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Secretin and Sleep in Children with Autism

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Abstract

The objectives of this pilot study were 1) to examine possible effects of secretin infusions on sleep-wake state organization in children with autism, and 2) to assess the feasibility of home recordings using time-lapse videosomnography in children with autism. Participants were a subset of subjects from two double blind, placebo-control, multi-center clinical trials. One trial, the UC Irvine study, assessed the effects of porcine secretin vs. saline infusions on children's behavior, language and IQ. The UC Davis trial assessed the effects of synthetic human secretin vs. saline infusions on behavior, language and gastrointestinal function. The sleep study enrolled some of the children from each of the two trials to observe possible secretin effects on sleep. To examine sleep, the UC Irvine trial used the Children's Sleep Habits Questionnaire and daily sleep diaries, whereas the UC Davis study used home-recorded time-lapse videosomnography. Because of the small sample size, the results from both trials are preliminary. They suggest that secretin, porcine or synthetic, does not improve sleep-wake state organization dramatically.

Keywords

autism; sleep; secretin

Autism is a severe neurodevelopmental disorder that is characterized by a triad of behavioral symptoms: 1) impairment in social interaction, 2) communication deficits and 3) restricted, repetitive behaviors.[1] Although these areas define autism diagnostically, other symptoms, such as tantrums, tactile hypersensitivity, self-injurious and destructive behaviors, cognitive impairment, and sleep problems, may coexist.[2,3] The prevalence rates of autism and Pervasive Developmental Disorders (PDD) appear to be on the rise, especially for younger preschool children.[4]

Recent research on children diagnosed with autism and autistic spectrum disorders has been directed at exploring secretin as a potential treatment for some of the language, behavioral and social interaction deficits that characterize the disorder.[5–8] The first clinical case report describing the beneficial effects of secretin on the gastrointestinal (GI) and behavioral symptoms of children with autism was published in 1998.[9] From this report of children whose autistic symptoms improved following a diagnostic secretin study for digestive disturbance, other case reports, press releases and electronic postings have suggested a wide range of effects, from marked improvement in GI symptoms, language, and social skills to no improvement at

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all.[9–12] In one open label trial,[13] it was noted that secretin reduced the number of middle-of-the-night awakenings and improved nighttime sleep in general. With the rapid and widespread dissemination of positive findings related to potential new treatments for autism in the popular press and on the internet, it is especially important that double blinded, random assignment trials be undertaken to verify or disprove the claims of success.

Secretin is an endogenous polypeptide that contributes to the digestive process by increasing pancreatic, biliary and gastric secretion. Porcine secretin is routinely used during endoscopy to assist gastroenterologists in diagnosing GI disturbances. The exact role that secretin plays in CNS function is unknown. Secretin and secretin receptors have been observed in central nervous tissue[14] and may act in the regulation of neurotransmitters.[15] The Autism Research Institute, an independent San Diego foundation, has gathered data from over 1000 children who have received single or multiple doses of porcine secretin. They noted only mild adverse events including hyperactivity, increased self-stimulation, aggression, diarrhea and reduced amounts of sleep.[13]

Open label trials[10] have supported the initial observation that the pancreatic-biliary fluid response to IV secretin is abnormal in those children with autism who have concomitant gastrointestinal problems. These children present with symptoms including constipation, abdominal pain, diarrhea, gaseousness, and/or foul smelling stools. Histological reports on 36 children with autism and GI symptoms have demonstrated that 69% of the children had grade I or II reflux esophagitis, 42% had chronic gastritis and 67% had chronic duodenitis.[10] Wakefield and colleagues described ileal lymphoid nodular hyperplasia and colitis, which they called autistic enterocolitis, in 12 children with autism.[16] The enterocolitis symptoms and some of the behavioral symptoms of this subgroup may show significant improvement on a gluten/casein-free diet. Thus, Wakefield and colleagues suggest a link between gastrointestinal allergy, behavioral symptoms, and a sub-type of autism.[16]

