Paroxetine in the Treatment of Primary Insomnia: Preliminary Clinical and Electroencephalogram Sleep Data

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Background: Primary insomnia is a persistent and recurrent disorder as well as a risk factor for depression. The goal of this study was to determine whether paroxetine, a nonsedating antidepressant, would be effective in the treatment of patients with primary insomnia.

Method: Fifteen patients meeting DSM-IV criteria for primary insomnia received paroxetine at bedtime for 6 weeks in an open, flexible-dose trial (median dose = 20 mg). Patients were assessed with daily sleep diaries, baseline and treatment polysomnography, and weekly standardized clinical evaluations.

Results: Of the 14 patients who completed the study (1 dropped out owing to side effects), 11 improved with treatment, and 7 of these 11 no longer met diagnostic criteria for insomnia. Although self-reported sleep quality (measured by the Pittsburgh Sleep Quality Index) and daytime well-being (measured by the Profile of Mood States) improved with treatment, the quantity of sleep, measured by diary and by polysomnography, did not change consistently with these improvements. Power spectral analysis suggested that paroxetine treatment may be associated with decreases in power in frequencies within the delta and alpha frequency ranges.

Conclusion: These results support the effectiveness of paroxetine in the acute treatment of primary insomnia. Further evaluation with controlled and longitudinal designs is warranted.

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Chronic insomnia is a common symptom with a prevalence of approximately 5% to 10%.[1] Individuals with chronic insomnia report elevated levels of anxiety, depression, distress, and general medical conditions.[1–4] Patients with chronic insomnia demonstrate interpersonal and occupational impairments when compared with good sleepers.[5–7] Chronic insomnia that extends over a 1-year period is a risk factor for the development of major depression, and longitudinal studies suggest that untreated chronic insomnia does not tend to remit with time.[1,8–10]

Despite relatively few outcome studies, clinicians have decreased benzodiazepine prescriptions for treatment of insomnia by 30% and increased the use of antidepressants as hypnotics by 100%.[11] Empirical support for the efficacy of antidepressants in patients with chronic insomnia in the absence of major mood disorders has been restricted to sedating antidepressants examined in limited clinical trials.[12] However, studies of nonsedating antidepressants, including the selective serotonin reuptake inhibitors (SSRIs), in patients whose insomnia is associated with a mood disorder suggest that mechanisms other than sedation may lead to improvements in sleep quality.[13–16] Given the relationship between chronic insomnia and depression, we chose to examine the effectiveness of paroxetine in treating patients with primary insomnia.[17] Paroxetine was selected because it allows for once-a-day administration, requires little dose titration, is reported to have fewer "activating" properties than other SSRIs, and is not considered sedating in the majority of patients.[18]

As our major aim, we hypothesized that at least 60% of patients treated with paroxetine would be "much improved" or "very much improved" on the Clinical Global Impressions-Improvement scale (CGI-I).[19] Our hypothesis was based on reports in the literature for benzodiazepine treatment of chronic insomnia, the usual pharmacologic intervention for chronic insomnia.[20] In addition, specific domains of primary insomnia, e.g., self-reported sleep quality, sleep quantity, daytime well-being, and daytime functioning, were also hypothesized to be associated with global treatment outcome. Exploratory analyses of automated measures of polysomnographic sleep (power spectral analyses) were conducted to characterize changes in pharmacoelectroencephalographic patterns.

METHOD

Study Design

Individuals aged 35 to 75 years with insomnia were identified through radio advertisement and physician referrals. DSM-IV diagnostic eligibility was determined using a structured sleep disorders interview and the Structured Clinical Interview for DSM-IV Axis I Disorders-Patient Edition (SCID-I/P).[21] Patients were given physical examinations, and screening laboratory work was done. Patients completed baseline sleep diaries for 2 weeks prior to beginning treatment and for each week during treatment. Patients were studied with laboratory polysomnography, using standard procedures as outlined in the Electroencephalogram (EEG) Measurement section below,[22] for 2 consecutive nights. Night 1 was used as an adaptation night and to screen for sleep apnea syndrome (apnea-hypopnea index > 10) and periodic limb movement disorder (periodic limb movement-arousal index > 10). Urine toxicology screening was performed for benzodiazepines and drugs of abuse. Patients had to be free of medications affecting sleep for at least 2 weeks prior to participation (4 weeks if fluoxetine had been taken). After a complete description of procedures and possible side effects was given to the subjects, written informed consent was obtained in accordance with institutional review board procedures.

