



SLEEP INTERNATIONAL

THE GLOBAL JOURNAL OF SLEEP MEDICINE

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CHRONIC FATIGUE SYNDROME
SLEEP NEWS AND PRODUCTS

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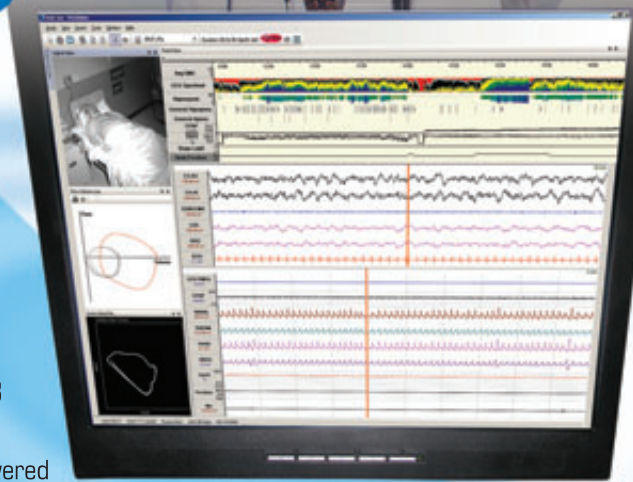
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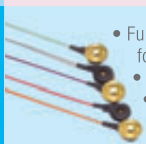
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shouldn't stuff themselves, avoid caffeine and medicine with stimulants, and the room should be quiet and cool.

DON'T WORRY!

Anxious or depressed mothers-to-be are at increased risk of having children who will experience sleep problems in infancy and as toddlers, according to a study by the University of Rochester, NY Medical Center. Sleep ranks as one of the most highly regarded indexes of healthy development, and plays a critical role in consolidating memory and facilitating learning, regulating metabolism and appetite, promoting good moods and sustaining both cardiovascular health and a vigorous immune function. The survey-based study, part of the Avon Longitudinal Study of Parents and Children (ALSPAC), assessed pregnant women living in Avon, England, who were due to give birth in a 21-month window. More than 14,000 women responded to questionnaires that gauged how depressed or anxious they were at multiple points early on in, late in, and after their pregnancy. Later on, the women were then asked to report on their child's sleep habits at 6, 18 and 30 months, detailing how long the child slept, how often the child awoke, and if he or she exhibited any of seven common forms of sleep problems, such as having nightmares, refusing to go to bed or having trouble falling asleep. Surprisingly, babies born to mothers classified as anxious or depressed while pregnant dozed just as long as their unstressed-pregnancy counterparts, about 12 hours, but children born to mothers who were depressed or anxious during pregnancy experienced more sleep problems. For instance, mothers classified as clinically anxious 18 weeks into pregnancy, compared to their non-anxious counterparts, were about 40% more likely to have an 18-month-old who refused to go to bed, woke early, and kept crawling out of bed. The child's rocky relationship with sleep often persisted until he or she was 30 months old. A similar effect was found in children born to mothers who were depressed during pregnancy. These prenatal mood disturbances worked as reliable predictors of children's sleep problems even when investigators controlled data for other factors already linked with poor sleep quality in children, including a mother's level of postnatal anxiety or depression, her smoking habit, or her social class. Related studies show that stress, which is associated with increased exposure stress hormones may disrupt a child's formation of a bundle of the suprachiasmatic nucleus in the brain, which acts as a signaling system that tunes the body's internal clock. The study noted that pregnant women concerned about how their own mood-disturbance may harm their unborn baby's sleeping habits may want to consider psychological treatment.

SET THE ALARM

Researchers at the University of Arkansas for Medical Sciences (UAMS) have discovered a new brain mechanism that might explain how we awaken. Researchers at the UAMS Center for Translational Neuroscience found that some neurons in the reticular activating system, a region of the brain that controls sleep-wake states, are electrically coupled. By finding drugs for increasing the electrical coupling of these cells, researchers said they can create a stronger pathway for potential sleep-wake control. The possible clinical applications range from the ability to wake people up from anesthesia more rapidly to stimulating someone in a comatose state to awaken if there are enough of these cells left alive to couple them. The study found that neurons in the subcoeruleus nucleus, a part of the brain believed to control the phase of deep sleep known as rapid-eye-movement (REM) sleep, joined in a way that allowed them to

News

□ October-November 2007

WET DREAMS

A detailed study about sexual dreams of men and women found that about eight percent of everyday dream reports from both genders contain some form of sexual-related activity. Women had more sex dreams, but researchers said it was probably because they were no longer shy about reporting them. The study focused on 3,500 home dream reports. Sexual intercourse was the most common type of sexual dream content, followed by sexual propositions, kissing, fantasies and masturbation. The study found that both men and women reported experiencing an orgasm in about four percent of their sexual dreams. Orgasms were described as being experienced by another dream character in four percent of the women's sexual dreams, but in none of the male dream reports. Current or past partners were identified in 20% of women's sexual dreams, compared to 14% for men, and public figures were twice as likely to be the object of women's sexual dream content. Multiple sex partners were reported twice as frequently in men's sexual dreams.

DRUG 'EM

Physicians frequently prescribe medications for sleep difficulties in children in US outpatient settings, according to a study at Ohio State University. The cross-sectional study on patients 17 years of age and younger with sleep difficulties from 1993-2004 used data from the National Ambulatory Medical Care Survey. About 18.6 million visits occurred for sleep-related difficulty in children. The highest percentage of visits was by school-aged children six to 12 years of age. Researchers found that 81% of visits among children with sleep difficulties resulted in a prescription for a medication, despite lack of FDA labeling for child use. Experts recommend that infants sleep between 14-15 hours a night, toddlers between 12-14 hours a night, pre-schoolers between 11-13 hours a night, and school-age children between 10-11 hours of sleep a night. Children should: Follow a consistent bedtime routine, establish a relaxing setting at bedtime, get a full night's sleep, not go to bed hungry, but

transmit electrical activity across the cells. The activity occurred spontaneously or could be induced by chemical agents that induce REM sleep. Researchers pointed to earlier work with animal models showing that stimulation of the reticular activating system produced electrical activity similar to that seen during waking and REM sleep. Electrical coupling would allow many cells to fire together, generating a rhythm that is transmitted to other parts of the brain to induce changes in sleep-wake states. In collaboration with the chemical transmitters that control the firing rates in individual cells, the two mechanisms could generate any of the frequencies seen in the EEG. Some anesthetics are known to block gap junctions, the channels by which electrical coupling takes place, while some stimulants increase electrical coupling.

THE NOSE KNOWS

Researchers at Johns Hopkins have found that symptoms in patients with obstructive sleep apnea and hypopnea can be significantly reduced through treatment with nasal insufflation (TNI), using a nasal cannula to deliver warm, humidified air at a high flow rate, and that TNI may offer a viable treatment alternative to patients with obstructive hypopneas and apneas. The study included 11 patients with mild to severe apnea-hypopnea disorders. Subjects were randomized to receive either no treatment or treatment with TNI at 20L/minute. Researchers measured airflow and supraglottic pressure and monitored body position, sleep arousals and respiratory events. At TNI of 10L/minute some improvement was noted but airflow limitations and snoring persisted. However, at TNI of 20L/minute, all patients showed a marked improvement. Results also showed that even patients with more severe disorders gained significantly from TNI. The authors noted that the minimally intrusive nasal interface of TNI may improve patient adherence, and may ultimately prove more effective at managing long-term morbidity and mortality of sleep apnea. Also, the fact that one flow rate and one cannula size were sufficient to stabilize breathing patterns in the majority of subjects suggested that titration of TNI may be unnecessary, streamlining the initiation of treatment.

UNDER YOUR SKIN

Physicians in the division of sleep medicine at the Medical College of Wisconsin are conducting a clinical research to assess a minimally invasive, implantable device as a treatment for sleep apnea. The study will evaluate the effectiveness of a small device that is implanted under the chin for the purpose of opening the airway and reducing or eliminating OSA. This device is implanted during a brief surgical procedure. Later, it is individually adjusted, as needed, for each individual patient, to reduce or stop collapse and open the airway. Researchers noted that many of the current treatments of sleep apnea are too poorly tolerated or too invasive and said that this device can be implanted during a minor surgical procedure and that side effects and complications may be very low. The study is being supported by Aspire Medical of Sunnyvale CA, developers of the Advance System.

GONE FOREVER

Researchers at Northwestern University have discovered that when animals are partially sleep deprived over consecutive days they no longer attempt to catch up on sleep, despite an accumulating sleep deficit. Their study showed that repeated partial sleep loss negatively affects an animal's ability to compensate for lost sleep. The body responds differently to

chronic sleep loss than it does to acute sleep loss. The ability to compensate for lost sleep is itself lost, which is said to be damaging both physically and mentally. In the study, the researchers kept animals awake for 20 hours per day followed by a four-hour sleep opportunity, over five consecutive days. The team monitored brain wave and muscle activity patterns in order to precisely quantify sleep-wake patterns. After the first day of sleep loss, animals compensated by increasing their intensity, or depth, of sleep, which is indicative of a homeostatic response. However, on the subsequent days of sleep loss, the animals failed to generate this compensatory response and did not sleep any more deeply or any longer than they did under non-sleep deprived conditions. At the end of the study, the animals were given three full days to sleep as much as they wanted, but they recovered virtually none of the sleep that was lost during the five-day sleep deprivation period. The findings support evidence that chronic partial sleep loss of even two to three hours per night has detrimental effects on the body, leading to impairments in cognitive performance, as well as cardiovascular, immune and endocrine functions. Sleep-restricted people also reported not feeling sleepy even though their performance on tasks declined.

BIG BULLY

SRBD, sleep-related breathing disorder, may be responsible for aggressive behavior and bullying by schoolchildren. A study at the University of Michigan found that schoolchildren who bully may be more likely to have an SRBD than their peers. Treatment of SRBD, a condition noted in 10% of children, was shown to improve other behaviors, and researchers surmised that it might work on bullying, too. The most severe form of an SRBD is obstructive sleep apnea, which occurs in about one percent to two percent of children.

HEY YOU, GET SOME SLEEP

Working an extended duration shift can pose a risk to not only the safety and well-being of medical interns, but also to that of their patients, according to research at Brigham and Women's Hospital in Boston, based on 2,737 physicians in their first post-graduate year who participated in a nationwide Web-based survey, completing a total of 17,003 monthly reports. A regression analysis was performed to determine the relationship between the number of extended duration work shifts (greater than or equal to 24 hours in length), reported medical errors and a self-reported measure of stress. The reporting of medical errors and the number of extended duration shifts worked in a month were both significant predictors of stress compared to months in which no extended duration shifts were worked. Interns working five or more extended duration shifts had seven times greater odds of reporting at least one fatigue-related significant medical error that resulted in an adverse patient event and reported 300% more fatigue-related preventable adverse events resulting in the death of the patient. Moreover, interns who reported a medical error that resulted in an adverse patient outcome were more than three times as likely to report high stress in that month.

SCARED OF CPAP

A study by the Mayo Foundation for Medical Education and Research interviewed 12 patients with newly-diagnosed OSA to learn more about their initial experiences. Two-thirds approached their evaluation with a hope for improvement in their overall quality of life. However, just half were open to CPAP, while 25% expressed outright fear and 17%, disappoint-

ment. Forty-two percent viewed CPAP as the lesser of two evils. Despite the proven reliability of continuous positive airway pressure in treating OSA, resistance and intolerance to CPAP poses limitations to its use. However, access to specialized services with a structured management protocol and close follow-up in a sleep center can improve CPAP compliance, according to a study by the Sleep Wellness Center of Pottstown, Pennsylvania. The study focused on 64 patients with OSA who were initially evaluated by a board certified sleep specialist and subsequently followed by a certified respiratory therapist. The subjects were educated about OSA and received printed AASM brochures on sleep apnea. The educational program was reinforced by technologists prior to their sleep studies. CPAP desensitization and mask fittings were conducted, followed by a specialized CPAP clinic where patients watched a video, were fitted with masks and received their CPAP with downloadable compliance cards. All patients had open access to the center and were seen on follow up at one month. Fifty-one patients used CPAP for more than four hours per night. The study was deemed particularly important as it was done in a community setting with resources exclusively provided from the center, and all patients had objective CPAP compliance data that was downloadable from their compliance card. Such data could also be tracked in follow up visits to initiate programs in the future to sustain and improve compliance further.