Children with autism frequently present with sleep problems as well.[2,17] When a sleep disorder is present, the symptoms most often reflect difficulties in going to bed and falling asleep at an appropriate hour, and/or middle-of-the-night awakenings that may result in wandering or in other disruptive behaviors.[2,18] Some investigators have speculated that daytime impairments in communication and in processing social cues may be associated with disturbed nighttime sleep.[2,19,20] Others have suggested that an accumulated sleep debt resulting from frequent nighttime disruptions leads to daytime inattention, restlessness and irritability, and that improved sleep leads to improved daytime behavior.[21] The question of whether disordered sleep patterns are associated with waking behaviors or are unrelated remains unanswered. Similarly, the question of whether the sleep problems of children with autism can be classified as dysomnias characterized by fragmented sleep and frequent night waking, or as phase delay syndromes characterized by delayed sleep onsets and late morning rise times, has been only partially addressed.[22]

The current preliminary investigation was undertaken to assess what effects, if any, secretin might have on nighttime sleep-wake state organization, given the report of a positive effect using an open label design.[13] The sleep study took advantage of two independent multi-center, double-blind, random assignment clinical trials of secretin and placebo infusions. Although the children who participated in the sleep studies were only a subset from each trial, any dramatic secretin effect on sleep should have been observable.

Methods

Both the University of California, Irvine (UCI) and the University of California, Davis (UCD) clinical trials were approved by their respective human subjects committees, and parents at

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both sites gave their informed consent for all investigative procedures. Each study's design was distinct (Figure 1a & 1b); however, in both studies, children were assigned randomly to one of two placebo-secretin conditions and, in both, parents and investigators were blind to the condition throughout the duration of the study. MANOVA statistics were used to analyze group differences for the UCI sample. Because of the small sample size, only descriptive statistics were used for the UCD sample.

UC Irvine (UCI) Study

The UCI study was part of a three-center (University of Chicago, University of California, Irvine and University of Utah) clinical trial, funded by NIMH and the University of California Davis M.I.N.D. Institute. In toto, 56 subjects (48 male), ages 3 to 12 years were enrolled. A sub-sample was recruited for the present sleep study consisting of 17 subjects (15 males) ranging in age from 3 to 8 years (M = 72 mos; S.D. ± 20). UCI participants were evaluated and diagnosed as having Autistic Spectrum Disorder (DSM-IV) by both the Autism Diagnostic Interview-Revised (ADI-R)[23] and the Autism Diagnostic Observation Schedule (ADOS).[24, 25] The sample was characterized as low functioning with a mean non-verbal IQ of 46 (S.D. ± 8) measured by the Mullen Scale of Early Learning.[26]

UCI children participated in a double-blind crossover design in which one half of the group was assigned to an initial placebo infusion, and the other half to an initial secretin infusion. Assignment to the initial treatment condition was random. After 4 weeks, participants were crossed and received an infusion of the opposite agent. Thus, each subject served as his/her own control. The active agent was porcine secretin, dosed at 2 cu/kg. The placebo was saline. Both were administered by IV infusion separated by 4 weeks.

The sleep measures in the UCI study included the Children's Sleep Habits Questionnaire (CSHQ) obtained on three occasions and a sleep diary completed daily over a two-week period at two time points (Figure 1a). Both instruments rely on parent report; however, each is based on a different time frame. The CSHQ[27] contains 46 items related to common sleep behaviors in children experienced in the previous week. Parents respond to items on a 3-point Likert scale (rarely = 0 to 1 nights per week; sometimes = 2 to 4 nights per week; usually = 5 to 7 nights per week). Eight sub-scales have been derived from factor analysis of these items with higher scores reflecting greater problems: Bedtime Resistance, Sleep Onset Delay, Sleep Duration, Sleep Anxiety, Night Waking, Parasomnias, Sleep Disordered Breathing and Daytime Sleepiness. The four that are of most interest to this study are Bedtime Resistance, Sleep Onset Delay, Sleep Duration and Night Waking. Test-retest reliability coefficients for CSHQ sub-scales range from .62 to .79; internal consistency ranges from .36 to .93.[27]

The sleep diary is a standardized, calendar-style form that asks the parent to note specific sleep-related events on a daily basis. Each form contains 7 days and nights of data with each calendar date clearly noted. The sleep-wake behaviors that are monitored include the child's bedtime, sleep-onset time, the time and duration of each nighttime awakening, the time and duration of each nighttime intervention and the morning rise time. Parents complete the diary each morning when their child awakens, reporting on the previous night's sleep. Each diary also contains an area for comments. Completion of the diary takes less than one minute. Three parents did not complete the diaries resulting in a sample size of n = 14 for this component.