Treatment duration was 6 weeks, followed by a 2-week taper. Patients met weekly with a clinician for standardized assessments of symptoms and side effects throughout the duration of the study. Sleep hygiene education was provided over the course of the treatment using the Sleep Hygiene Awareness and Practices Scale (SHAPS) to structure the intervention.[23] Paroxetine was initiated at 10 mg to be taken within 1 hour of desired bedtime and adjusted every 2 weeks up to 30 mg based on progress quantified by the CGI-I (a 7-point Likert scale completed by patient and by clinician that reflects global changes during treatment) and side effects by the UKU Side Effect Rating Scale[24] (UKU, a checklist scale for psychotropic drugs). The median dose of paroxetine at the end of the trial was 20 mg (range, 5–30 mg). Sleep diaries and pill counts served as measures of compliance. At the end of week 6, patients completed outcome measures and repeated 2 nights in the sleep laboratory, the first being a repeated adaptation night. Outcome clinical assessment included questions from the structured sleep interview to assess the symptoms of primary insomnia. The SCID-I/P was not repeated.

Subjects (Table 1)

Of 80 potential patients, 50 were excluded during phone screening, primarily for current psychiatric disorders or psychoactive medication use; 10 were excluded during the clinical evaluation, primarily for current psychiatric disorders. After the polysomnogram, 3 patients were excluded for a diagnosis of periodic limb movement disorder, 1 patient was excluded for obstructive sleep apnea, and 1 patient declined to participate. Of the 15 patients eligible and agreeing to participate, 14 completed the trial and 1 withdrew after the first day of treatment owing to nausea attributed to paroxetine. Of the 14 who completed the trial, 1 patient declined the repeat polysomnogram, but agreed to the remainder of the outcome assessment.

Table 1. Demographic Information

Variable	Baseline Value
Age, y, mean ± SD	52.9 ± 11.6
Sex, female, N (%)	9 (64)
Race, white, N (%)	14 (100)
Duration of insomnia symptoms, y, mean ± SD	17 ± 10
History of depression, yes, N (%)	6 (43)
History of insomnia treatment, yes, N (%)	13 (93)
History of antidepressant exposure, yes, N (%)	9 (64)

Although not an inclusion criterion, either diary or polysomnogram severity characteristics typical for hypnotic trials, e.g., sleep onset latency or wake after sleep onset of longer than 30 minutes, more than 3 awakenings at night, or a total sleep time of less than 6 hours, were demonstrated by all 14 patients. As shown in Table 2, the baseline mean Hamilton Rating Scale for Depression (HAM-D)[25] scores and the mean Beck Depression Inventory (BDI)[26] scores reflect modest levels of depressive symptoms. The baseline Hamilton Rating Scale for Anxiety (HAM-A),[27] Spielberger State-Trait Anxiety Inventory (STAI),[28] and the Brief Symptom Inventory (BSI)[29] scores reflect modest levels of anxiety and distress symptoms. The SCID-I/P assessment and the modest levels of distress, depression, and anxiety are consistent with chronic insomnia and congruent with the construct of primary insomnia, i.e., insomnia not resulting from another psychiatric disorder such as minor depression (see Gwirtsman et al.[30]) or dysthymia (see Philipp et al.[31]).