SLEEP PRODUCTS

SLEEPING LESSONS

SleepTech, LLC launched its REST: Resources for Expert Sleep Training program. The nation's newest sleep school opened its doors in mid April to great excitement and anticipation. Even though it is a "new" program, REST has already achieved A-STEP accreditation by the American Academy of Sleep Medicine for its introductory 80 hour sleep course through its affiliation with SleepTech, LLC. The REST program is based on the proven internal courses offered by its host, a leader in the sleep diagnostics market. The company has trained its technologists to a higher standard for over 14 years. After a short approval process, SleepTech gained the coveted designation as an A-STEP provider in October 2006. The REST program is offering many workshops in addition to the A-STEP introductory course. Scoring, EKG and BRPT Registry Exam Prep workshops can offer up to 13.75 continuing education credits to current RPSGT attendees per class. This is one of the few A-STEP courses being offered in the Northeast and it is also unique as it offers additional real world skills like EKG and scoring workshops that will make an immediate impact on the technologist's work and help earn continuing education credits. To learn more about the REST: Resources for Expert Sleep Training program, visit the website at rest-education.com. Classes and workshops are scheduled through 2007 and new offerings for 2008 will be announced by mid-July. Pricing and dates may also be found on the website and students may register online for future courses. SleepTech, LLC is a sleep disorder diagnostics and services provider with partner-based facilities nationwide. It is held by Flaga Group, a worldwide market leader in the sleep industry. Contact communications@sleeptech.com.

NEW TECH

Hi-Tech Medical introduces these new products: Type 444 Plus Hose, a tube technology breakthrough, this product can be completely stretched or crushed and will return to its original dimensions and shape immediately. Smooth interior for excellent flow characteristics. Type 444 Plus is an excellent choice for home or institutional medical equipment applications. The tubing is available with plain ends or injection molded cuffs. The Type 480 Hydro Hose is Hi-Tech Medical's first Medical hose that has the ability to absorb moisture from the interior of the hose and transfer it in a directional manner to the exterior atmosphere. This product is a great solution to ending "rainout" in CPAP and other respiratory equipment applications. The Type 1250 Hose Life is a new CPAP system accessory that allows for suspension of the CPAP system hose over the bed. This system is uniquely light in weight, durable in construction, super compact for travel, and easy to set up. The Type 1260 Hose Wrap is a new style of hose cover that assists in controlling vapor condensation in CPAP and other respiratory circuits while providing a super soft tubing surface. The ease of inserting and withdrawing the hose from the wrap is due to the unique end finish and fabric design. These Hi-Tech products are engineered to allow for use by those who are physically challenged. Contact hitechmedical.net.

EXECUTIVE PROFILES

Atlanta School of Sleep Medicine

Russell Rosenberg, PhD

Russell Rosenberg is President and Chief Executive Officer, Atlanta School of Sleep Medicine and President and Chief Executive Officer, NeuroTrials Research, Inc, Atlanta, GA. Dr Rosenberg is a clinician, researcher and educator who specializes in sleep disorders medicine and psychology. For 16 years, he served as the Director of the Sleep Medicine Institute at Northside Hospital. In 1992, his interest in sleep medicine education led to the development of the Atlanta School of Sleep Medicine, premier provider of continuing medical education and training for sleep technologists and physicians. An investigator in numerous research studies in the fields of sleep disorders, neurology and psychiatry, Dr Rosenberg also leads NeuroTrials Research, Inc. an independent clinical trials organization devoted to investigational drug research and diagnostic testing. He serves on the board of the National Sleep Foundation.

Describe the Atlanta School of Sleep Medicine and its unique features.

Education and training at The Atlanta School of Sleep Medicine (ASSM) is designed exclusively for physicians and technologists interested in learning the practice of sleep medicine and technology. Physicians and technologists both attend the school, taking introductory courses in the fundamentals of polysomnography and clinical sleep medicine. The educational program is both cutting edge and very practical; faculty members have at least a decade of experience in the field and maintain a clinical practice. ASSM faculty members stay abreast of sleep medicine research and integrate advances in the field by continually updating their course presentations. Classes are small, giving students access to instructors and facilitating the opportunity

for group discussion and peer interaction. The school's new facility is state-of-the art and students may do practical on-site training at Northside Hospital's 6-bed, American Academy of Sleep Medicine (AASM), accredited sleep laboratory. Introductory courses for doctors teach the basic fundamentals of sleep medicine, including polysomnographic interpretation and formulation of treatment strategies. Technologists gain a strong rudimentary understanding of the technical data acquisition process—applying electrodes, marking and measuring for EEG, and placing other electrodes and sensors for a sleep study. Students come to the school with varying levels of experience, but all leave with the tools they need to become proficient in sleep technology with ongoing education, experience, and supervision. The school is approved by the American Association of Sleep Technology (AAST) to provide continuing education units. Registered sleep technologists must earn 50 hours of continuing education units (CEUs) every five years. ASSM is also accredited by the Accreditation Council for Continuing Medical Education (ACCME) for physician CME credits. For the past two years, ASSM has jointly sponsored the National Sleep Foundation's annual symposium, attended by sleep professionals from throughout the country.

How does the school directly affect patient care?

Sleep medicine is a rapidly growing area of medical practice, with more than 70 million Americans acknowledging difficulty sleeping on a regular basis. Communities, hospitals and physicians in many specialties—family practice, internal medicine, pediatrics, neurology, psychiatry, pulmonary medicine and more—are helping people by diagnosing and treating their sleep disorders. Due to this increased interest in sleep medicine, the services of well-trained, qualified technologists are in high demand. The ASSM helps meet that need by providing consistent, standardized education and training for technicians. Since the training program at the school covers an intense short time frame, students are expected to receive mentoring and practical experience in the work environment. The training they receive at ASSM provides them with the background and framework they need to make the most of their practical experience after completing the course.

What are the latest advances in educational programming in sleep medicine? What new technology is having the greatest impact on your area of expertise?

The school's web-based e-learning program went online this summer. In keeping with the American Academy of Sleep Medicine's A-STEP (Accredited Sleep Technologist Education Program), AASM is raising the bar and leading the way in sleep technologist educational programming. Our goal is to make training accessible and manageable, using advances in educational technology where possible to help meet the growing need for highly trained and qualified sleep professionals. The requirement for sleep technologist training will increase to 80 hours of combined classroom and practical experience. Students will have four weeks to complete a 30-hour online portion of the educational program prior to attending the school. Studying basic human physiology and anatomy as it relates to sleep medicine and understanding the variety of sleep disorders will equip students well for the 50-hour intense "hands-on" coursework in Atlanta. This new program is also well suited to potential technologists who may not have had traditional allied healthcare schooling. With this new, in-depth training program, the Atlanta School of Sleep Medicine has sought accreditation by the Academy as a provider of A-STEP

training. The A-STEP course at ASSM is expected to launch in early November 2007.

What sets the Atlanta School of Sleep Medicine apart from others in the field?

The ASSM offers a comprehensive and practical approach to education and training in the field of sleep medicine that is consistent and encompasses the tremendous expansion in the field. Our distinguished, internationally known faculty provides "real world" case-presentations, focuses on interpretation skills and is available and accessible to students. We have developed a more pragmatic, less theoretical approach—a unique combination that offers students the best possible training for their work in sleep medicine.

Discuss your research and development process, including end-user input.

Faculty and staff actively solicit course participants' opinions through course evaluations and additional feedback from attendees at professional meetings. Responding to technologists' suggestions, faculty teach with an interactive component, demonstrating patient set-up, CPAP preparation and titration, and scoring, while maintaining comprehensive didactic, in-class content. The school continues to be responsive to the demographics and needs of current and prospective participants. The ASSM has added additional course locations in recognition of the significant percentage of students located west of the Mississippi. We now offer a four-day course for physicians in San Diego in February, August and October, 2007. An annual course offered in San Antonio attracts students from the Southwest. Courses covering topics of special interest and advancement have also been created in response to student interests, including specialty courses in Surgical Treatment of Obstructive Sleep Apnea; Keys to a Successful Sleep Business Practice; and Pediatric Sleep Medicine. These special course offerings allow both new and former students to increase their knowledge in the field.

How do you use conferences, seminars and such to promote the school?

Faculty and staff from the ASSM speak, exhibit and attend select professional conferences to educate potential students about the training they need to pursue a career in sleep medicine. Physicians and technologists alike benefit from ASSM's presence during professional meetings, gaining access to some of the nation's preeminent sleep professionals.

Stellate

Dr Jean Gotman

Dr Jean Gotman, President & CEO, Stellate.

Describe your product(s) and its unique features.

Stellate provides comprehensive solutions in the areas of Sleep Diagnostics, EEG, Epilepsy Monitoring and ICU Monitoring. Our products feature several proprietary data analysis tools based on original research and are designed for exceptional ease of use, simplified workflows and enhanced efficiencies. Our design approach ensures easy upgrading of features and the option of multiple applications (such as Sleep Diagnosis and EEG) on the same platform.

How does your product directly affect patient care?

Stellate products include advanced event detection algorithms that significantly enhance diagnostic accuracy, enabling users to promptly capture critical events as they occur and take appropriate action. Powerful and flexible analysis tools provide additional information to resolve difficult diagnostic situations. Components of our systems that directly interface with the patient are designed with a high emphasis on patient comfort and safety.

Tell us about the latest advances in the area your product serves.

Recent guideline changes published by the AASM for the recording and scoring of sleep studies provide additional opportunities for the development of new automated event detection and classification tools. Stellate's extensive work in this area allows our products to fulfill these requirements easily.

What sets your product apart from others in the field?

Our comprehensive suite of recording & analysis tools in conjunction with our extremely flexible, rugged hardware platform & outstanding customer service provide our users with the most effective turnkey solution for polysomnography. In addition our extensive commitment to research & development allows us to bring innovative tools to our users.

Discuss your R&D process, including end-user input.

Stellate's R&D process uses two distinct approaches. Firstly, we actively seek input from our customers through focus groups, periodic surveys and the day-to-day interaction that our sales and customer support teams have with them, to identify what is really important to make their jobs easier. Secondly, we actively collaborate with many hospitals and academic institutions to develop cutting edge analysis techniques that subsequently find their way into our final products. We also run all our new features through a rigorous beta testing process to ensure their ease of use and effectiveness.

What are your goals for R&D in the near future?

In the arena of Sleep, the clinical use of ideas such as Flow-Volume and Sleep Microstructure will play an important role in the next several years. Our R&D initiatives will focus on incorporating advanced analysis techniques into everyday tools that will become part of routine clinical usage. We will continue to develop solutions to simplify the assessment of electrophysiological data for fast and accurate patient care in line with emerging networking technologies.

Discuss the educational services you offer for use of your product.

We offer comprehensive applications and product training delivered by a highly qualified team of individuals that includes Polysomnography and EEG technologists who have strong clinical experience. On-site and web-based training options customized to specific needs are made available to our customers. Our R&D staff offer seminars, presentations and lectures at important forums including major industry conferences to discuss advancements in the area.

Discuss the role of critical care providers in developing and upgrading your product.

Stellate actively seeks and uses inputs from clinicians from leading hospitals and clinics during new product development and ongoing product improvement. All new products are put

through customer use tests to ensure they fully meet customer requirements and necessary modifications are incorporated before final product release.

What new technology do you see as having the greatest impact on your area of expertise?

Advances in communication technology enabling faster remote viewing of data with larger number of channels, faster CPUs leading to speedier data processing and developments in sensor technology enabling incorporation of additional physiological information are some of the major developments that we see as having an impact on sleep diagnostic equipment. The most important developments, however, will come from improved software technology, including analysis algorithms and user interface, which will greatly improve the accuracy and efficiency of sleep clinicians in performing their diagnostic and treatment work.

Discuss the international scope of your testing/marketing/development efforts.

Stellate has an international presence in over 30 countries around the world. We maintain strong relationships with leading clinicians and researchers in these countries and our product development process takes into account unique needs identified by our international customers. Our presence in international markets enables us to be aware of new developments as they arise.

Tell us how you utilize conferences, seminars and such to promote your product.

We participate in leading national, international and regional conferences through exhibits and presentations. Product demonstration is actively conducted at such venues. Our products show their real value when the clinician goes through a scoring session and sees the impact of the many features that facilitates their work and allow in-depth analysis.

SLEEP PRODUCTS REVIEW

Complex Sleep Apnea and VPAP Adapt SV

Michael Farrell

Michael Farrell is Senior Vice President, Sleep Strategic Business Unit, ResMed.