For the UCI participants, the CSHQ was completed for the week prior to the first infusion, the week prior to the second infusion and for the week 1 month after the second infusion. The daily sleep diary was completed daily over a two-week period immediately following each of the two infusions (Figure 1a).

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The UC Davis (UCD) Study

The University of California, Davis (UCD) study also was part of a multi-center clinical trial, supported by grants from a proprietary company, the UC Davis M.I.N.D. Institute and the Children's Miracle Network Telethon. One hundred twenty six participants were enrolled at 5 sites: UC Davis, University of Maryland, the Mayo Clinic, the Southwest Autism Research Center/Phoenix Children's Hospital and the Rochester Institute for Digestive Diseases and Science. At UCD, 12 children completed an extensive diagnostic battery, including ADI-R and ADOS assessments, to confirm the diagnosis of autistic disorder (DSM-IV), establish the severity of GI symptoms, and determine the level of cognitive function. UCD children were randomly assigned to either a placebo (control) or synthetic secretin (treatment) group. Both parents and investigators were blind to the assignment group. Each child remained in the original group of assignment for 3 infusions of either saline or synthetic secretin separated by 3-week intervals. Assessment batteries were completed prior to the first infusion and then following each infusion. The baseline, pre-infusion Childhood Autism Rating Scale[28] scores ranged from 34 to 44.5 (M = 39.8, S.D. ± 4.0). The average IQ was 58 (range = 36–80). Synthetic secretin was dosed at 2 cu/kg.

Seven of the 12 enrolled children were initially recruited for the sleep protocol but one family withdrew before completing the protocol. The remaining 6 children (3 secretin, 3 placebo) who participated in the sleep study ranged in age from 3.5 to 7 years (M = 5.5, S.D. ± 2.7). Time-lapse videosomnography recorded sleep-wake behaviors on 4 consecutive nights (2 nights prior to and 2 nights following) the first infusion, and 4 consecutive nights (2 nights prior to and 2 nights following) the second infusion. Thus, a total of 8 nights of sleep were obtained for each subject (Figure 1b). Parents were asked to start the recording before the child entered the bed and end the recording after the child got up in the morning.

The time-lapse video system has been described previously.[29,30] In brief, sleep-wake behavior is recorded using a portable time-lapse video system consisting of a time-lapse videocassette recorder (Panasonic AG-6740P), a low level illumination camera (e.g., Sanyo VDC-9212) on a tripod next to the child's bed, a 12″ video monitor, and a microphone to record sound. Video and audio signals are recorded using the 18-hour time-lapse mode so that a full 18-hours can be recorded on one 2-hour standard VHS videotape. A time code generator records "real" clock time on the tape.

The method of scoring time-lapse videotapes in human infants also has been described previously.[29,31] The following sleep-wake indices were scored from the videotapes: Time to bed and the time of sleep onset (sleep latency), the longest continuous sleep period during the night (LSP), the number and duration of middle of the night awakenings, and the time of awakening in the morning. Each awakening of two or more minutes in duration, occurring at least ten minutes after initial sleep onset, was considered a *nighttime* awakening, regardless of the actual clock time. Awakenings lasting at least 30 seconds, but not 2 minutes, were scored as arousals. Awakenings and arousals were summed. Also scored were the use of sleep aids and all parent interactions with a wakeful child during the night. All of the nighttime awakenings or arousals were scored by at least 2 investigators. Differences of opinion were resolved by consensus. All videotapes were scored blind to the treatment condition. For this study, the proportion of REM and NREM sleep states were not scored.

Results

The UCI Study

Analysis by MANOVA of changes in the CSHQ item and sub-scale scores, regardless of order (secretin-placebo, placebo secretin), revealed no dramatic secretin effects. As summarized in

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Table 1, the possibility of a non-significant trend can be observed for Bedtime Resistance, Sleep Onset Delay and Sleep Duration scores. Lower scores suggested slight improvement from baseline to post infusion for both groups whether or not children began the trial on secretin or placebo. In the follow up period, one month after the second infusion, Bedtime Resistance, Sleep Onset Delay and Sleep Duration continued to improve slightly for the group who received secretin initially.