Clinical Measures

Given the pilot nature of the study, a variety of measures were used to assess patients' performance. These measures are presented in Tables 2 and 3. The primary outcome was clinical improvement measured as symptomatic improvement quantified by the CGI-I and by DSM-IV diagnostic criteria for primary insomnia. These measures were used to analyze data obtained through the structured sleep interview to categorize patients as responders and nonresponders.

In addition, rating scales were selected to reflect the individual diagnostic criteria of the DSM-IV construct of primary insomnia: self-reported sleep quality, sleep quantity, daytime well-being, and daytime functioning. Subjective sleep quality was measured by the Pittsburgh

Table 2. Outcome of Clinical Measures[a]

	Baseline		Outcome				
Clinical Measure	Mean	SD	Mean	SD	F	df	p
Self-report outcome (primary dependent measure)[b]	...	...	…	…	5.51	4,10	.01
Subjective sleep quality							
PSQI, less medication item	10.1	3.3	7.0	3.3	11.27	1,13	.01[c]
Daytime well-being							
POMS	21.1	28.2	2.9	23.1	21.37	1,13	< .01[c]
Daytime functioning							
MOS-SF36, physical subscale	49.0	10.5	49.5	7.7	0.06	1,13	.80[c]
MOS-SF36, mental subscale	43.8	12.8	49.4	10.8	6.76	1,13	.02[c]
Other clinical measures							
Depression symptoms							
HAM-D, 17-item	10.1	3.1	4.9	3.2	...	...	...
HAM-D, less sleep items	6.3	3.3	3.4	3.1	...	...	...
BDI	8.5	6.4	4.7	4.0	...	...	...
BDI, less sleep item	7.5	5.8	4.4	3.9	...	...	...
Anxiety symptoms							
HAM-A	8.6	3.5	3.0	1.7	...	...	...
STAI	45.44	4.4	42.4	4.3	...	...	...
Distress							
BSI	0.46	0.43	0.22	0.30	...	...	...
Sleep scales[d]							
DBQ	44.8	11.8	38.6	7.9	...	...	...
SHAPS Knowledge subscale	20.5	5.9	17.9	5.6	...	...	...
SHAPS Practices subscale	20.5	7.4	16.1	7.3	...	...	...
Side effects							
UKU	15.3	8.2	6.1	5.6	...	...	...

[a]Abbreviations: BDI = Beck Depression Inventory, BSI = Brief Symptom Inventory, DBQ = Dysfunctional Beliefs and Attitudes About Sleep Questionnaire, HAM-A = Hamilton Rating Scale for Anxiety, HAM-D = Hamilton Rating Scale for Depression, MOS-SF36 = Medical Outcomes Study 36-Item Short-Form Health Survey, POMS = Profile of Mood States, PSQI = Pittsburgh Sleep Quality Index, SHAPS = Sleep Hygiene Awareness and Practices Scale, STAI = Spielberger State-Trait Anxiety Inventory, UKU = UKU Side Effect Rating Scale. Symbol: ... = not applicable.
[b]One group MANOVA, repeated measures.
[c]Bonferroni-corrected level of significance: .05/4 = .0125.
[d]Lower number represents better clinical state.

Sleep Quality Index (PSQI).[32] Daytime well-being was measured by the Profile of Mood States (POMS).[33] Daytime functioning was measured by the Medical Outcomes Study 36-Item Short-Form Health Survey (MOS-SF36).[34] Sleep quantity was measured by 2 methods, the Pittsburgh Sleep Diary (PghSD)[35] and polysomnography. This was done because self-report and EEG-defined methods may provide different information about sleep.[15] The variables selected a priori to reflect sleep quantity were sleep onset latency, wake after sleep onset, and total sleep time, since each of these characterize the sleep quantity complaints of patients with insomnia.

The structured sleep and psychiatric interviews established diagnostic inclusion and exclusion criteria. However, because diagnostic reliability is marginal in distinguishing primary from psychiatric insomnia,[36] psychiatric symptom rating scales were included to demonstrate the modest levels of mood and anxiety symptoms at baseline. Depressive symptoms were measured by the BDI and the HAM-D. Anxiety symptoms were measured by the STAI and the HAM-A. Global distress was measured by the BSI. The Dysfunctional Beliefs and Attitudes About Sleep Questionnaire (DBQ)[37] was used to measure knowledge, practices, and cognitions affecting sleep.