Recently, the topic of complex sleep apnea has stimulated much inquiry and discussion among researchers and clinicians in the sleep industry. At this year's SLEEP conference in Minneapolis, complex sleep apnea was a key focal point with the introduction of new clinical data, four oversubscribed standing-room-only sessions and numerous poster presentations. The sentiment at SLEEP clearly reflected a growing recognition of the importance of effectively identifying and treating complex sleep apnea patients.

Complex sleep apnea is characterized by the emergence and persistence of central apneas and/or hypopneas during attempts

to treat obstructive events with standard continuous positive airway pressure (CPAP) or bilevel devices. Patients with complex sleep apnea generally exhibit predominately obstructive or mixed apneas when they are analyzed during the diagnostic portion of the sleep study, without CPAP or bilevel therapy. Sleep physicians and technologists find that these patients cannot be adequately treated with conventional therapy due to the emergence of central events while under treatment with standard CPAP or bilevel systems. They experience residual symptoms (fatigue, sleepiness, depression) and are often intolerant of conventional therapy. As a result, their sleep-disordered breathing cannot be completely resolved: this presents a frustrating challenge to clinicians.

While difficult-to-treat types of sleep apnea have long been observed in sleep labs, there was a lack of specification and definition of this emerging central sleep apnea problem. Peter Gay, MD and Tim Morganthaler, MD from the Mayo Clinic (along with other key opinion leaders from around the globe) have better defined this particular SDB disease state and, importantly, have given it a name: complex sleep apnea (CompSA). Much of the excitement surrounding CompSA appears to be driven by recent clinical successes in treating patients who have historically been difficult to treat. The adaptive servo-ventilation technology was originally launched by ResMed in Europe in 2001 with a focus on Cheyne-Stokes respiration combined with underlying central sleep apnea as well as mixed sleep apnea in heart failure patients. The additional medical potential of this adaptive technology to treat and normalize CompSA patients was found with the help of key researchers like Dr Gay and Dr Morganthaler.

ResMed took the lead in the Americas central sleep apnea treatment space over two years ago when we introduced the first device to gain FDA clearance for the treatment of central and mixed sleep apnea as well as periodic breathing in August 2005. The VPAP Adapt SV device constantly measures, learns and matches the patient's breathing rate and minute ventilation, ensuring optimal delivery of positive airway pressure therapy. The Adapt SV has an established history of success and its adaptive servo-ventilation technology has been clinically validated in U.S. as well as European-based peer-reviewed clinical studies. By August 2007, it was relied upon by over 1,000 hospitals and institutions – a number growing literally every week.

Recently, another treatment option for complex sleep apnea has been introduced to the US market. While there is healthy discussion and debate about the best forms of therapy for complex sleep apnea patients, we believe it is important for respiratory specialists to understand the key differences between the two technologies. One clear differentiator is that ResMed's adaptive servo-ventilation technology utilizes a sophisticated respiratory learning algorithm based upon the fundamental measurement and normalization of minute ventilation. The competing auto servo technology is based upon measurement of a different metric: peak flow - this is a significantly noisier parameter than minute ventilation. Moreover, ResMed's adaptive servo-ventilation technology has passed extensive clinical review, setting it apart from other treatment options. There are over eight (8) peer-reviewed articles (with more in press) showing the clinical efficacy of ResMed's adaptive servo-ventilation technology, with data showing improvement in AHI, sleep architecture and arousals,

as well as improvement in many other cardiovascular and physiological parameters. We have included a subset of these references at the end of this article for your review.^{1,2,3,4,5,6}

In this area of sophisticated algorithms and treatment of complicated disease states like complex sleep apnea, we believe that peer-reviewed clinical efficacy is a critical factor to consider in choosing the most effective ventilation algorithm. Other companies recognizing CompSA presents an important medical opportunity for companies and clinicians in the respiratory therapy area to find ways to effectively identify, diagnose and treat these patients. To date, the Adapt SV has successfully treated well over 12,000 patients with 7 years of extensive use worldwide. We continue to receive testimonials from physicians who have successfully managed their difficult-to-treat patients with the Adapt SV. At the SLEEP 2007 conference, the clinical database of the Adapt SV technology was expanded with two new additional clinical studies reinforcing the effectiveness of the technology in treating complex sleep apnea.^{7,8}

The sleep industry is entering an exciting time in the treatment of complex sleep-disordered breathing and other complicated sleep disorders. As a combined team of clinicians and companies serving this market, we are better-equipped to treat a wider range of clinical and patient needs than ever before. ResMed's dedication to patient care continues to fuel our investment in R&D with the goal of developing new technologies to meet the clinical needs of a growing patient population. We look forward to working with respiratory therapists as well as sleep physicians and technologists to continue to meet emerging needs in complex sleep apnea as well as other new, unmet medical needs in respiratory medicine.

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SLEEP ROUNDTABLE

SleepSense

Sarah Bond

Sarah Bond is Marketing/Sales Coordinator for SleepSense.

How do you foresee the next 5 years in sleep related reimbursement? Is this changing product development trends?

We believe reimbursement will increase significantly for ambulatory testing, and new apnea therapy modalities besides CPAP which will be introduced in the near future. Naturally, the mix of our products and future R&D plans are geared to cater for the expected market needs.

What patient populations could be considered for home sleep testing? What are the indications for a home sleep test?

We believe almost every patient should be considered for home testing, but continuing with an in-lab study if there is any doubt about the accuracy of the ambulatory study. We believe the number of these ambulatory studies will increase to such an extent, that overall the number of in-lab studies will not decrease significantly.

What is the standard by which we should evaluate new home sleep testing diagnostics?

We see more and more home testing devices that are, in fact, just smaller versions of the in-lab equipment. We think that the overall accuracy of ambulatory testing is perfectly acceptable, and that new devices must be evaluated by any added value they can present to the medical system—longer follow-up, easier use, lower cost and more.

What are the advantages of home sleep diagnostics over traditional in-lab polysomnography?

Improved patient compliance, larger customer base, availability to experts of various disciplines.

Braebon

Michael Clark

Michael Clark is Director of Marketing and Sales for Braebon

How do you foresee the next 5 years in sleep related reimbursement? Is this changing product trends?

I believe there will be some big changes in sleep medicine over the next 5 years with respect to reimbursement as we know it now. In September, the Centers for Medicare Services (CMS) will hold a public meeting to reassess the National Coverage Determination (NCD) for diagnosis and treatment of obstructive sleep apnea to include home sleep testing as an alternative to traditional in lab polysomnography. This was looked at 2 years ago and turned down but the pressure from groups such as the American Academy of Otolaryngology Head and Neck Surgery and others have forced CMS to take another look. If in some way CMS approves reimbursement for home studies then I believe you will see a number of sleep equipment vendors offering portable testing products that range from type 3

screening devices to full PSG systems. Portable testing in the home will most likely become a factor that will affect reimbursement rates since full in-lab PSG testing may not be required for a large percentage of “obvious” obstructive sleep apnea patients.

What patient populations could be considered for home sleep testing? What are the indications for a home sleep test?

Home sleep testing would be beneficial for a number of patients that for whatever reason cannot be tested in a traditional sleep laboratory. These include a percentage of patients that would be difficult to study in-lab such as bariatric, pediatric, elderly or patients that are too sick or live in a rural area where a sleep lab is not practically accessible. There is also a group of patients that simply refuse to be tested in a sleep lab because they may be concerned about their safety at night or they think it is too much like a hospital.

Patients who complain about the obvious symptoms of sleep apnea indicated by a simple sleep questionnaire are usually good candidates for a home sleep test. Most often they are overweight with a thick neck that the “janitor could recognize.” In certain cases if the AHI exceeds 15 and the events are clearly obstructive and the patient has had a proper physical examination by a sleep physician then one could argue this person may not need a traditional in lab sleep study and might benefit going directly to therapy.

What is the standard by which we should evaluate new home sleep testing diagnostics?

Without any question home sleep testing systems or portable monitoring devices should be compared to the “gold standard” of laboratory polysomnography. They should be statistically compared side by side with a conventional in-lab digital PSG system over a number of patients for both accuracy and reliability. This would include both type 2 (minimum of 7 channels that include EEG, EOG, chin EMG, ECG, airflow, respiratory effort and oximetry) and type 3 (minimum of 4 channels that include airflow, respiratory effort, ECG and oximetry) recording units. Type 4 monitors that record only one or two parameters should not be used for home sleep testing since they do not have the ability to distinguish between obstructive sleep apnea and central, mixed or complex sleep apnea. Although most portable devices automatically score the recording the raw data should be accessible for technical review and physician interpretation.

What are the advantages of home sleep diagnostics over traditional in-lab polysomnography?

There has been a long-standing debate between at home and in lab polysomnography and what is actually best for the patient. From a technical perspective my experience has indicated the “gold standard” in-lab study still generates the best data. However there are many reasons the patient may be reluctant or unable to be tested this way leading to a situation where they might not get the treatment they need. Given the choice most patients would prefer to be tested at home for obvious reasons related to the unfamiliar environment of a sleep testing facility. Although the technology of portable recording systems has advanced over the years there will still be problems with the sensor/human interface and the technical issues of recording in a more hostile environment. Nevertheless home sleep diagnostics used as a screening tool for sleep apnea is very

useful and will become more popular as physician awareness of sleep disorders increases.

How are your products integrated for hybrid labs, in terms of studies and for homecare?

Our Pursuit Sleep2 system was designed specifically to perform both stationary laboratory and portable at home sleep studies. This means that the same amplifier system can be conveniently used to record studies in both the traditional sleep lab and in the patients home. The amplifier itself called the MediPalm because it can fit into the palm of your hand has several design features making it ideal for hybrid recording environments. For instance the MediPalm can be powered directly from a computer or run on internal batteries. Since it has an onboard microprocessor and memory this amplifier can function with or without a computer and also back the study internally. So even if the power goes out or the computer hard drive fails you will still be able to complete the study.

What is the role of repeated measures in sleep testing? Will this help reduce the inherent night-to-night variability that we observe from sleep studies?

Although there are studies that demonstrate there is a percentage of night-to-night variability between sleep studies it is not cost effective to perform this procedure on a regular basis. If the sleep testing facility provides a comfortable recording environment for the patient and the staff performs a quality study from a technical perspective then in most cases the test will not need to be repeated. On occasion there will be the need to repeat a study but this should be less than 5% of all patients tested. This may be of more importance with unattended portable home studies since the risk for technical problems will increase. Our MediByte 10 channel type 3 screening device for snoring and sleep apnea has a software feature that allows the unit to be programmed for back to back night studies. This would reduce the chance of not getting a good recording and also measure the night-to-night variability between 2 studies.

Actigraph, LLC

Rick W. Finch

Rick W. Finch is Senior Vice President of ActiGraph, LLC.

How do you foresee the next 5 years in sleep related reimbursement? Is this changing product development trends?

ActiGraph is actively fighting for reimbursement. Once more permanent billing codes are established, there is a great deal of pull-through that will be necessary at the regional CMS levels as well as private plans before consistent reimbursement will be unilateral. To categorize a strategic five year plan at this juncture would literally be a shot in the dark. However, there are some good things happening that are encouraging, and hopefully we will see our hard work come to fruition sooner rather than later.

What patient populations could be considered for home sleep testing? What are the indications for a home sleep test?

Prime patient populations consist of individuals that may be suspect of having a sleep disorder (screening) or those who

have been prescribed post diagnostic testing of the efficacy of a specific course of therapy. Testing in these areas benefits everyone involved: the patient, the physician, and the lab conducting the diagnostic testing or prescribing the follow up.

What is the standard by which we should evaluate new home sleep testing diagnostics?

Most physicians have indicated to me that we should evaluate based on the validity of the diagnostic measure, by the direct and indirect costs associated with the measure, and by the ease of patient use/compliance. Actigraphy has benefits in all these areas, and additionally, over a three day wear of the device, it may also show other metric indications of overall activity throughout the day. These indications may also have an effect on an individual's sleep habits as well as other health related risks.

What are the advantages of home sleep diagnostics over traditional in-lab polysomnography?

The science of accelerometry is not yet intended to diagnose a specific illness like apnea or RLS. Rather, we are focused on using this technology as a measure of screening prior to in-lab testing and/or follow-up post therapy to ensure efficacy of a particular treatment in a patient's own environment.

How are your products integrated for hybrid labs, in terms of studies and for homecare?

ActiGraph algorithms are validated for the detection of motion. The ease of use/compliance makes them particularly attractive for homecare...with applications beyond the realm of sleep medicine and including, but not limited to diabetes, obesity intervention and activity rehabilitation.

