				X		X	
HAM-D	X							X				X		X	
TFEQ		X												X	
EAT	X														
Sheehan Disability Scale		X												x	
Dispense Sleep and Night-Eating Diary		X	X	X		X		X		X		X			
Review Sleep and Night-Eating Diary			X	X	X	X	X	X	x	X	x	X	X	X	
Record Adverse Events		X	X	X	X	X	X	X	X	X	X	X	X	X	X
Dispense Study Medication			X	X	X	X	X	X	x	X	x	X	x	X	
Collect study medication and perform drug accountability				x		x		X		X		X		x	X

*Creatinine also tested at visit 1

ATTACHMENTS

Attachment 1
Medical Outcome Study (MOS) Sleep Scale

1. How long did it usually take you to fall asleep during the past 4 weeks? (circle one)

0-15 minutes……...	1
16-30 minutes…….	2
31-45 minutes…….	3
46-60 minutes…….	4
More than 60 minutes…….	5

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2. On the average, how many hours did you sleep each night during the past 4 weeks?

Write in # of hours per night _____

How often during the past 4 weeks did you…. (circle one number on each line):

		All of the Time	Most of the Time	A Good Bit of the Time	Some of the Time	A Little of the Time	None of the Time
3.	feel that your sleep was not quiet (moving restlessly, feeling tense, speaking, etc., while sleeping)?	1	2	3	4	5	6
4.	get enough sleep to feel rested upon waking in the morning?	1	2	3	4	5	6
5.	awaken short of breath or with a headache?	1	2	3	4	5	6
6.	feel drowsy or sleepy during the day?	1	2	3	4	5	6
7.	have trouble falling asleep?	1	2	3	4	5	6
8.	awaken during your sleep time and have trouble falling asleep again?	1	2	3	4	5	6
9.	have trouble staying awake during the day?	1	2	3	4	5	6
10.	snore during your sleep?	1	2	3	4	5	6
11.	take naps (5 minutes or longer) during the day?	1	2	3	4	5	6
12.	get the amount of sleep you needed?	1	2	3	4	5	6

Attachment 2
Epworth Sleepiness Scale

How likely are you to doze off or fall asleep in the following situations, in contrast to feeling just tired? This refers to your usual way of life in recent times. Even if you have not done some of these things recently, try to work out how they would have affected you.

Use the following scale to choose the most appropriate number for each situation:

0 = Would **never** doze

1 = **Slight** chance of dozing

2 = **Moderate** chance of dozing

3 = **High** chance of dozing

SITUATION	**CHANCE OF DOZING**
Sitting and reading	_____
Watching TV	_____
Sitting, inactive in a public place (e.g. a theatre or a meeting)	_____
As a passenger in a car for an hour without a break	_____
Lying down to rest in the afternoon when circumstances permit	_____
Sitting and talking to someone	_____
Sitting quietly after lunch without alcohol	_____
In a car, while stopped for a few minutes in traffic	_____
Total Score:	_____

EPWORTH SLEEPINESS SCALE SCORE

A score of <8	indicates normal sleep function
A score of 8-10	indicates mild sleepiness
A score of 11-15	indicates moderate sleepiness
A score of 16-20	indicates severe sleepiness
A score of 21-24	indicates excessive sleepiness

Attachment 3: Hamilton Rating Scale for Depression (HAM-D)

1. Depressed mood (Sadness, hopeless, helpless, worthless)

0 = Absent
1 = Gloomy attitude, pessimism, hopelessness
2 = Occasional weeping
3 = Frequent weeping
4 = Patient reports highlight these feelings states in his/her spontaneous verbal and non-verbal communication.

2. 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 punishment
4 = Hears accusatory or denunciatory voices and/or experiences threatening visual hallucinations. Delusions of guilt.

3. Suicide

0 = Absent
1 = Feels life is not worth living
2 = Wishes he/she were dead, or any thoughts of possible death to self
3 = Suicide, ideas or half-hearted attempt
4 = Attempts at suicide (any serious attempt rates 4)

4. Insomnia, early

0 = No difficulty falling asleep
1 = Complaints of occasional difficulty in falling asleep i.e. more than half-hour
2 = Complaints of nightly difficulty falling asleep

5. Insomnia, middle

0 = No difficulty
1 = Patient complains of being restless and disturbed during the night
2 = Walking during the night – any getting out of bed rates 2 (except voiding bladder)

6. Insomnia, late

0 = No difficulty
1 = Waking in the early hours of the morning but goes back to sleep
2 = Unable to fall asleep again if he/she gets out of bed