EEG Measurement

Bedtime and wake-up time were at subjects' habitual times as determined by their 2-week sleep diaries. Patients were studied in the Western Psychiatric Institute and Clinic Sleep Laboratory in individual rooms connected by cables to central EEG equipment. All patients were recorded starting within 30 minutes of their habitual sleep times. Polysomnographic technologists used standard criteria for scoring sleep visually,[38] with periodic checks of interrater reliability ($\kappa = 0.76$ to 0.85 for most major sleep variables). All sleep was visually scored in 60-s epochs by raters blinded to clinical data. Unpublished data from our laboratory (available upon request) indicate comparability between the use of 60-s and 30-s epoch ratings on most sleep parameters.

Sleep was recorded on a 24-channel polygraph (78B Grass Instrument Division, Astromed, Inc., West Warwick, R.I.), and measurements included an EEG, an electro-oculogram (EOG), and a submental chin electromyogram (EMG).[39–41] The EEG consisted of a single C3

Table 3. Sleep Diary and Polysomnographic Measures[a]

Clinical Measure	Baseline Mean	Baseline SD	Outcome Mean	Outcome SD	F	df	p
Sleep quantity outcome (primary dependent measure)[b]	...	...	...	...	5.463	6,6	.03
Diary[c]							
Sleep onset latency, min	43.0	39.5	30.1	39.5	2.49	1,11	.14[d]
Wake after sleep onset, min	67.3	44.7	57.3	48.6	0.38	1,11	.55[d]
Time spent asleep, min	363.4	79.9	388.0	79.3	0.76	1,11	.40[d]
Polysomnography							
Sleep onset latency, min	18.1	12.1	24.7	10.9	4.29	1,11	.06[d]
Wake after sleep onset, min	66.1	62.9	49.2	39.3	0.53	1,11	.48[d]
Total sleep time, min	372.4	49.8	379.3	49.4	0.14	1,11	.72[d]
Other diary and polysomnographic measures							
Diary							
Time in bed, min	442.8	64.7	451.7	52.6	...	...	...
Sleep efficiency, %	77.6	13.9	82.8	11.7	...	...	...
No. of awakenings	2.3	1.2	2.7	1.1	...	...	...
Sleep quality VAS,[e] %	44.9	16.1	60.7	18.9	...	...	...
Waking mood VAS,[e] %	55.6	22.1	67.9	21.8	...	...	...
Alertness on waking VAS,[e] %	41.6	22.1	56.2	25.9	...	...	...
Polysomnography							
Total recording period, min	452.0	57.1	456.3	37.8	...	...	...
Sleep efficiency, %	82.4	11.4	84.9	8.0	...	...	...
No. of wakings	7.0	3.4	12.3	7.5	...	...	...
Stage 1, min	26.0	9.8	41.6	16.0	...	...	...
Stage 2, min	205.6	54.7	250.5	29.3	...	...	...
Stage 3, min	33.0	22.9	29.5	32.7	...	...	...
Stage 4, min	10.0	14.1	6.3	12.1	...	...	...
REM time, min	94.5	24.9	57.7	26.1	...	...	...
REM latency (minus awake), min	67.4	34.6	170.2	75.6	...	...	...
Stage 1, %	7.2	2.8	10.9	4.3	...	...	...
Stage 2, %	55.1	9.8	65.5	10.1	...	...	...
Stage delta, %	12.0	9.7	8.8	9.0	...	...	...
Delta sleep ratio	1.1	0.6	2.2	0.2	...	...	...