What is the role of repeated measures in sleep testing? Will this help reduce the inherent night-to-night variability that we observe from sleep studies?

I don't think anyone will argue that the best chance for a true sleep "snapshot" is in the comfort of one's own environment. Even then, there will be shifting variables that will continue to have an effect on one's ability to sleep...whether in a clinic or in one's own bed. Periodic testing/screening is really the only objective measurement we have, and Actigraphy offers an inexpensive and objective view acutely and over time.

Embla

Mike Longman

How do you foresee the next 5 years in sleep related reimbursement? Is this changing product development trends?

While it is hard to say with any degree of certainty how reimbursement models may change, we believe, as many in the industry do, that the US health care reimbursement model for sleep disorders will follow the current European model which allows for home sleep testing. Product development trends industry-wide have begun to change in the US. While many manufacturers are just now developing small, portable home based screeners and diagnostic tools, our Embletta has been the gold standard for ambulatory and PG in Europe for nearly 6 years.

What patient populations could be considered for home sleep testing? What are the indications for a home sleep test?

There are a number of questionnaires available to both patients and clinicians that can provide enough information to determine the likelihood that a patient has sleep apnea. Patients with a strong likelihood are well served by home monitoring because the severity of their condition can be determined and therapy can be administered more quickly than with a traditional sleep test. Likewise, patients may refuse to submit to an in-lab sleep test for various reasons, including cases where a sleep lab test presents a financial burden.

What is the standard by which we should evaluate new home sleep testing diagnostics?

First, it is important to remember that the parameters being recorded in home sleep testing have been recorded successfully for many years. An example of such recordings include respiratory recording in apnea monitors, ECG in Holter, EEG in ambulatory, actigraphy, body position and oximetry. These recordings have been performed in unattended home monitoring studies since the 1970s. That being said, the standards applied in attended studies should be applied to home studies. The recorded signals in the unattended study should be of high quality and reliability.

What are the advantages of home sleep diagnostics over traditional in-lab polysomnography?

The advantages are vast and affect all components of the sleep diagnostic process including clinicians, patients, and sleep facilities. Home sleep testing also fosters an improved continuum of care so that patients can be assessed at regular intervals. Home sleep tests create the opportunity for patients to be tested in a timelier manner since the issue of backlog and resistance to visit a sleep lab are eliminated. The equipment is less expensive, less labor intensive, and therefore the cost of the procedure is less, which will open the door for patients who do not have the financial means to have a sleep test in a lab setting. The advantage for clinicians and patients alike is clear—expedient diagnostic testing leads to more immediate therapy and therefore better quality of life.

How are your products integrated for hybrid labs, in terms of studies and for homecare?

We give our customers the flexibility to perform a range of diagnostic testing from simple screening to a full PSG using the same software application. We also offer full integration to HIS or laboratory management systems with our Embla Enterprise software, a business management solution. Embla Enterprise facilitates electronic management of patient records, provides efficiency statistics including tools to monitor patient compliance, tracks referral patterns, and assists with accreditation procedures. We believe that easier access to information, efficient management of patients, and effective follow up and reporting tools leads to better patient care. Additionally, we offer a full sensor line to accompany our products, as well as other PSG systems, including our unique XactTrace technology and Respiratory Inductive Plethysmography (RIP) belts.

What is the role of repeated measures in sleep testing? Will this help reduce the inherent night-to-night variability that we observe from sleep studies?

Our position on this topic is that the population is best served

by home testing and that a single night will provide sufficient data to determine the appropriateness of therapy. An individual with sleep apnea experiences events every night and therefore the variability from night to night is more a question of severity not a positive versus negative test. Furthermore, it is our belief that repeated measures should be applied within the continuum of care. Using home diagnostic testing devices, patients could and should be tested at regular intervals to determine the efficacy of the therapy. The high cost of in-lab testing prevents many from ever being re-tested and therefore the effectiveness of therapy is largely based on subjective information through self reporting.

Compumedics USA

Tom Lorick

Tom Lorick is VP Marketing, Compumedics USA.

How do you foresee the next 5 years in sleep related reimbursement? Is this changing product development trends?

Compumedics foresees a shift in reimbursements for sleep diagnostics that would continue to follow the general trend of healthcare reimbursement in the United States. While that might seem like a general decline across the board, we think it is more a focus on the optimum use of more expensive, resource intensive procedures such as a full PSG. Thus the trend will most likely reflect a shift in focus towards appropriately identifying the best candidates for complete PSG exams so that reimbursement is commensurate with the required physician guided resource utilization and resulting patient treatment. Therefore it is appropriate that more screening type of tests will be considered and selected for reimbursement. Reimbursement for the screening or limited PSG indicator testing would necessarily be lower to reflect the reduced resources required to arrive at the correct patient treatment regimen. As focus in sleep medicine continues to shift to outcomes of care, there will be more reimbursement related to follow-up evaluations, especially unattended studies.

What is the standard by which we should evaluate new home sleep testing diagnostics?

Very simply put, home testing needs to meet the standards a physician requires to appropriately treat the patients. That standard may change based on the severity or type of disorder with which an individual patient may present. A home sleep study may provide the information a physician needs for proper treatment, or may indicate the need to have an attended study performed. Regardless, the home study needs to provide reliable, quality data that is diagnostic in nature. If the home study results consistently leave questions in the physicians mind, or results in the request for an attended study in a high percentage of cases, then the type of study conducted may need to be reviewed. With current technology there is no need to compromise on the quality of the sleep study recording done at home. A full 16-channel PSG can be done in the home which meets all the new AASM guidelines for in-lab PSG. Compumedics has been a leader in portable PSG systems since it first developed the P-Series in 1995. The Compumedics Somté line of portable recorders cover the range from 5-channel to 18-channel recordings.

What are the advantages of home sleep diagnostics over traditional in-lab polysomnography?

Probably the first advantage would be that the patient is tested in their own environment. This may put the patient at ease or possibly uncover issues that may not be seen in a lab setting. (what is the bed like, what about the pillows, do they sleep with a partner, etc.). A second advantage would be the reduced resources and physical space required for the home exam versus a sleep lab. In addition fewer technologists can set-up and initiate testing on more patients than in a traditional lab.

How are your products integrated for hybrid labs, in terms of studies and for homecare?

Compumedics has long made products that are suitable for attended, ambulatory and home environments. Our newest product the SomtePSG is a true hybrid in that it allows for up to 17 channels of data to be tracked and recorded on a data card for an unattended study or via wireless Bluetooth for an attended study. The device is compact and provides all of the required physiologic measures to comply with the newest AASM recommendations. Our Siesta and Safiro systems also offer fixed and ambulatory capabilities that are suitable for lab or home-based use. Most importantly all of these devices utilize the same software and user interface so that the data, analysis and reporting is the same for all of the devices easing the training and resource requirements on the technologists and physicians.

What is the role of repeated measures in sleep testing? Will this help reduce the inherent night-to-night variability that we observe from sleep studies?

The literature well documents the “first night effect” and night-to-night variability in sleep studies. The cost of testing in the sleep lab prevents us from routinely doing multiple night recordings, but the lower cost of home studies would make multiple-night recordings feasible. From a practical standpoint, patients who clearly demonstrate moderate or severe sleep apnea patterns during a single diagnostic study will not likely have any added benefit from a second nights recording. Patients who demonstrate results that are not consistent with their complaint of excessive daytime sleepiness may benefit from a second night and of course, patients who are placed on treatments such as CPAP or oral appliance therapy could very likely benefit from repeated studies that are performed days or weeks after they accommodate to the therapy.

Cardinal Health/Viasys Healthcare Respiratory Care

Steve Birch

Steve Birch is Director of Marketing Sleep Diagnostics and Therapy

How do you foresee the next 5 years in sleep related reimbursement? Is this changing product development trends?

The growing pressure of healthcare costs from all sectors will impact reimbursement and sleep reimbursement will not be exempt. In fact, as most patients with obstructive sleep apnea remain undiagnosed and the costs to manage this population continue to grow we can expect that there will be pressure to control or reduce these costs. Product development in the area of sleep diagnostics is expanding the options for home sleep

testing and also adjusting to the changing needs of the sleep diagnostic centers where the types of patients that will be tested there may change. On the sleep therapy side of the equation reducing cost while improving quality and expanding feature sets has become the standard and this can be expected to continue. Improvements in compliance monitoring and mechanisms for enhancing compliance will be added to new devices with increasing regularity.

What patient populations could be considered for home sleep testing? What are the indications for a home sleep test?

Clearly there are some patients with frank obstructive sleep apnea that can be qualified for home sleep testing with a standard history and physical and possibly the addition of a sleep questionnaire. The concern is that co-morbidities might be missed with a less comprehensive home sleep test. There does not appear to be interest in testing patients other than those with OSA in the home setting. This is in large part due to the size of the potential OSA population and general lack of technologies that are capable of being used for diagnosis of other sleep disorders. The indications for home sleep testing will likely be bed-partner observed snoring and/or apnea, excessive daytime sleepiness, morning headache and inability to focus upon awakening, obesity and a neck circumference of 17 inches or more. I expect that CMS in concert with sleep professionals will take the lead in formally establishing these indications.

What is the standard by which we should evaluate new home sleep testing diagnostics?

The standard for evaluation of home sleep testing technologies is not facility based polysomnography because the conditions for use are very different. The technologies should be evaluated based on four criteria. First, the device should utilize sensor technology and monitor parameters that are closely allied with those used in facility based sleep centers. This helps to assure a uniform understanding of what is being measured and how this relates measurements made on other systems and in turn to the patients sleep disorder. Secondly, the device and sensors must be easy to apply, the device easy to set-up and operate and the data easy to download and score. A key concern about home sleep testing is that there will be sensor failures or other device related problems that require retesting and that this will eliminate the anticipated financial benefit of home sleep testing. Thirdly, the device should be capable of storing multiple nights of data. This improves the likelihood of getting good results and can be used to compensate for first night effect. Lastly, the device should download data to a program that provides both automated scoring and manual processing. This allows for the management of artifacts and the generation of an acceptable report.

How are your products integrated for hybrid labs, in terms of studies and for homecare?

The SomnoStar platform which is used for our facilities based and portable polysomnography products also supports home sleep testing devices. The SomnoStar Orbit is a 9 channel device that can provide data files to the SomnoStar software for scoring and report generation. Homecare providers can provide the home sleep test device to the patient, but can also download data and generate reports if they acquire the SomnoStar software.

What are the advantages of home sleep diagnostics over traditional in-lab polysomnography?

Ideally home sleep testing can improve access for patients not

currently served by a sleep center, reduce the time to make a diagnosis and provide a cost effective diagnosis of OSA. The home sleep testing technology can address the first night effect, particularly in pediatric patients, multi-night variability can be cost effectively evaluated and follow-up studies of CPAP function can be conducted.

What is the role of repeated measures in sleep testing? Will this help reduce the inherent night-to-night variability that we observe from sleep studies?

Auto-CPAP technology has shown us that some patients have significant variability in their pressure requirements from night-to-night. So some of the variability seen in sleep studies is likely real. Home sleep test devices can be used to assess therapeutic effectiveness from night-to-night; however auto-CPAP technology with an integrated monitor can provide the same or even better information regarding this. The first night effect may be reduced or eliminated with home testing, although I believe that this has yet to be demonstrated in adults. Patient follow-up is a key component in establishing a successful therapeutic regime for OSA. Part of the follow-up is a determination of therapeutic effectiveness. Home sleep testing with the ability to monitor CPAP pressure can provide important information regarding the clinical benefit experienced by the patient. Patients at increased medical risk or in high risk occupations should be tested routinely.

CleveMed

Hani Kayyali

Hani Kayyali is President of CleveMed.

How do you foresee the next 5 years in sleep related reimbursement?

We believe that the reimbursement for home procedures will become a reality soon. These procedures will include home screening of obstructive sleep apnea, CPAP titration, and CPAP follow-up. Reimbursement for non-CPAP alternatives is expected to grow, such as oral appliances and surgery.

Is this changing product development trends?

Reimbursement for home procedures will most definitely change product development. In fact, product development has been changing for awhile in anticipation of the new reimbursement environment. Portable devices that offer highly reliable recordings will be in demand, and wireless and internet-based capabilities that permit seamless and secure data transfer between patients, DME providers, and doctors will be required. The role of sophisticated data analysis will increase as well, whether it is to improve ongoing methods like auto-scoring algorithms for breathing or sleep behavior events or to start new applications like identifying airway collapse site.

What patient populations could be considered for home sleep testing?