Of interest, though again not statistically significant, is a further observation of higher mean Night Waking scores following secretin infusion in both conditions. In other words, parents did not report less night waking in their children following secretin infusion, regardless of the infusion sequence (secretin-placebo or placebo-secretin). Night Waking scores were comparable (4.4 ± 1.7 vs. 4.1 ± 1.4) following secretin infusion when secretin preceded saline and when saline (pre-secretin) preceded secretin infusion (4.1 ± 1.4 vs. 4.4 ± 1.3). Because of inadequate power related to the small number of participants, no definitive conclusions can be drawn from this observation. However, the expected marked decrease in awakenings was not evident.

The CSHQ sub-scale scores of the children with autism in the UCI sample, in general, were comparable to scores obtained from a large sample of children with PDD,[22] suggesting that parents completing the CSHQ in this study were not different in responding to questions about sleep than a much larger group of comparable parents. The scores, on average, also were similar to those reported for a population of children referred for sleep problems to a sleep disorder's clinic, and higher than scores reported for a normally developing control group.[27]

Similar to the observations reported for the CSHQ data, the sleep diaries did not show any systematic changes related to secretin infusion. Sleep variables for the 14 participants with diary data failed to demonstrate dramatic improvements between the secretin and placebo infusions. On average, children in both groups had a sleep latency of 30 minutes, slept for 9.5 hours a night and awakened 2 times per week. Again, like the CSHQ responses, the sleep diary responses from the UCI sample resembled the sleep diary responses from a comparable, but larger sample.[22]

The UCD Study

Videosomnography revealed several interesting sleep-wake differences between the placebo group and the secretin group. As portrayed in Table 2 and Figures 2 and 3, the sleep latency time, the length of nighttime arousals and awakenings, and the total sleep time did not differ between the two groups; however, the total number of arousals and awakenings per night and the longest sleep period differed over both infusion periods. The number of arousals/awakenings per night increased after both secretin infusions; most notably, after the second infusion (3.6 ± 1.4 to 7.6 ± 1.0), while the number of arousals/awakenings for the children receiving placebo remained relatively constant. With more arousals, the longest continuous sleep period for the children receiving secretin decreased after each infusion (287 minutes to 219 minutes from pre- to post-infusion #1; and, 209 minutes to 144 from pre- to post-infusion #2). The small size of the sample precluded formal MANOVA testing; however, the directions of change in the secretin group are consistent and warrant replication.

Since this is the first video study of sleep in children with autism, it should be noted that videosomnography was tolerated by all of the children. Three children routinely slept in bed with either one or both of their parents or siblings. All of the children but one had delayed or atypical sleep onsets and late bedtimes. For the 3 children who slept alone, all required more than 20 minutes to fall asleep at the beginning of the night. Two of the children regularly fell asleep away from their beds and were placed in their bed already asleep. Several of the children used sleep aids to comfort themselves at sleep onset and following a middle-of-the-night

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arousal. The sleep aids were a soft object such as a blanket or cloth. Moreover, it was anecdotally observed that children who frequently co-slept with one or both parents tended to move closer to the adult(s) in bed upon awakening or arousing.

Discussion

The results of this study do not readily support the previously reported open trial, anecdotal observations of improved sleep in some children with autism following secretin infusion.[13] None of the children in either of the double blind clinical trials demonstrated significant changes in their sleep-wake state organization following secretin compared to placebo. The lack of any demonstrable dramatic change was observed both following infusions of either porcine secretin or synthetic human secretin, and after single or repeat infusions. Indeed, the observations from this study suggest, if anything, the possibility of more arousals rather than improved sleep following secretin. Given the small sample size, however, replication of these findings with a larger sample is required. The UC Davis sample was a group of children who, in addition to being diagnosed as having autism, were selected because they also had gastrointestinal symptoms, and for whom secretin was predicted most likely to be effective in eliminating GI discomfort. The results of the UC Davis study did not demonstrate any dramatic improvement in sleep following secretin infusion in children with this medical condition.