[a]One patient completed diary incorrectly at outcome; 1 patient completed protocol but declined repeat polysomnogram. Abbreviations: REM = rapid eye movement sleep, VAS = visual analog scale.
[b]One-group MANOVA, repeated measures.
[c]Diary averaged over 1 week.
[d]Bonferroni-corrected level of significance: .05/6 = .008.
[e]Higher value represents better clinical state.

or C4 scalp placement referenced to linked mastoids. All electrode impedances were determined to be < 5000 Ω. Filter settings for the EEG were 0.3 to 100 Hz. The EMG was bipolar, with filter setting of 10 to 90 Hz. The paper speed was 10 mm/s, and a 50-μV signal was calibrated to produce a 10-mm deflection at a sensitivity setting of 5. For each EEG channel, the high-pass filter on the polysomnograph amplifier was set to 0.3 Hz and the low-pass filter to 100 Hz. EEG signals were first low-pass filtered by an anti-aliasing filter (70 Hz; 24 dB/octave). Amplified EEG signals were then analog-to-digital converted (sampling rate = 256 Hz). The digital EEG signals were band-limited to 50 Hz by a digital finite impulse response (FIR) filter before being decimated from 256 Hz to 128 Hz. EEG power spectra were calculated on the 128-Hz signals for consecutive 4-s epochs and 0.25-Hz frequency band widths by a fast fourrier transform (FFT) routine. Artifact-laden 4-s epochs were identified by automated procedures.[42] Each 60-s spectrum was the average of the 4-s spectra for each 60 seconds of EEG that had excluded awake time based on visual scoring and that did not contain artifacts based on the automated artifact detection routine. For comparison of power spectra, the 0.25-Hz bins were collapsed into the following frequency ranges: delta (0.5–3.75 Hz), theta (4.0–8.0 Hz), alpha (8.25–12.5 Hz), and sigma (12.75–15.0 Hz).

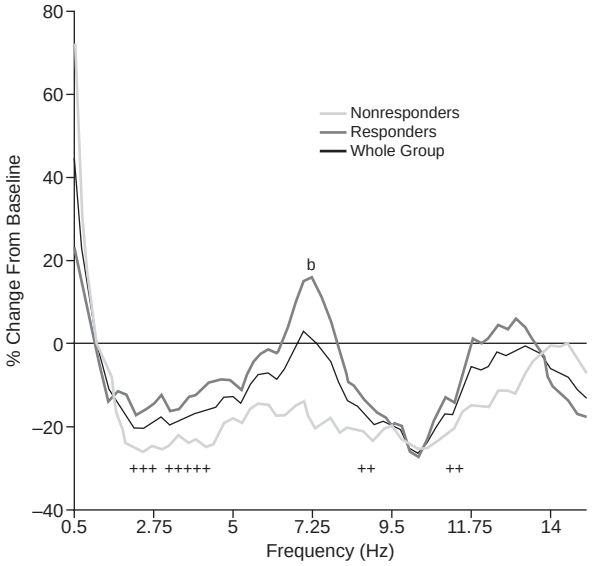
Analyses

Results of the clinical rating scales (PSQI, POMS, MOS-SF36) were analyzed by 1-way multivariate analysis of variance for repeated measures (time = pre-paroxetine to post-paroxetine). The PSQI score was adjusted to remove the medication item, since the outcome score would be artificially inflated by placing subjects on paroxetine. The sleep diary and polysomnography variables of sleep quantity (sleep onset latency, wake after sleep onset, and total sleep time) were analyzed in a separate 1-way multivariate analysis of variance for repeated mea-

sures (time = pre-paroxetine to post-paroxetine). For the diary data, the mean for 1 week at baseline and the last week of treatment, prior to the second 2 nights in the laboratory, was used. A square root or logarithmic transformation was used for variables violating normality or homogeneity of variance. The level of significance was set at $p \leq .05$ (2-tailed) for each multivariate model. The level of significance for univariate follow-up contrasts within each MANOVA was corrected with the Bonferroni adjustment.