7. Work and activities

0 = No difficulty
1 = Thoughts and feelings of incapacity related to activities: work or hobbies
2 = Loss of interest in activity – hobbies or work – either directly reported by patient or indirectly seen in listlessness, in decisions and vacillation (feels he/she has to push self to work or activities)
3 = Decrease in actual time spent in activities or decrease in productivity. In hospital, rate 3 if patient does not spend at leas three hours a day in activities
4 = Stopped working because of present illness. In hospital rate 4 if patient engages in no activities except supervised ward chores

8. Retardation : Psychomotor (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 = Interview impossible

9. Agitation

0 = None
1 = Fidgetiness
2 = Playing with hands, hair, obvious restlessness
3 = Moving about; can't sit still
4 = Hand wringing, nail biting, hair pulling, biting of lips, patient is on the run

10. Anxiety, psychic

Demonstrated by: subjective tension and irritability, loss of concentration, worrying about minor matters, apprehension, fears expressed without questioning, feelings of panic, feeling jumpy

0 = Absent
1 = Mild
2 = Moderate
3 = Severe
4 = Incapacitating

11. Anxiety, somatic

Physiological concomitants of anxiety such as:

- gastrointestinal,:dry mouth, wind, indigestion, diarrhea, cramps, belching
- cardiovascular: palpations, headaches
- respiratory: hyperventilation, sighing
- urinary frequency
- sweating
- giddiness, blurred vision
- tinnitus

0 = Absent
1 = Mild
2 = Moderate
3 = Severe
4 = Incapacitating

12. Somatic symptoms: gastro-intestinal

0= None
1= Loss of appetite but eating without encouragement from others. Food intake about normal.
2= Difficulty eating without urging from others. Marked reduction of appetite and food intake.

13. Somatic symptoms: general

0 = None
1 = Heaviness in limbs, back or head; backaches, headaches, muscle aches, loss of energy, fatigability
2 = Any clear-cut symptom rates 2

14. Genital Symptoms

Symptoms such as: loss of libido, menstrual disturbances

0 = Absent
1 = Mild
2 = Severe

15. Hypochondriasis

0 = Not present
1 = Self-absorption (bodily)
2 = Preoccupation with health
3 = Strong conviction of some bodily illness
4 = Hypochondrial delusions

16. Loss of Weight
Rate either 'A' or 'B':

A When rating by history:
0 = No weight loss
1 = Probable weight loss associated with present illness
2 = Definite (according to patient) weight loss

B Actual weight changes (weekly):
0 = Less than 1 lb (0.5 kg) weigh loss in one week
1 = 1-2 lb (0.5 kg-1.0 kg) weight loss in week
2 = Greater than 2 lb (1 kg) weight loss in week
3 = Not assessed

17. Insight
0 = Acknowledges being depressed and ill
1 = Acknowledges illness but attributes cause to bad food, overwork, virus, need for rest, etc.
2 = Denies being ill at all

TOTAL SCORE: ___

Attachment 4: Eating Attitudes Test (EAT)

Please do not consider episodes of eating while you are asleep when answering this questionnaire

Please check a response for each of the following statements:

I . . .	Always	Usually	Often	Sometimes	Rarely	Never
1. Am terrified about being overweight.	□	□	□	□	□	□
2. Avoid eating when I am hungry.	□	□	□	□	□	□
3. Find myself preoccupied with food.	□	□	□	□	□	□
4. Have gone on eating binges where I feel that I may not be able to stop.	□	□	□	□	□	□
5. Cut my food into small pieces.	□	□	□	□	□	□
6. Aware of the calorie content of foods that I eat.	□	□	□	□	□	□
7. Particularly avoid food with a high carbohydrate content (i.e. bread, rice, potatoes,etc.)	□	□	□	□	□	□
8. Feel that others would prefer if I ate more.	□	□	□	□	□	□
9. Vomit after I have eaten.	□	□	□	□	□	□
10. Feel extremely guilty after eating.	□	□	□	□	□	□
11. Am preoccupied with a desire to be thinner.	□	□	□	□	□	□
12. Think about burning up calories when I exercise.	□	□	□	□	□	□
13. Other people think that I am too thin.	□	□	□	□	□	□
14. Am preoccupied with the thought of having fat on my body.	□	□	□	□	□	□

(continued on next page)

Attachment 4: Eating Attitudes Test (EAT)
continued

Please do not consider episodes of eating while you are asleep when answering this questionnaire