Initially, home testing will target OSA patients. However, we foresee sleep technology for the home to grow in sophistication to handle the more complicated patient cases. Sleep disordered breathing patients with comorbidities like stroke, diabetes, COPD, and others ultimately could be diagnosed and treated in the home.

What are the indications for a home sleep test?

A number of indicators, like a patient's ability to conduct the test by themselves at home, the complexity of a patient's health status, and clinical indicators (obesity, sleep habits, etc) will play a factor in prescribing home tests. However, at the end of the day, home testing should not create more work for everyone involved (the patient, sleep physician and insurance carriers). Instead, home testing should improve the process, making it more convenient for the patient, reliable for the doctor and cost effective for the payer. A simple to use home sleep monitor with reliable yet powerful recordings will certainly be needed.

What is the standard by which we should evaluate new home sleep testing diagnostics?

First and foremost is patient care and comfort. Are we diagnosing and treating patients faster in a manner that is reliable and accurate? Then there is cost. Are we saving the health care system money by home testing? This will ultimately rely on the sensitivity and specificity of home testing.

What are the advantages of home sleep diagnostics over traditional in-lab polysomnography?

Testing patients in the comfort of their own home is ideal for patients who may have difficulty coming to the sleep lab, such as pediatric patients, the elderly, or those suffering from chronic pain. Since sleep labs are able to increase the volume of patients being tested, patients can be diagnosed more quickly, thereby decreasing the time it takes to start them on a treatment plan. From an economic standpoint, labs can increase the volume of patients seen and payors are likely to realize cost savings.

How are your products integrated for hybrid labs, in terms of studies and for homecare?

CleveMed's line of diagnostic sleep products are ideal for expanding the reach of the sleep lab. In addition to our complete wireless PSG systems for traditional in-lab use, we offer a 9-channel sleep screener for advanced home screening. Recognizing the need for PSG testing in the hospital inpatient setting, CleveMed's iPSG inpatient PSG system allows for patients to be monitored in hospital rooms by a technologist remotely - even if the sleep lab is far away. For virtually attended sleep studies in the home setting, PSG@Home is available this Fall. With this system sleep studies can be done in patient homes or hotel rooms using a bedside system controlled by the sleep lab technologist remotely. This proprietary technology uses mobile phone broadband internet service to transmit patient data and video in real time from the patient's home to the technologist, allowing studies to be conducted anywhere in the world where cell phone service is available. With CleveMed, sleep labs can perform PSG anywhere: attended, virtually attended or unattended.

What is the role of repeated measures in sleep testing?

It is not clear if this will be required for home testing. Regardless of the final CMS ruling in this regard, home devices should have the capability to run multiple nights with minimal hassle to the patient such as no battery changes, no memory download, no special sensors handling or storage.

Will this help reduce the inherent night-to-night variability that we observe from sleep studies?

Yes. Multiple consecutive night recordings should help improve the accuracy of the results.

Sleep Characteristics of Persons With Chronic Fatigue Syndrome and Non-Fatigued Controls: Results From A Population-Based Study

William C. Reeves, Christine Heim, Elizabeth M. Maloney, Laura Solomon Youngblood, Elizabeth R. Unger, Michael J. Decker, James F. Jones, David B. Rye

Abstract

Background: The etiology and pathophysiology of chronic fatigue syndrome (CFS) remain inchoate. Attempts to elucidate the pathophysiology must consider sleep physiology, as unrefreshing sleep is the most commonly reported of the 8 case-defining symptoms of CFS. Although published studies have consistently reported inefficient sleep and documented a variable occurrence of previously undiagnosed primary sleep disorders, they have not identified characteristic disturbances in sleep architecture or a distinctive pattern of polysomnographic abnormalities associated with CFS.

Methods: This study recruited CFS cases and non-fatigued controls from a population based study of CFS in Wichita, Kansas. Participants spent two nights in the research unit of a local hospital and underwent overnight polysomnographic and daytime multiple sleep latency testing in order to characterize sleep architecture.

Results: Approximately 18% of persons with CFS and 7% of asymptomatic controls were diagnosed with severe primary sleep disorders and were excluded from further analysis. These rates were not significantly different. Persons with CFS had a significantly higher mean frequency of obstructive apnea per hour ($p = .003$); however, the difference was not clinically meaningful. Other characteristics of sleep architecture did not differ between persons with CFS and controls.

Conclusion: Although disordered breathing during sleep may be associated with CFS, this study generally did not provide

evidence that altered sleep architecture is a critical factor in CFS. Future studies should further scrutinize the relationship between subjective sleep quality relative to objective polysomnographic measures.

Background

Chronic fatigue syndrome (CFS) presents a diagnostic and management challenge. A case of CFS is defined by: 1) clinically unexplained, persistent or relapsing fatigue of at least 6 months' duration that is not the result of ongoing exertion, is not substantially alleviated by rest, and results in substantial reduction in previous levels of occupational, educational, social, or personal activities, and; 2) concurrent occurrence of at least 4 accompanying symptoms (unusual post-exertional malaise, unrefreshing sleep, significant impairment in memory/concentration, headache, muscle pain, joint pain, sore throat and tender lymph nodes).¹ No characteristic physical signs or diagnostic laboratory abnormalities herald CFS. Thus, diagnosis depends on evaluation of self-reported symptoms and ruling out medical or psychiatric conditions that could cause the illness. Similarly, the pathophysiology of CFS remains inchoate and as yet there is no definitive treatment; rather, therapy (both pharmacologic and nonpharmacologic) is directed toward relieving symptoms and improving function.²

Attempts to elucidate the pathophysiology of CFS must consider sleep physiology. Unrefreshing sleep is the most common of the 8 CFS-defining symptoms, reported by 88 to 95% of cases identified in population studies^{3,4} and 70 to 80% of patients in clinic-based studies.⁵ Most of the postulated etiologies of CFS (eg, infection, immune and hormone perturbations) affect sleep; and, conversely, primary sleep disorders, sleep deprivation and experimental disruption of sleep produce many of the features of CFS (eg, fatigue, impaired cognition, joint pain and stiffness).⁷⁻¹⁰ Indeed, untreated primary sleep disorders, such as sleep apnea and narcolepsy, preclude diagnosis of CFS.^{1,11}

The aforementioned issues raise a central question. Does CFS account for the accompanying sleep disturbances or does an underlying sleep abnormality result in or contribute to CFS?

Authors Reeves, Maloney, Youngblood, Unger and Jones are with the Viral Exanthems & Herpesvirus Branch, Division of Viral & Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control & Prevention; Heim is with the Department of Psychiatry and Behavioral Sciences and Decker and Rye are with the Department of Neurology, Emory University School of Medicine, Atlanta, GA. Reprinted from BMC Neurology, © 2006 Reeves et al; licensee BioMed Central Ltd. This is an Open Access article distributed under the terms of the Creative Commons Attribution License.

Table 1: Analysis of Sleep Architecture in CFS and Controls, Measured on Night 2 and Adjusted for Medication Use

	CFS n = 35 Adjusted Mean*	NF n = 40 Adjusted Mean*	P-Value**
Total sleep time (min)	400.3	407.9	0.52
Sleep period time (min)	453.8	457.8	0.79
Latency to sleep onset (min)	21.3	17.1	0.47
REM latency (min)	98.4	106.8	0.40
Sleep efficiency (%)	88.3	90.2	0.32
Wake after onset (min)	53.8	44.0	0.69
Wake % Sleep Period	11.7	9.8	0.72
# Arousals	105.7	110.2	0.81
Arousal index	15.9	16.3	0.82
Stage 1 (% TST)	9.6	9.5	0.79
Stage 2 (% TST)	48.2	50.8	0.28
Stage 3/4 (% TST)	19.9	17.4	0.20
REM (% TST)	22.3	23.3	0.98

* Mean values adjusted for medication use (yes/no)

** P-values generated using 2-factor analysis of variance

Studies of sleep in persons identified with CFS through tertiary care clinics have not contributed substantially to answering this question.^{6,12-16} Although previous studies have consistently reported inefficient sleep and documented a varying occurrence of previously undiagnosed primary sleep disorders, they have not identified characteristic disturbances in sleep architecture or a distinctive pattern of polysomnographic abnormalities associated with CFS. As with many studies of CFS, published evaluations of sleep pathology have not uniformly applied the case definition of CFS and often lack appropriate comparison groups. People with CFS use a number of prescriptions and over the counter medications that affect sleep;¹⁷ yet most

studies do not mention whether or not medications have been considered. Finally, we are aware of no published studies of CFS that have utilized multiple-night polysomnography, nor are we aware of any published studies that address sleep pathology in a population-based sample of persons with CFS. Because an overwhelming majority of persons with CFS remain undiagnosed,^{4,18} results of studies on CFS patients identified through physician practices may not be generalizable.

The objective of this study was to describe clinical and polysomnographic sleep characteristics of persons with CFS identified from the general population of Wichita, Kansas,⁴

Table 2: Distribution of Breathing and Movement Abnormalities During Sleep

Clinical Sleep Variable	CFS (n = 35)	NF (n = 40)	P-value*
Hypopnea			
Mean event/hr	2.66	1.79	P = 0.24
Range	(0.00 – 16.03)	(0.00 – 14.66)	
Obstructive Apnea			
Mean event/hr	0.94	0.59	P = 0.003
Range	(0.00 – 12.11)	(0.00 – 10.70)	
Central Apnea			
Mean event/hr	0.36	0.15	P = 0.18
Range	(0.00 – 2.44)	(0.00 – 1.89)	
Mixed Apnea			
Mean event/hr	0.14	0.15	P = 0.58
Range	(0.00 – 2.28)	(0.00 – 3.15)	
Snore Index			
Mean	5.31	4.57	P = 0.95
Range	(0.00 – 27.50)	(0.00 – 34.30)	
Respiratory Distress Index			
Mean	4.11	2.69	P = 0.009
Range	(0.10 – 21.21)	(0.00 – 20.35)	
Periodic Leg Movements			
Mean events/hr	4.42	4.56	P = 0.35
Range	(0.00 – 25.74)	(0.00 – 39.37)	
Periodic Leg Movements with Arousals			
Mean events/hr	1.03	0.87	P = 0.62
Range	(0.00 – 11.57)	(0.00 = 7.09)	

*P-values were generated using zero-inflated Poisson regression, adjusting for use (yes/no) of sleep medications. Mean values represent arithmetic means. Leg movement was not measured in 9 CFS cases and 1 control.

compared to non-fatigued controls matched for sex, race, age, and body mass index who were randomly selected from the same population. All study participants were admitted to a research ward in Wichita for 2 days.¹⁹ They underwent a complete physical and psychiatric evaluation, their medications were reviewed and they completed 2-overnight polysomnographic studies and a multiple sleep latency (MSLT) evaluation. This report evaluates associations of sleep disorders and variations in sleep architecture with CFS.

Methods

Participants: This study adhered to U.S. Department of Health and Human Services human experimentation guidelines and received Institutional Review Board approval from the CDC and collaborating institutions. All participants gave informed consent.

Between January and July 2003, we conducted a 2-day in-hospital study of adults identified with CFS from the general population of Wichita.¹⁹ The in-hospital study enrolled people who had participated in the 1997 through 2000 Wichita Population-Based CFS Surveillance Study.⁴ Participants in the in-hospital study were fatigued adults with medically/psychiatrically unexplained chronic fatigue identified during the surveillance study. Fifty-eight had been diagnosed at least once with CFS and 59 had unexplained chronic fatigue that was not CFS. Controls were randomly selected from the cohort who participated throughout surveillance, who did not have medical or psychiatric exclusions, and who had not reported fatigue of at least 1-month duration; they were matched to CFS cases on sex, age, race/ethnicity, and body mass index. Upon admission to this study, subjects were reevaluated for CFS symptoms and exclusionary medical and psychiatric conditions (discussed below). The 43 who, at the time of the in-hospital study, met 1994 criteria for CFS (discussed below) comprise the cases in this report. Controls are 43 individuals who had never reported fatigue during the surveillance study, who were not fatigued at the time of this in-hospital study and who had no exclusionary medical or psychiatric condition identified at the time of study (following section). Because current classification of CFS was not completely in accord with recruitment classification, strict matching was not maintained, though cases and controls were demographically comparable. Thirty-six (84%) of the 43 with CFS and 38 (88%) of the 43 controls were women; most (40 CFS and 42 controls) were white; their mean ages were 50.6 and 50.3 years, respectively; and body mass index was 29.4 and 29.3, respectively.