For the power spectral analyses, the analytic strategy of Van Bemmel et al.[43] was used. Frequencies from 0.5 Hz to 15 Hz for non–rapid eye movement sleep period 1 (NREM1) in 0.25-Hz frequency bins and in frequency bands (delta, theta, alpha, sigma) were analyzed for the whole group, and in responders compared with nonresponders. Both approaches were used because differences manifested in smaller frequency bins may be obscured when collapsed into broader frequency bands. Frequency bins were compared by 2-way analysis of variance for repeated measures (group = responder, nonresponder; time = pre-paroxetine treatment to post-paroxetine treatment). Frequency bands were analyzed by multivariate analysis for repeated measures (group = responder, nonresponder; time = pre-paroxetine to post-paroxetine treatment). The level of significance was set at $p \leq .05$ (2-tailed).

Figure 1. Change in NREM1 Spectral Power With Paroxetine Treatment as a Function of Frequency[a]



[a]Figure depicts the effects of paroxetine on spectral power in patients with primary insomnia after 6 weeks of treatment; 2-group ANOVA, repeated measures (df = 1,10) for each 0.25 Hz. Symbol: + = effect of paroxetine in the whole group (main effect for time significant [$p \leq .05$]). See text for multivariate analysis of frequency bands.
[b]Responders differ from nonresponders (interaction term significant [$p \leq .05$]).

RESULTS

At the conclusion of the study, 11 (79%) of 14 patients were "much improved" or "very much improved" on the CGI-I. Seven (50%) of 14 patients no longer met DSM-IV criteria for primary insomnia. Tables 2 and 3 summarize the results for all of the clinical, diary, and laboratory measures. The self-reported domains selected a priori to reflect DSM-IV diagnostic criteria improved with treatment, significantly so for sleep quality and daytime well-being, marginally so for daytime mental functioning. The physical functioning subscale, however, did not reflect this improvement. The overall test for changes in sleep quantity demonstrated significant changes with treatment, although univariate contrasts for each individual measure were not significant. Examination of means of the sleep quantity measures demonstrated inconsistent relationships between diary and polysomnography measures. Mean values for diary sleep onset latency, wake after sleep onset, and total sleep time improved. Mean values for polysomnography sleep onset worsened. Mean values for polysomnography wake after sleep onset and total sleep time improved.

Figure 1 shows the power spectral plots of 0.25-Hz bins for NREM1 (the results are similar for whole night and for total NREM plots). The main finding is that paroxetine treatment was associated with decreases in mean power in frequencies within the delta and alpha frequency ranges. Responders and nonresponders did not differ in any of the baseline demographic, clinical, or sleep measures listed in Tables 2 or 3. In Figure 1, examination of the responder profile compared with the nonresponder profile suggests that paroxetine resulted in increases in mean power in theta frequencies for responders, but decreases in mean power in theta frequencies for the nonresponders. A similar but not statistically significant pattern is also seen in the faster alpha frequencies. Table 4 presents the analysis on spectral bands, derived from collapsing the 0.25-Hz bins. There was an overall group-by-time interaction suggesting that the responders and nonresponders differed in their EEG-measured changes after treatment, but results of univariate post hoc tests for specific frequency bands were not significant.

DISCUSSION

Eleven of 14 patients with primary insomnia were much improved after 6 weeks of treatment with paroxetine, and half no longer met diagnostic criteria for an insomnia disorder. Global changes were accompanied by improvements in subjective sleep quality and daytime well-being. Changes in sleep quality as reported by patient diary were inconsistent with changes measured using

Table 4. Power Spectral Bands for NREM1 Before and After Paroxetine Treatment[a]