Improved sleep also was not apparent in the UCI sample in which children with gastrointestinal symptoms were not over-represented. Parental reports of more wakefulness at night on the CSHQ following secretin infusion in the UCI sample complemented the findings of more observed arousals/awakenings on videotape in the secretin group in the UC Davis sample. Although the nightly sleep diaries from UCI did not corroborate the increased wakefulness reported by the CSHQ, the increase in brief arousals, noted on the UCD videotapes, are usually not observed by parents who complete nightly sleep diaries.

The observations from the UC Davis and UCI samples are corroborative in several other respects. First, neither porcine nor synthetic human secretin dramatically improved sleep. Overall total sleep time at night was not increased by secretin compared to placebo, even after two infusions. Secondly, the observations from both studies raise the question that secretin infusion may have an arousing effect. Although differences between secretin and placebo participants after both infusions for the UC Davis cohort were suggestive regarding the number of middle-of-the-night awakenings/arousals and in the longest continuous sleep period, the sample size is too small and statistical power too limited to draw statistically meaningful inferences. In the secretin group, the number of arousals increased on both recording nights following each of the two infusion periods. Also, the longest sleep period decreased significantly after secretin from baseline to the final video recording period after the second infusion. These shifts suggest that secretin potentially may have an immediate arousing effect rather than a sedative effect. The potentially arousing effect during sleep of secretin in children with autism requires replication and further exploration. The lack of a dramatic secretin effect on sleep-wake organization, noted in both of these clinical trials, however, supports a recent report of minimal secretin effects on autistic daytime behaviors.[11]

Given the many reports in the literature of disrupted sleep in children with autism and PDD, it is important to note that most previous studies have used parent descriptions of sleep.[2] Actigraph and polygraph studies are rare and sample sizes are small because the recording technology poses a special challenge for children with autism who generally respond negatively to the novelty of instrumentation and laboratory settings.[17,32] The current study describes, for the first time in this population, the use of time-lapse videosomnography as an objective method of recording sleep-wake behavior in the natural setting of the home without the use of instrumentation. The successful application of videosomnography makes further research on

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sleep in autism promising. A better understanding of sleep-wake organization and the nature of sleep disorders in children with autism is critical for designing more effective interventions.

Using the video technology, the six children studied in the UC Davis sample all exhibited tentative signs of a sleep onset problem, and possibly a circadian sleep disorder with delayed sleep onsets. Because half of the children co-slept in a family bed, it is difficult to know whether the arousals and awakenings that were noted might have resulted in even more fragmented sleep had the parents or siblings not been in the bed. Further research using videosomnography is planned to untangle fragmented sleep (dysomnias) from sleep onset (circadian) disorders and to determine how prevalent co-sleeping is in this population.

The videotapes also clearly demonstrated that children with autism use sleep aids to help in self-soothing following a nighttime awakening. Some of the co-sleeping children moved closer and physically reached out to touch an adult sleeping in their bed. This latter behavior resembles the comfort and proximity seeking behaviors described in attachment research and observed in laboratory studies of children with autism.[33,34] These are the first reported observations of such behaviors in children with autism at night.

Time-lapse videosomnography has been shown to be reliable and valid in coding REM and NREM sleep states, wakefulness and out of crib times in infants.[29] No validity studies exist for children with autism. However, sleep and waking as manifested by arousals, full awakenings, bedtimes, sleep onset times, out-of-bed times, morning rise times and parent-child nighttime interactions were easily and reliably coded by 3 experienced coders in these children with autism.

There are some limitations to the use of videosomnography with this population at these ages. In infant studies, the video camera is placed on a tripod immediately adjacent to the crib. For these older children with autism, all of the parents suggested that the camera be placed some distance from the bed and that it be as unobtrusive as possible. These distances, using our customary non-telephoto lens, precluded the fine resolution required for scoring REM and NREM sleep states, but did not prevent scoring awakenings and time in bed. Additionally, when children co-sleep with parents or siblings, maintaining an unobstructed view of the target child on the videotape can be challenging.