Assessment and classification of CFS: Subjects who agreed to participate were admitted to a Wichita hospital research unit for 2 days. Subjects brought all their current medications so that clinic staff could record this data and maintain medication profiles throughout the study. To identify medical conditions specified by the case definition as exclusionary for CFS,^{1,11} participants provided a standardized past medical history, a review of current medications, underwent a standardized physical examination, and provided blood and urine for routine analysis.^{1,11} To identify psychiatric conditions exclusionary for CFS, licensed and specifically trained psychiatric interviewers administered the Diagnostic Interview Schedule for current Axis I disorders.²⁰ Exclusionary psychiatric illnesses specified by the case definition were current melancholic depression, current and lifetime bipolar disorder or psychosis, substance abuse within 2 years and eating disorders within 5 years. A panel of

physicians and psychiatrists/psychologists reviewed this information and identified subjects with disorders exclusionary for the diagnosis of CFS. Subjects with no exclusionary conditions were considered to be CFS if they met empirically measured parameters¹⁹ of the 1994 CFS case definition.¹ Non-fatigued controls met none of the parameters.

Medication use: As noted, clinic staff reviewed all current (prescription and over the counter) medications that study participants were taking. Study investigators (DBR, MJD, CH, JFJ, WCR), and other Emory University Department of Psychiatry and Behavioral Sciences collaborators, reviewed all medications and classified them as affecting (inducing sleep, inhibiting sleep or with mixed effects) or not affecting sleep. Those classified as affecting sleep included analgesics (e.g., hydrocodone, Lortab, oxycodone, Propoxyphene), antidepressants (eg, Celexa, amitriptyline, imipramine, Lexapro, Wellbutrin, Effexor, Prozac, Zoloft, Paxil, fluoxetine), anti-anxiety (Alprazolam), antihistamines (eg, diphenhydramine, chlorpheniramine, benadryl, promethazine), decongestants (eg, pseudoephedrine, guaifenesin), anticonvulsants (eg, Topamax, Neurotin, clonazepam), anti-sleep phase disorder (melatonin), blood pressure controlling (eg, Clonidine, Proamatine), antipsychotics (eg, Seroquel, Zyprexa, Fluvoxamine), stimulants (eg, methylphenidate, Provigil), peristaltic stimulants (Metoclopramide), and muscle relaxants (cyclobenzaprine). Medications affecting sleep were handled as a binary measure (ie, they used or did not use one or more of those named above). Analyses took into account use of sleep affecting medications, as noted below.

Polysomnographic and Multiple Sleep Latency Techniques: Nocturnal polysomnography and daytime multiple sleep latency testing (MSLT) were conducted in a 4-bed laboratory established at Wesley Medical Center, Wichita, KS, and consisted of polysomnography on night #1, MSLT the following day and another polysomnography on night #2. Patients were asked to arrive 3 hours before their typical bedtime on Night 1 to allow adequate time for electrode application and standard biocalibrations. "Lights out" and "lights on" time were 22:00 and 07:00, respectively. The daytime MSLT testing schedule was adjusted for other measures being collected; MSLT began at 11:00 and consisted of three additional naps at 13:00, 15:00, and 17:00.

Electrophysiological measures of wakefulness and sleep were acquired and recorded with the Flaga/Medcare N7000 digital polysomnographic system on a Windows XP platform using proprietary software (Flaga/Medcare Somnologica Studio). We employed a sampling rate of 256 Hz to allow for Fast Fourier Transform of EEG signals. Standard gold cup electrodes were employed for recording of EEG, EOG, and EMG for sleep staging and appreciation of sleep architecture. Respiration was measured with inductance plethysmography-like belts placed around the chest and abdomen. A pressure transducer, positioned in close approximation to the nares provided indices of airflow. A pulse oximeter probe was applied to either the right or left index finger, to measure arterial oxygen saturation (SaO₂). Electrocardiogram (ECG) was recorded with standard snap electrodes (NeuroSupplies, Waterford, CT). The following signals were recorded: central (C₃-A₂/C₄-A₁) and occipital (O₁-A₁/O₂-A₂) EEG, left and right monopolar EOG, surface mentalis EMG, ECG (modified V3), respiratory airflow and effort and surface EMG from the right and left anterior tibialis.

The polysomnographic outcome variables used in our analyses included: total sleep time (TST) (in minutes), sleep efficiency (% of time spent in bed asleep), the percentage of TST spent in non-REM (NREM) and REM sleep, sleep latency (in minutes) to three consecutive epochs of sleep, and REM Latency, defined as the time between the first epoch of any stage of sleep and the first epoch of REM-sleep. Brief arousals were scored following criteria set forth by the American Academy of Sleep Medicine, and the number of arousals expressed as a rate per hour of sleep adjusted for TST. Periodic leg movements both with and without accompanying arousals, were scored according to conventional criteria,²² and expressed as an index of the rate of leg movements per hour of sleep, and a separately derived index of those accompanied by an American Academy of Sleep Medicine -defined arousal.²³

Daytime sleepiness was measured with the MSLT, which has demonstrated objective sensitivity to the effects of sleep deprivation, sleep fragmentation, sleep restriction, insufficient sleep, hypersomnia, and in disease states such as sleep apnea and narcolepsy.²⁴⁻²⁶ Multiple sleep latency tests were performed and scored according to standard guidelines with the exception that four naps were recorded at 11:00, 13:00, 15:00, and 17:00. The mean sleep latency on the MSLT was defined as the mean time from lights out to the first 30-second epoch scored as sleep. A sleep onset REM was defined as one or more epochs of REM sleep occurring within 15 minutes of the first epoch scored as sleep. Mean MSLT values of 5 or less are considered to represent pathological sleepiness, scores between 5–10 are consistent with a degree of daytime sleepiness. Scores of 10 and above are considered normative and believed to denote a lack of daytime sleepiness. Because mean values on the MSLT may adversely be affected by a spurious sleep latency on a single nap opportunity²⁷ possibly due to what might be perceived as stressful inter-nap activities,²⁸ median values were also computed for each subject.

Interpretation of polysomnography data: Polysomnography data were scored by an Emory University registered polysomnology technologist (blinded as to subjects' fatigue classification). An Emory University Department of Neurology American Board of Sleep Medicine certified physician (DBR), also blinded to the subjects' fatigue classifications, interpreted results. The polysomnology technologist manually scored each recording in 30 second epochs as wake, NREM, Stages 1–4 sleep, or rapid eye movement (REM) sleep. Criteria for scoring respiratory variables were based upon those of the Sleep Heart Health Study.²¹ Briefly, apnea was scored if airflow decreased to less than or equal to 25% of the immediately preceding baseline for a period of at least 10 seconds. Hypopnea was scored if either airflow or thoracic-abdominal excursion decreased by at least 30% of baseline, for at least 10 seconds, with a concomitant reduction in SaO₂ of 4% or greater. The Respiratory Distress Index (apneas + hypopneas corrected for hour of sleep) was derived from these scored events. To determine the technologist's level of reproducibility, 12 randomly selected studies were scored twice, with at least a six-week interval separating the original scoring and the repeat scoring. Comparison between original and repeat scorings with Kappa analyses yielded a Kappa coefficient of 0.88.

Diagnostic criteria for sleep disorders exclusionary for CFS: The CFS case definition specifies sleep apnea and narcolepsy as conditions that could explain fatigue and symptoms of CFS and therefore exclude the diagnosis of CFS.^{1,11}

Obstructive sleep apnea: Obstructive sleep apnea was considered clinically significant and therefore exclusionary if an individual's Respiratory Distress Index was ≥ 30 on either night, or was between 10 and 30 and the individual had an abnormal mean sleep latency of < 5 minutes during MSLT.²⁹

Narcolepsy: Narcolepsy was diagnosed if 2 out of 4 MSLTs were positive for REM sleep and mean sleep onset during MSLT was < 5 minutes.²⁹

Statistical analysis: Data were analyzed by Systat (Systat Software Inc, Richmond, CA) and SAS (SAS Institute Inc, Cary, NC). We used a 2-factor analysis of variance using PROC GLM to measure the associations between case status and medication use (yes/no) with polysomnographic variables. Log transformed values of polysomnographic variables were used when necessary to satisfy the assumption of normally distributed outcomes. Mean values for each polysomnographic variable were adjusted for medication use using the least square method (LSMEANS). All mean values presented in this paper represent arithmetic means. We also used standard and exact logistic regression models to compute odds ratios as estimates of relative risks and 95% confidence intervals for CFS associated with dichotomous polysomnographic variables (cut-offs based on 25th or 75th percentiles). Measurement of clinical sleep variables included a high number of zero values. Zero-inflated Poisson Regression was used to regress case status and medication use (yes/no) on continuous values of clinical sleep variables. For this final analysis, we used SAS version 9.0 (PROC NL MIXED) and an inflation probability determined by the regressors. Analyses were also performed excluding participants taking medications that affect sleep. Estimates were unchanged when analyses excluded participants taking sleep-affecting medications. For this reason, the results presented in this report do not exclude participants taking such medications, but rather adjust for them in the analysis. We used the χ^2 statistic or Fisher's exact test to evaluate associations between CFS and dichotomous variables.

Results

Primary sleep disorders: Eleven study participants had sleep disorders exclusionary for CFS (obstructive apnea $n = 8$, narcolepsy $n = 3$). Persons with CFS had a higher frequency of exclusionary sleep disorders (8 of 43, 18.6%) than non-fatigued controls (3 of 43, 7%), but the difference was not statistically significant ($p = .16$). The remainder of this presentation considered the remaining 35 individuals with CFS and 40 controls.

Sleep architecture and MSLT: There were no statistically significant differences in standard polysomnographic measurements between those with CFS and controls on either night 1 or night 2. As expected, total sleep time increased in both groups between nights 1 and 2; latency to sleep onset and to REM onset decreased in both groups; and, waking after sleep onset was less common in both groups on night 2 (data not shown). As night 1 was considered to be an adaptation night, data is shown for night 2 (Table 1). Mean values, adjusted for medication use, did not differ between participants with CFS and non-fatigued controls. Interestingly, regardless of case status, medication use was independently associated with both REM latency and Stage 1 % total sleep time. Both REM latency and Stage-1 percent of total sleep time were significantly longer in study participants who reported using any sleep medications

at the time of the study ($P = .02$, $P = .01$, respectively). In addition to comparing polysomnographic measurements as continuous variables between people with CFS and non-fatigued controls, we used regular and exact logistic regression to examine possible associations. We dichotomized measurements based on 25th and 75th percentiles among non-fatigued controls. As with the previous analyses there were no significant differences (data not shown). Virtually identical results were obtained when analysis was restricted to subjects who did not use sleep-altering medications. Finally, evaluation of multiple sleep latency testing studies yielded similar distributions of classifications; (39% normal, 35% borderline and 26% abnormal) between CFS and controls.

Disordered breathing and periodic leg movements during sleep:

Subjects with CFS had significantly more episodes of obstructive apnea and a higher Respiratory Distress Index than did the non-fatigued controls (Table 2). Nonetheless, the difference between the groups in mean obstructive episodes per hour of total sleep was not of a magnitude recognized to have a clinical impact. All other measures of disordered breathing and periodic leg movements were not different between the two groups. Use of medications affecting sleep was independently associated with a higher rate of hypopnea and leg movements episodes per hour, after adjusting for case status ($P = .03$, $P = .05$, respectively). However, use of sleep altering medication was associated with a lower rate of obstructive apneic episodes per hour ($P < .0001$).

Discussion

To our knowledge, this represents the most comprehensive polysomnographic analysis of a community sample of rigorously evaluated people with CFS and frequency-matched non-fatigued controls. There were no significant differences in rates of primary sleep disorders between CFS cases and NF controls. Thus, in spite of additional attention to methodological issues, our findings are in agreement with prior studies of CFS patients identified through clinical referral.^{6,12-16} Similarly, there were no differences in any measured sleep parameters, with the exception of the frequency of obstructive apnea per hour of nighttime sleep and these differences were not clinically meaningful. While subtle breathing problems during sleep might plausibly contribute to CFS, the most striking finding of this study in fact is the absence of readily identifiable differences in objective, polysomnographically defined, sleep parameters between subjects with CFS and non-fatigued controls. Similarly, there were no differences between persons with CFS and non-fatigued controls with respect to daytime multiple sleep latency tests. The lack of differences in overnight sleep parameters and MSLT is in contrast to the participants' self-reported symptoms. For example, 97% of persons with CFS in this study reported unrefreshing sleep compared with 20% of controls. As noted by others, persons with CFS may suffer from an element of sleep-state misperception.³⁰ Future studies should further scrutinize the association between subjective sleep quality and objective polysomnographic results in persons with CFS.