	Baseline				Outcome										
	Responders (N = 7)		Nonresponders (N = 5)[c]		Responders (N = 7)		Nonresponders (N = 5)		Group		Time		Group × Time[b]		
Band	Mean	SD	Mean	SD	Mean	SD	Mean	SD	F	p	F	p	F	df	p
Overall	...	...	...	...	...	...	...	...	1.065	.44	5.521	.03	5.119	4,7	.03
Delta	55.97	25.06	32.21	17.48	46.87	15.61	28.89	16.85	4.604	.06	1.085	.32	0.235	1,10	.64[d]
Theta	4.79	2.66	3.87	1.92	4.67	3.06	3.07	1.66	0.786	.40	1.832	.21	1.032	1,10	.33[d]
Alpha	2.41	2.06	1.86	1.10	1.71	1.05	1.41	0.72	0.312	.59	3.751	.08	0.182	1,10	.68[d]
Sigma	0.83	0.30	0.76	0.37	0.80	0.40	0.68	0.25	0.252	.63	0.697	.42	0.122	1,10	.74[d]

[a]Abbreviation: NREM1 = non-REM sleep period 1.
[b]Two-group MANOVA, repeated measures.
[c]One patient's recording unusable for technical reasons.
[d]Bonferroni-corrected level of significance: .05/4 = .0125.

polysomnography. Medication was well tolerated, and overall side effect reporting diminished with treatment.

Although patients were rigorously assessed for current psychiatric syndromes, 43% had prior histories of depression. Two thirds had also received sedating antidepressants, in low doses and for brief durations, in the past. Sedating antidepressants and benzodiazepine hypnotics, when used acutely and intermittently, may temporarily improve sleep quantity but not affect the longitudinal course of the disorder.[12] In this study, the median dose of paroxetine was 20 mg used for 6 weeks, a strategy more consistent with traditional antidepressant treatment. Because patients with chronic insomnia are in a high-risk group for depression, paroxetine may serve as both an intervention strategy for persistent insomnia as well as a preventive strategy for depression.

Paroxetine was effective despite the inconsistency between changes in diary and those in polysomnography sleep quantity. On the one hand, a larger sample or more than 6 weeks may be necessary for serotonergic manipulation to be manifested in reliable changes in sleep quantity (and for more robust effects on daytime functioning). On the other hand, the discrepancy between subjective and objective measures of sleep is also seen in patients with chronic insomnia who receive benzodiazepine hypnotics for more than 3 or 4 weeks and in patients with depression treated with antidepressants.[15,16,44] Daytime well-being and functioning may be more meaningful markers of treatment outcome than the quantity of nighttime sleep. Alternatively, the effect of paroxetine on serotonergic systems may serve to improve affect, which leads to reappraisals of daytime well-being and functioning. This leaves open the question of whether paroxetine treatment merely changes distressed poor sleepers into nondistressed poor sleepers or whether, in addition to symptomatic relief, the long-term health risks associated with chronic insomnia, e.g., major mood disorders, are also reduced.

While the macro-architecture of sleep did not show consistent changes in the quantity of sleep, the micro-architectural aspects of sleep as reflected in power spectral analyses did demonstrate changes in the mean power of delta and alpha frequencies with treatment. Quantitative EEG methods provide a measure that may be useful in determining biological correlates of treatment response. However, more research is needed to determine the physiologic meaning of changes in frequencies or frequency bands. We collected EEG data from the standard C3 or C4 sites. However, additional research is also needed to examine how different sites, and the relationships between sites, may offer unique physiologic information.

The interpretation of data in this pilot study is constrained by the lack of a control group and the small number of subjects. Positive treatment effects could be attributed to sleep hygiene education, placebo effects, positive expectancy by the investigators and patients, and the self-monitoring that accompanied the structure of the study. Treatment effects may also be related to other changes observed in the EEG measures of sleep as described in Table 3. However, given the limited sample, only the a priori selected measures above were examined for statistical significance. A randomized, double-blind, placebo-controlled longitudinal trial is warranted to confirm and extend these preliminary findings. Although linking outcome to DSM-IV diagnostic criteria provides a measure of clinical relevance, more work is needed to identify rating scales and measures that reflect changes in these individual criteria to improve the understanding of the mechanisms by which different treatments change various aspects of insomnia syndromes.

Drug name: paroxetine (Paxil).

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