There were additional limitations with the study itself. This was an exploratory study, examining 2 double-blind trials of secretin infusions. Because of the constraints of the two clinical trials, methods for recording sleep in each trial differed even though the methods of assessment for making the diagnosis of autism were consistent. That is, the population of children in both samples was reliably diagnosed as having autism, although the UC Davis sample was particularly selected because of accompanying GI symptoms. With small sample sizes, inadequate power and differing methods of data collection in the two cohorts, extensive statistical analyses were not possible. Nevertheless, descriptively, the data from both studies appear consistent and suggest that, preliminarily, secretin has no major effect on improving sleep over the course of several infusions. The results are also consistent with findings from the larger clinical trials that have reported no major general benefits of secretin as a therapeutic agent for children with autism.

Summary

The use of secretin to treat some of the behavioral symptoms of autism has received much public attention recently related to isolated case reports of dramatic improvement in some children. A small pilot study attempted to explore the potential effects of secretin on the sleep-wake patterns of children with autism. Participants were a subset of subjects from two double blind, placebo-control, multi-center clinical trials. One trial assessed the effects of porcine

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secretin vs. saline infusions on children's behavior, language and IQ. The other assessed the effects of synthetic human secretin vs. saline infusions on behavior, language and gastrointestinal function. The sleep study enrolled some of the children from each of the two trials and used different methodologies to assess sleep and waking behavior. One trial used the Children's Sleep Habits Questionnaire and daily sleep diaries, while the other used home-recorded time-lapse videosomnography. Because of small sample sizes and inadequate power, the results from both trials are primarily observational. They suggest that secretin, porcine or synthetic, does not dramatically improve sleep-wake state organization. Instead, it is possible that secretin may have an immediate arousing, rather than sedating, effect. The use of time-lapse videosomnography was tolerated well by the children and families in this study and provides an objective method to quantify bedtimes, sleep onset times, and arousals/awakenings from sleep. A larger sample of children with autism is necessary to replicate these tentative observations, and to more fully explore the potential effects of secretin on sleep and waking.

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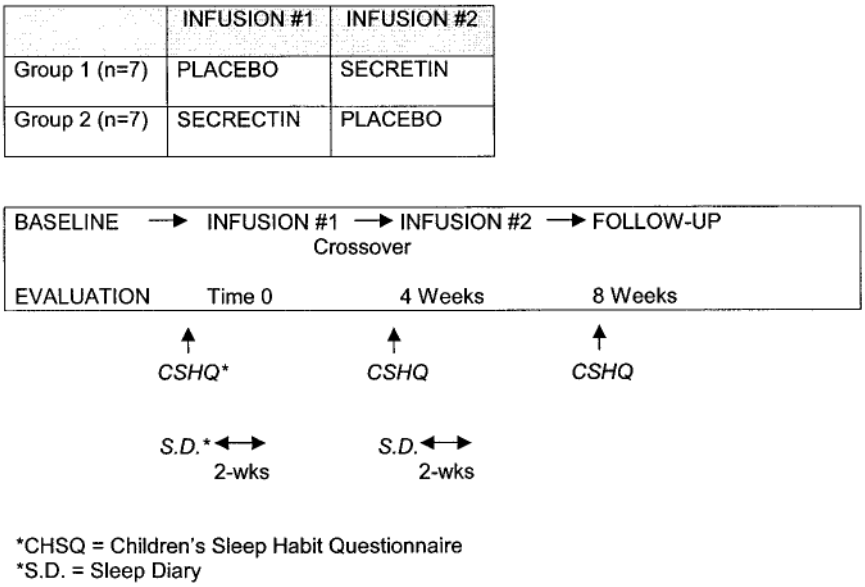

Figure 1a.

The Research Design for the University of California, Irvine (UCI) Study (1a) Portrays a Double Blind Crossover Study with Each Subject Serving as Its Own Control (n = 17)
Note: The Children's Sleep Habit Questionnaire was administered on 3 occasions, prior to infusion 1, 4 weeks later prior to infusion 2 and 4 weeks later at follow-up. The Sleep Diary (SD) was completed twice for 2-week intervals immediately following Infusions #1 and #2.