Disorders of sleep were common in both CFS cases and controls in this study. Indeed primary sleep disorders that may respond to therapy were identified in 13% of the overall study population. These findings were unexpected; as the population-based nature of the study eliminated referral bias and potential participants were excluded from the study if they reported diagnosed narcolepsy or sleep apnea disorders during screening

interviews. Despite this, sleep apnea and narcolepsy of clinically significant severity were identified in 11 participants, requiring their exclusion from the study. As participants with sleep disorders were not identified until polysomnographic studies were performed, it is arguable that in clinical situations, referral of subjects with unexplained fatigue to a sleep laboratory should be considered in an effort to identify disorders that may respond to intervention. In research settings case ascertainment does not usually include formal sleep studies. Thus, the potential impact of including subjects with primary sleep disorders in the CFS diagnosis should be considered when interpreting results from such studies, and when designing CFS studies. Finally, MSLTs were borderline or abnormal in 60% of subjects. This may be attributed to the occurrence of sleep disorders in our study population, or to environmentally induced sleep disruption occurring during the night preceding the MSLT.

The study has several weaknesses that should be considered while evaluating the results. While one of the largest studies identifying CFS cases and NF controls from the general population to date, the small numbers of identified subjects with current CFS may not be sufficient to identify small but biologically significant differences in sleep architecture. Second, our subjects spent two nights in the sleep lab (to allow accommodation) and (although adequate to detect primary sleep disorders) this may not produce an accurate picture of subtle nocturnal sleep behaviors. Moreover, sleep-altering medications were frequently used by both CFS cases and controls and their use was much more common among CFS cases. Some of these medications have opposite effects on sleep and we chose to lump them as sleep-altering. While we employed statistical corrections for their use, may have been inadequate to fully correct for the varied impact of the different formulations. It should nonetheless be noted that stratified analyses restricted to those without sleep-altering medications yielded similar findings compared to the total sample, although the greatly reduced numbers further limited the power of the examination. Finally, the median duration of CFS in the Wichita population was 7.3 years;⁴ thus, findings in this study of prevalent cases may not be applicable to those with shorter illness duration.

Conclusion

In conclusion, although this study evaluating associations between sleep physiology and CFS addressed the major limitations and methodological issues of previous studies, we could not confirm statistically significant associations between sleep parameters and CFS. Sleep abnormalities therefore are an unlikely contributor to the pathophysiology of CFS and the illness may include sleep-state misperception. However, 18% of persons with CFS had previously unrecognized clinically severe apnea or narcolepsy, demonstrating the importance of evaluating persons with otherwise unexplainable chronic fatigue for sleep disorders. Additional, sufficiently powered, studies with CFS cases identified from the population should be conducted.

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Parent-Rated Behavior Problems Associated With Overweight Before and After Controlling For Sleep Disordered Breathing

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Abstract

Background: Researchers and clinicians are seeking to develop efficacious behavioral interventions to treat overweight children; however, few studies have documented the behavioral correlates of overweight children in community samples. The goal of this study was to determine the nature and prevalence of behavior problems for overweight school-aged children versus normal weight peers before and after controlling for the effect of sleep disordered breathing.

Methods: Hispanic and Caucasian children were invited to participate in a study of sleep through public elementary school classrooms. Anthropometric evaluation and behavioral ratings were collected for 402 children aged 6–11 years. Overweight was calculated using the Centers for Disease Control age- and gender-specific guidelines. Children were classified as overweight if they were at or above the 95th percentile for their age and gender group. Behavior problems were measured using the Conners' Parent Rating Scales-Revised and the Child Behavior Checklist. Sleep disordered breathing was assessed using in-home overnight polysomnography.

Results: Approximately 15% (59/402) of the sample was classified as overweight. Simple odds ratios indicated that overweight children were more likely to have clinically relevant levels of internalizing symptoms (OR 2.23, CI 1.05–4.72), psychosomatic complaints (OR 2.15, CI 1.02–4.54), withdrawal (OR 4.69, CI 2.05–10.73), and social problems (3.18, 1.53–6.60). When odds ratios were adjusted for level of sleep disordered breathing, withdrawal (OR 3.83 CI 1.59–9.22) and social problems (OR 2.49 CI 1.14–5.44) remained significantly higher for overweight subjects.

Conclusion: After controlling for the effect of sleep disordered breathing, behaviors such as withdrawal and social problems, are common in overweight children and need to be taken into account in the design of interventions and services as they may act to moderate the efficacy of behavioral treatments.

Background

The prevalence of childhood overweight has been reported frequently in the research literature and popular media. Recent epidemiological studies estimate that pediatric overweight has increased dramatically in the last generation, that as of 2000 approximately 15% of children aged 6–11 are overweight,¹ and that 25–31% of children and adolescents in the US are overweight or at risk of being overweight.^{2–5} The health consequences related to childhood overweight include insulin resistance, type 2 diabetes, hypertension, and heart disease later in life.^{6,7}

Psychological or behavioral problems in childhood have been examined as both causes and effects of overweight. That is, overweight has been hypothesized as a possible result of psychological symptoms and psychological symptoms have been hypothesized to be a result of overweight.^{8–11} Further evidence for the relationship between overweight and behavioral problems is provided by treatment studies that have shown decreased levels of psychological and behavioral problems in children subsequent to treatment for overweight.^{12–14}

Clinical, referred, or screened samples have found relationships between overweight and depression,^{15,16} social problems, withdrawal,¹⁵ and both internalizing and externalizing behaviors.¹⁶ One longitudinal study found relationships between chronic overweight and oppositional defiant disorder for boys and girls and with depression for boys.¹⁰ Alternatively, an epidemiological study of adolescents and young adults found a relationship between body mass index (BMI) and depression only in girls.¹⁶ Mixed samples have found lowered social and physical perceived self-competence and well-being compared to normal weighted peers.¹⁷ Community-based studies have found depression¹⁸ and overweight related in girls and non-specific

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Table 1: Descriptive statistics for the sample (N = 402).

Variable	Mean (SD) or Percent	Range
Age (years)	8.8 (1.61)	6.0 – 11.9
Gender (female)	48.3 %	
Hispanic	38.6 %	
Caucasian	61.4 %	
Overweight	14.7 %	
BMI	18.0 (4.48)	10.9 – 48.1
Parent Education*	13.6 (3.24)	1–21

*(N = 287) Many parents did not report educational level.

patterns of behavior problems associated with overweight.⁸ In overweight children and adolescents, quality of life measures indicate a lower overall quality of life as well as lower self-esteem and physical functioning.^{19,20}

Sleep disordered breathing and obesity are comorbid in adults.²¹ There is some support for this relationship in children. Children diagnosed with sleep disordered breathing (SDB) may have a greater probability of comorbid overweight²² and children who are overweight have been found to have a greater probability of SDB.²³ However, in previously published analyses, the TuCASA study (from which the current analyses are derived), have not confirmed this relationship.²⁴

There are several limitations to the studies currently available linking overweight to behavior in children. Studies using non-referred samples have been screened for specific psychological disorders,¹⁰ are conducted within other cultures,¹⁷ or have used overweight categorizations that are not age- and gender-specific.^{15,16} While behavioral problems have been linked to SDB, such as cognitive problems, hyperactivity, and externalizing behaviors²⁵⁻²⁷ and behavior problems have been linked to overweight (as described above), ideally weight and SDB should be considered simultaneously in estimating their relationships with behavior.

Identification of behaviors uniquely related to obesity could inform development of behavioral interventions and services for children. Clinicians working in this area could benefit from understanding the independent contribution of overweight on behavioral problems both in the presence and absence of SDB. Thus, the goal of the current research was to provide a description of the nature and prevalence rate of behavior problems, in a general population cohort, for overweight and normal weight school children after controlling for the presence of sleep disordered breathing. We hypothesized that externalizing behaviors would be less related to overweight after taking into account levels of SDB.

Methods

Participants: Subjects in the current analyses were enrolled in a study of sleep in children, the Tucson Children’s Assessment of Sleep Apnea.^{24,27,28} This study recruited 6 through 11 year old Hispanic and Caucasian children to undergo home polysomnography, a sleep questionnaire, and neurocognitive testing. A detailed description of recruitment procedures has been previously published.^{24,27,28} Briefly, recruitment was accomplished by soliciting the cooperation of 19 selected elementary schools in the Tucson Unified School District (TUSD). A short sleep-habits screening questionnaire was sent home with all children in a “notes home” folder. Parents were asked to complete the questionnaire and to provide contact information if they agreed to allow study personnel to call and schedule a polysomnogram and neurocognitive testing for their child. Sleep and demographic questionnaire data, child weight and height measures were acquired in the family home at the time of the polysomnogram. Behavioral questionnaire data were collected from parents when the child subsequently underwent neurocognitive testing within the Department of Pediatrics. The TUSD Research Committee and the University of Arizona Institutional Review Board approved the study protocol. Parents or guardians completed approved consent forms and children completed assent forms before participating in the study. Children were excluded from the study if there was a history of head injury, tonsillectomy, mental retardation, or asthma. Families were paid \$25 for completing the sleep study and \$25 for completing the behavioral evaluation.

Measurement

Weight: Children were classified as overweight if their BMI was at or over the 95th percentile for age- and gender-specific normative values.²⁹ Children below the 95th percentile were classified as “normal weight”. The group referred to as “normal weight” included those children at risk for overweight (between the 85th and 94th percentiles for their sex and age).

Behavior: The Conners’ Parent Rating Scale – Revised (CPRS-

Table 2: Descriptive statistics and tests of differences between normal weight versus overweight subjects.

	Normal Weight Mean (SD) or Percent (N = 343)	Overweight Mean (SD) or Percent (N = 59)	F (sig) or Chi ² (sig)
Age	8.7 (1.6)	9.2 (1.5)	F 4.42 (.04)
Gender (% Female)	50.1%	37.3%	Chi 3.33 (.07)
Hispanic %	35.6%	55.9 %	Chi 8.81 (.00)
RDI*	0.92 (2.15)	0.81 (1.21)	F 0.19 (.66)
Parent Education	13.7 (3.3)	13.2 (2.8)	F 0.90 (.34)

*Respiratory Disturbance Index

Table 3: Odds ratios and percentages for probability that a subject who is overweight will be classified within the clinical range for each problem behavior on the CPRS-R.

Scale name	% Normal Weight in Clinical Range	% Overweight in Clinical Range	Unadjusted Odds Ratio (95% CI)	Adjusted Odds Ratio* (95% CI)
Oppositional	9.4	16.7	1.69 (0.76–3.74)	1.62 (0.71–3.72)
Cognitive Problems	11.7	20.0	1.68 (0.80–3.49)	1.46 (0.68–3.16)
Hyperactivity	17.3	16.7	0.84 (0.39–1.82)	0.86 (0.39–1.88)
Anxious Shy	12.3	15.0	1.29 (0.59–2.81)	1.21 (0.54–2.72)
Perfectionism	6.4	5.0	0.78 (0.22–2.69)	0.68 (0.18–2.49)
Social Problems	8.5	15.0	1.63 (0.71–3.76)	1.26 (0.51–3.09)
Psychosomatic	9.4	20.0	2.15 (1.02–4.54)	1.59 (0.71–3.56)
ADHD index	12.0	11.7	0.81 (0.32–2.00)	0.64 (0.24–1.69)
Global Index- Total	12.3	10.2	0.65 (0.2–41.73)	0.62 (0.23–1.69)
DSM Inattentive	12.3	16.7	1.25 (0.57–2.73)	1.05 (0.46–2.40)
DSM Hyperactive	17.6	18.3	0.94 (0.45–1.95)	0.98 (0.46–2.09)
DSM Total	14.4	13.3	0.78 (0.33–1.82)	0.67 (0.27–1.63)

* Note: Odds Ratios controlled for level of sleep disordered breathing.

R) is a well validated 80-item behavior rating scale that measures symptoms of attention deficit hyperactivity disorder (ADHD; hyperactivity, impulsivity, and inattention) as well as comorbid behaviors such as oppositional behavior, anxiety, and somatic complaints.³⁰ All 12 CPRS-R scales focus on behaviors central to a diagnosis of ADHD such as Cognitive Problems and Hyperactivity or measure behaviors that are commonly comorbid with inattention and hyperactivity, such as social problems. Three scales on the CPRS-R are considered internalizing correlates of ADHD (Anxious-Shy, Perfectionism, and Psychosomatic Complaints). Seven of the scales on the CPRS-R are derived directly from the Diagnostic and Statistical Manual-IV criteria for ADHD.³¹ Behaviors are rated on a 4-point scale that ranges from Very True to Not True. A t-score is derived for each scale, based on a large age and gender specific normative sample. A t-score (M = 50, SD = 10) over 65 is considered to indicate moderate to severe clinical impairment.