Please check a response for each of the following statements:

I . . .	Always	Usually	Often	Sometimes	Rarely	Never
15. Take longer than others to eat my meals.	□	□	□	□	□	□
16. Avoid foods with sugar in them.	□	□	□	□	□	□
17. Eat diet foods.	□	□	□	□	□	□
18. Feel that food controls my life.	□	□	□	□	□	□
19. Display self-control around food.	□	□	□	□	□	□
20. Feel that others pressure me to eat.	□	□	□	□	□	□
21. Give too much time and thought to food.	□	□	□	□	□	□
22. Feel uncomfortable after eating sweets.	□	□	□	□	□	□
23. Engage in dieting behavior.	□	□	□	□	□	□
24. Like my stomach to be empty.	□	□	□	□	□	□
25. Have the impulse to vomit after meals.	□	□	□	□	□	□
26. Enjoy trying new rich foods.	□	□	□	□	□	□

Total Score_____

Attachment 5: Three Factor Eating Questionnaire (TFEQ)

Please do not consider episodes of eating while you are asleep when answering this questionnaire

Part I: Read each of the following 36 statements carefully. If you agree with the statement or feel that it is true as applied to you; answer true by circling the appropriate letter (T). If you disagree with the statement, or feel that it is false as applied to you, answer false by circling the appropriate letter (F).

1.	When I smell a sizzling steak or see a juicy piece of meat, I find it very difficult to keep from eating, even if I have just finished a meal.	T	F
2.	I usually eat too much at social occasions, like parties and picnics.	T	F
3.	I am usually so hungry that I eat more than three times a day.	T	F
4.	When I have eaten my quota of calories, I am usually good about not eating anymore.	T	F
5.	Dieting is so hard for me because I just get too hungry.	T	F
6.	I deliberately take small helpings as a means of controlling my weight.	T	F
7.	Sometimes things just taste so good that I keep on eating even when I am no longer hungry.	T	F
8.	Since I am often hungry, I sometimes wish that while I am eating, an expert would tell me that I have had enough or that I can have something more to eat.	T	F
9.	When I feel anxious, I find myself eating.	T	F
10.	Life is too short to worry about dieting.	T	F
11.	Since my weight goes up and down, I have gone on reducing diets more than once.	T	F
12.	I often feel so hungry that I just have to eat something.	T	F
13.	When I am with someone who is overeating, I usually overeat too.	T	F
14.	I have a pretty good idea of the number of calories in common foods.	T	F
15.	Sometimes when I start eating, I just can't seem to stop.	T	F
16.	It is not difficult for me to leave something on my plate.	T	F
17.	At certain times of the day, I get hungry because I have gotten used to eating then.	T	F
18.	While on a diet, if I eat a food that is not allowed, I consciously eat less for a period of time to make up for it.	T	F
19.	Being with someone who is eating often makes me hungry enough to eat also.	T	F
20.	When I feel blue, I often overeat.	T	F
21.	I enjoy eating too much to spoil it by counting calories or watching my weight.	T	F
22.	When I see a real delicacy, I often get so hungry that I have to eat right away.	T	F
23.	I often stop eating when I am not really full as a conscious means of limiting the amount that I eat.	T	F
24.	I get so hungry that my stomach often seems like a bottomless pit.	T	F
25.	My weight has hardly changed at all in the last ten years.	T	F
26.	I am always hungry so it is hard for me to stop eating before I finish the food on my plate.	T	F
27.	When I feel lonely, I console myself by eating.	T	F
28.	I consciously hold back at meals in order not to gain weight.	T	F
29.	I sometimes get very hungry late in the evening or at night.	T	F
30.	I eat anything I want, any time I want.	T	F
31.	Without even thinking about it, I take a long time to eat.	T	F
32.	I count calories as a conscious means of controlling my weight.	T	F
33.	I do not eat some foods because they make me fat.	T	F
34.	I am always hungry enough to eat at any time.	T	F
35.	I pay a great deal of attention to changes in my figure.	T	F
36.	While on a diet, if I eat a food that is not allowed, I often then splurge and eat	T	F

other high calorie foods.

Part II. Each question I this section is followed by a number of answer options. After reading each question carefully, choose the one option which most applies to you and circle the appropriate number.