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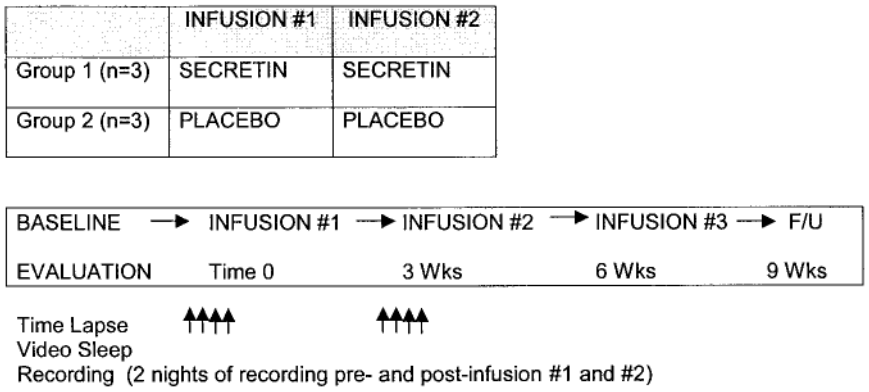

Figure 1b.

The Research Design for the University of California, Davis (UCD) Study (n = 6)

Note: Figure 1b portrays a double blind secretin-placebo (control) group study. Videosomnography was obtained on 4 consecutive nights (2 nights pre-infusion and 2 nights post-infusion) around each of the first 2 infusions.

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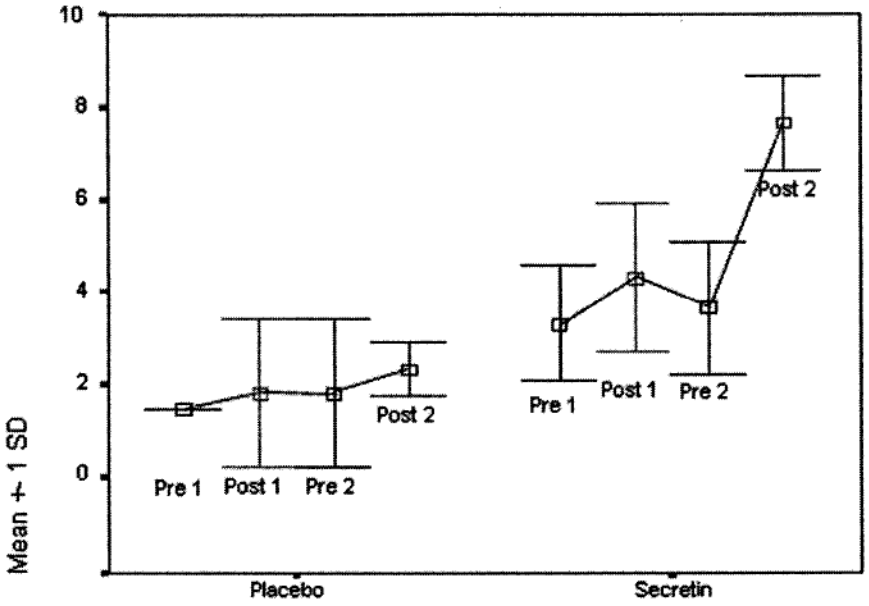

Figure 2.
Number of Night Wakings, UC Davis Study
Note. The number of arousals/awakenings are increased following each of the two secretin infusions compared to the placebo infusions (Mean ± s.d.).