37. How often are you dieting in an conscious effort to control your weight?	1 Rarely	2 Sometimes	3 Usually	4 Always
38. Would a weight fluctuation of 5 lbs. affect the way you live your life?	1 Not at all	2 Slightly	3 Moderately	4 Very Much
39. How often do you feel hungry?	1 Only at meal times	2 Sometimes between meals	3 Often between meals	1 Almost always
40. Do your feelings of guilt about overeating help you to control your food intake?	1 Never	2 Rarely	3 Often	4 Always
41. How difficult would it be for you to stop eating halfway through dinner and not eat for the next four hours?	1 Easy	2 Slightly difficult	3 Moderately difficult	4 Very Difficult
42. How conscious are you of what you are eating?	1 Not at all	2 Slightly	3 Moderately	4 Very Much
43. How frequently do you avoid "stocking up" on tempting foods?	1 Almost never	2 Seldom	3 Usually	4 Almost Always
44. How likely are you to shop for low calorie foods?	1 Unlikely	2 Slightly likely	3 Moderately likely	4 Very likely
45. Do you eat sensibly in front of other and splurge alone?	1 Never	2 Rarely	3 Often	4 Always
46. How likely are you to consciously eat slowly in order to cut down on how much you eat?	1 Unlikely	2 Slightly likely	3 Moderately likely	4 Very likely
47. How frequently do you skip dessert because you are no longer hungry?	1 Almost never	2 Seldom	3 At least once a week	4 Almost every day
48. How likely are you to consciously eat less than you want?	1 Unlikely	2 Slightly likely	3 Moderately likely	4 Very likely
49. Do you go on eating binges even though you are not hungry?	1 Never	2 Rarely	3 Sometimes	4 At least once a week
50. To what extent does this statement describe your eating behavior? "I start dieting in the morning, but because of any number of things that happen during the day, by evening I have given up and eat what I want, promising myself to start dieting again tomorrow."	1 Not like me	2 Little like me	3 Pretty good description of me	4 Describes me perfectly

Part III:

51. On a scale of 1 to 6, where 1 means no restraint in eating (eat whatever you want, whenever you want it) and 6 means total restraint (constantly limiting food intake and never "giving in"), what number would you give yourself?

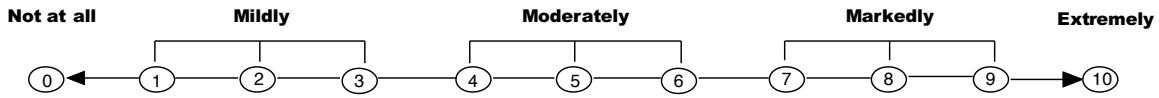
1. eat whatever you want, whenever you want it
2. usually eat whatever you want, whenever you want it
3. often eat whatever you want, whenever you want it
4. often limit food intake, but often "give in"
5. usually limit food intake, rarely "give in"
6. constantly limiting food intake, never "giving in"

Attachment 6:
Sheehan Disability Scale (SDS)

Instructions: Please mark ONE box for each scale based on your symptoms over the past week.

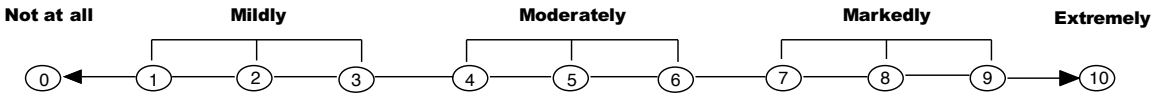
WORK / SCHOOL

The symptoms have disrupted your work / school work:



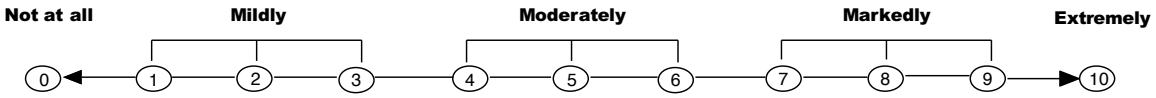
SOCIAL LIFE

The symptoms have disrupted your social life:



FAMILY LIFE / HOME RESPONSIBILITIES

The symptoms have disrupted your family life/home responsibilities:



Please answer the following questions about how much your symptoms of Sleep-Related Eating Disorder affect you emotionally.

1. How worried or distressed are you by your symptoms of Sleep-Related Eating Disorder?
(*circle one number*)

Not Worried										Very Worried
0	1	2	3	4	5	6	7	8	9	10

2. How ashamed are you of your symptoms of Sleep-Related Eating Disorder?
(*circle one number*)

Not Ashamed										Very Ashamed
0	1	2	3	4	5	6	7	8	9	10