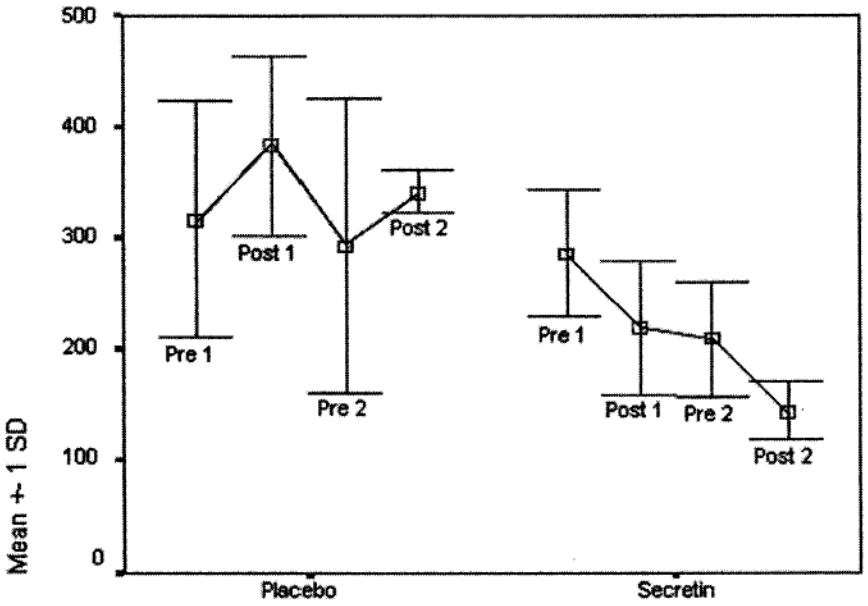

Figure 3.
Longest Sleep Period, UC Davis Study
Note: The Longest Sleep Period (LSP) in minutes decreases following each of the two secretin infusions compared to the placebo infusions (Mean ± s.d.).

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Table 1

UCI Study: Mean (SD) and (Range) of CSHQ Variables After Infusions

	Secretin-Placebo Sequence (n = 8)			*Placebo-Secretin Sequence (n = 9)*		
	Pre-Secretin Baseline	***Post-Secretin Pre-Saline***	***Post-Saline Follow-up***	***Pre-Saline Baseline***	***Post-Saline Pre-Secretin***	***Post-Secretin Follow-up***
Sleep Onset Delay	2.1 (.8)	1.7 (.7)	1.6 (.7)	1.6 (.7)	1.3 (.5)	1.6 (.7)
Range	(1.0–3.0)	(1.0–3.0)	(1.0–3.0)	(1.0–3.0)	(1.0–2.0)	(1.0–3.0)
Sleep Duration	4.7 (1.8)	4.4 (1.3)	4.3 (1.9)	3.8 (1.4)	3.8 (1.2)	3.6 (1.2)
Range	(3.0–7.0)	(3.0–6.0)	(3.0–8.0)	(3.0–6.0)	(3.0–6.0)	(3.0–6.0)
Bedtime Resistance	9.0 (3.7)	8.2 (2.9)	8.0 (2.4)	9.6 (3.8)	8.8 (4.0)	9.6 (3.5)
Range	(6.0–17.0)	(6.0–15.0)	(6.0–13.0)	(6.0–16.0)	(6.0–16.0)	(6.0–16.0)
Night Waking	4.1 (1.4)	4.4 (1.7)	3.7 (.86)	4.8 (1.7)	4.1 (1.4)	4.4 (1.3)
Range	(3.0–7.0)	(3.0–7.0)	(3.0–5.0)	(3.0–8.0)	(3.0–6.0)	(3.0–6.0)

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Table 2

UCD Study: Mean (SD) for Two Nights of Video Sleep Recording Pre- and Post-Infusion

	Secretin (n = 3)				*Placebo (n = 3)*			
	Infusion #1		*Infusion #2*		*Infusion #1*		*Infusion #2*	
Variables[a]	*Pre*	*Post*	*Pre*	*Post*	*Pre*	*Post*	*Pre*	*Post*
Sleep Latency	10(4)	10(9)	34(59)	17(24)	24(27)	20(8)	43(40)	8(14)
# of Awakenings	3.3 (1.2)	4.3(1.6)	3.6 (1.4)	7.6 (1.0)	1.5(0)	1.8(1.6)	1.8(1.6)	2.3(.5)
Length of Awakening	3.3 (2.7)	17.7 (25.1)	5.8 (6.8)	2.7 (1.3)	3.9(5.4)	1.8 (2.02)	.9(.9)	26.2 (40.0)
Longest Sleep Period	287 (57)	219(60)	209 (51)	144 (25)	316 (106)	383(80)	292 (132)	341(18)
Total Sleep Time	528 (50)	510(19)	413 (70)	480 (72)	413 (142)	510(53)	455(19)	522(38)

[a] Variables are in minutes except for number of awakenings.