The Child Behavior Checklist (CBCL)³² allows assessment of 118 parent-reported behavioral and emotional problems of children aged 4–18. Parents rate their child's behavior on a 3-point scale (Not True, Somewhat True, or Very/Often True). The CBCL includes 8 syndrome scales, a Total problem score, and higher order Internalizing and Externalizing scales. Internalizing scales include Anxious/Depressed, Withdrawn, and Somatic Complaints. Externalizing scales include Aggressive Behavior

and Delinquent Behavior. Three syndrome scales, Social Problems, Thought Problems, and Attention Problems, are not part of the internalizing/externalizing dimensions. A t-score over 65 was considered to indicate moderate to severe clinical impairment.

Polysomnography: Home visit procedures and methods for obtaining PSG data have been described previously. Briefly, a 2-person mixed-gender team arrived at the home approximately 1 hour prior to the child's typical bedtime. Institutional Review Board-approved informed consent was obtained from the parent, and an assent form was signed by the child. Questionnaires were administered, and anthropometric and other physiologic measurements were completed. The oral airway was examined by a trained technician and rated with a value from 1 (unobstructed) to 3 (tonsils encroaching upon airway). Unattended overnight polysomnograms were obtained using the Compumedics PS-2 system (Abbotsford, Victoria, Australia). The following signals were acquired as part of the TuCASA montage: C₃/A₂ and C₄/A₁ electroencephalogram, right and left electrooculogram, a bipolar submental electromyogram, thoracic and abdominal displacement (inductive plethysmography bands), airflow (nasal/oral thermister), nasal pressure cannula, finger pulse oximetry, electrocardiogram to detect major arrhythmias (single bipolar lead), snoring microphone, body position (mercury gauge sensor), and

Table 4: Percentages, unadjusted, and adjusted odds ratios for probability that a subject who is overweight will be classified within the clinical range for each problem behavior on the CBCL.

Scale name	% Normal Weight in Clinical Range	% Overweight in Clinical Range	Unadjusted Odds Ratio (95% CI)	Adjusted Odds Ratio* (95% CI)
Aggressive Behavior	7.4	10.2	1.12 (0.41–3.06)	0.96 (0.33–2.79)
Anxious/Depressed	9.5	16.9	1.69 (0.76–3.75)	1.46 (0.63–3.40)
Attention Problems	14.0	11.9	0.69 (0.28–1.07)	0.54 (0.20–1.42)
Somatic Complaints	10.1	16.9	1.58 (0.72–3.50)	1.21 (0.51–2.85)
Withdrawn	4.5	20.3	4.69 (2.05–10.73)	3.83 (1.59–9.22)
Social Problems	8.0	23.7	3.18 (1.53–6.60)	2.49 (1.14–5.44)
Thought Problems	9.2	8.5	0.70 (0.24–2.07)	0.57 (0.18–1.81)
Delinquent Behavior	11.3	10.2	0.72 (0.27–1.91)	0.73 (0.26–1.98)
Total Score	12.2	18.6	1.46 (0.68–3.11)	1.38 (0.63–3.03)
Internalizing	9.2	20.3	2.23 (1.05–4.72)	1.84 (0.83–4.10)
Externalizing	7.8	10.2	1.08 (0.39–2.92)	0.92 (0.32–2.65)

* Note: Odds Ratios controlled for level of sleep disordered breathing.

ambient light to determine sleep period time (sensor attached to the vest to record on/off).

The Compumedics software system was used to process all PSG data. Scoring has been described in detail previously.²⁸ Briefly, sleep stages were scored according to Rechtschaffen and Kales criteria. Arousals were identified using criteria published by the American Academy of Sleep Medicine. Apneas were scored if the amplitude (peak to trough) of the airflow signal using the thermister decreased below at least 25% of the amplitude of baseline breathing (identified during a period of regular breathing with stable oxygen levels), if this change lasted for more than 6 seconds or 2 breath cycles. Hypopneas were designated if the amplitude of any respiratory signal decreased below (approximately) 70% of the amplitude of baseline and if the thermister signal did not meet the criterion for apnea. Central events were marked if no displacement was noted on both the chest and abdominal inductance channels. Otherwise, events were scored as obstructive. After full scoring, analysis software was used to link each event to data from the oxygen saturation and arousals from the electroencephalogram channels.

The Respiratory Disturbance Index (RDI) was used as an indicator of SDB and defined as the number of respiratory events (apneas and hypopneas) per hour of the total sleep time. Breathing “events” were scored during sleep if total inspiratory volume went below 50% of baseline and was associated with a 3% decrease in blood oxygen levels.^{28,33,34} For this analysis, a 3% oxygen desaturation was required for an event to be counted in the total RDI. We considered a child to have SDB if their RDI was greater than or equal to 1 event per hour of total sleep time. Use of this definition is supported by previous evidence that an RDI of one, based on events with a 3% oxygen desaturation, is clinically significant.³⁵

Data analyses: Data were analyzed using SPSS version 13 for Windows (SPSS, Inc., Chicago, IL). One-way ANOVA or Chi2 tests were used to test differences in demographic statistics between overweight and normal weight children. Simple odds ratios and adjusted odds ratios were calculated to determine the probability of behavior problems given the presence of overweight using the behavioral measures CBCL and CPRS-R. Adjusted odds ratios were calculated for the behavioral measures and controlled for the level of sleep disordered breathing using the respiratory disturbance index (RDI), described above.

Results

Of the 7,055 initial surveys distributed throughout the schools, 2,327 (32.9%) were returned. Of the 1,219 (52.4%) who gave permission to be contacted further, 503 (41.3%) met inclusion criteria and agreed to participate. Of those 503, 480 had sleep studies of sufficient quality. Of the 480 sleep studies completed, 402 (83.7%) had complete anthropometric and behavioral data.

Descriptive summary statistics for the sample are in Table 1. There were approximately equal numbers of boys and girls, and more Caucasians than Hispanics. Overweight was present in 14.7% of the total sample. There were significantly more Hispanic subjects in the overweight (55.9%) group compared to the non-overweight group (35.6%). Descriptive statistics are provided separately for the overweight and normal weight subjects in Table 2. The overweight subjects tended to be

slightly older than the normal weight subjects. Although there was a trend toward gender differences, there were no significant differences between the groups on RDI, gender, or parent education.

Table 3 shows percentages of overweight and normal weight subjects who were classified as having clinically relevant levels of behavioral problems (moderate to severe) for the Conners' Parent Rating Scale-Revised (CPRS-R). Table 3 includes simple odds ratios indicating the probability of overweight children being classified with clinically relevant levels of behavior problems. Odds ratios, adjusted for SDB, are also shown in Table 3. Although odds ratios were significant for several CPRS-R scales, confidence intervals were wide and only the Psychosomatic scale was statistically significant. Twice as many children were classified as having psychosomatic complaints in the overweight versus normal weight groups. When odds ratios were adjusted for level of SDB, psychosomatic complaints were no longer significantly different across the groups.

Table 4 shows percentages of overweight and normal weight subjects who were classified as having clinically relevant levels of behavioral problems (moderate to severe) for the Child Behavior Checklist, simple odds ratios, and adjusted odds ratios controlling for SDB. Significant unadjusted odds ratios were observed for the Withdrawn, Social Problems and Internalizing scales. When SDB was controlled, the Withdrawn (3.83, CI 1.59–9.22) and Social Problems (2.49, CI 1.14–5.44) odds ratios remained significantly different between the groups.

Discussion

Within this sample, 15% of the subjects were overweight. Overweight was more prevalent in Hispanic and male subjects. Overweight children had increased parent reports of psychosomatic complaints, social problems, withdrawal, and general internalizing behaviors. When SDB was taken into account, overweight was no longer associated with psychosomatic complaints and general internalizing symptoms. However, levels of withdrawal for the overweight subjects were still almost 4 times higher and social problems were 2.5 times higher than that of normal weight subjects. Hyperactivity, oppositional, and externalizing behaviors were not elevated in the overweight group and showed minimal change after accounting for SDB.

While both obesity and SDB may have behavioral consequences, each may be related to different types of behavioral problems and each may affect behavior through unique causal mechanisms. For example, SDB may cause externalizing types of behavior problems through associated nocturnal hypoxia and disrupted sleep architecture. Reactions to and maladaptive coping with functional limitations and social stigma may moderate the relationship between overweight and behavior problems. The Conners' psychosomatic complaints scale, which was related to overweight before but not after controlling for SDB, included items related to headaches, stomach aches in general, stomach aches before school, vague complaints that are not supported by physical illness, and fatigue. While in overweight children these behaviors may be more related to avoidance of school or other social situations, vague bodily pain, malaise and fatigue could also be related to poor quantity or quality sleep associated with sleep disordered breathing.

The most prevalent problem behaviors reported by parents on

the CBCL were those related to social problems and withdrawal. The CBCL withdrawn scale includes items related to shyness, preference for being alone, secretiveness, sulking, underactive, sadness, withdrawal, and not talking. Although overweight has been hypothesized to be a result of some psychiatric symptoms,⁸ these behavioral problems could result from living with overweight. Social problems on the CBCL were reported much more frequently by parents of overweight children than by parents of normal weight children. Social problems scale items are related to immaturity, not being liked by peers, teased by peers, overweight, and clumsiness. Children who are overweight may be subject to bullying or face functional limitations.³⁶ They may be ostracized by their peers or feel less physically competent compared to their peers.¹⁷ Withdrawal may be a reaction to judgment by peers or other social problems.

Oppositional behavior has been linked to chronic overweight, when overweight is present from childhood through adolescence.¹¹ The current results do not support the idea that oppositional or externalizing behaviors, such as aggression, are salient at this developmental stage in the context of overweight. Another large cross-sectional study that found a relationship between overweight and overall behavior problems did not fit specific patterns related to externalizing (nor internalizing) problems.⁸ It may be that the current sample was not chronic enough to be at risk for externalizing behaviors.

A limitation to this study is that only one informant was used to measure behavioral problems. Although cross-informant behavioral agreement is generally low,³⁷ it does provide contextual perspectives on behavior and may be used to generate alternate explanations for results. Additionally, this study is descriptive and the data do not allow for strong inferences regarding the etiology of the behaviors reported by parents. Finally, more data on these families would have been helpful to determine if familial nutrition habits, parental obesity, and/or socioeconomic status related to behavior problems. However, this study did examine a broad variety of problem behaviors derived from a population-based sample of school children. Overweight was defined as age- and gender-specific, however, the overweight group was predominantly Hispanic. Epidemiological studies have documented the relatively high rate of overweight in young Hispanic males found here.³

Overweight may contribute to behavior problems independent of SDB. It is possible that the behaviors for which overweight adds predictive value above SDB are those that are influenced by social factors such as teasing or other peer behaviors. Overweight children do face discrimination and stigmatization and this may impact their global self-worth.³⁸⁻⁴⁰ Further research with larger samples should examine the extent to which emotional response to overweight is moderated by environmental and social pressures such as exclusion or individual differences in the need for relatedness or social acceptance.

The current cross-sectional study allows limited causal inference. As Freidman and Brownell⁴¹ have emphasized in adults, many important questions about etiology and treatment may only be answered through longitudinal research that allows for an examination of multiple risk factors. Although emotional and behavioral problems may influence the efficacy of interventions in obesity, many trials to date have not measured

or examined the moderating effect of behavioral problems on outcomes. The current study indicates that behaviors associated with overweight, such as withdrawal and social problems, may need to be taken into account in the design of interventions and services as they may act to moderate the efficacy of behavioral treatments. Additionally, the predisposition toward behavioral problems in the context of childhood overweight may be influenced by long-term attitudes surrounding overweight and the extent of obesity within the family. Psychologists and health administrators seeking to create services responsive to the rates in U.S. childhood overweight could benefit from further information regarding the psychosocial mechanisms of any behavioral problems.

Conclusion

In conclusion, after controlling for the effect of sleep disordered breathing, behaviors such as withdrawal and social problems, were present in some overweight children and should be considered in the design of interventions and services as they may act to moderate the efficacy of behavioral treatments for obesity.

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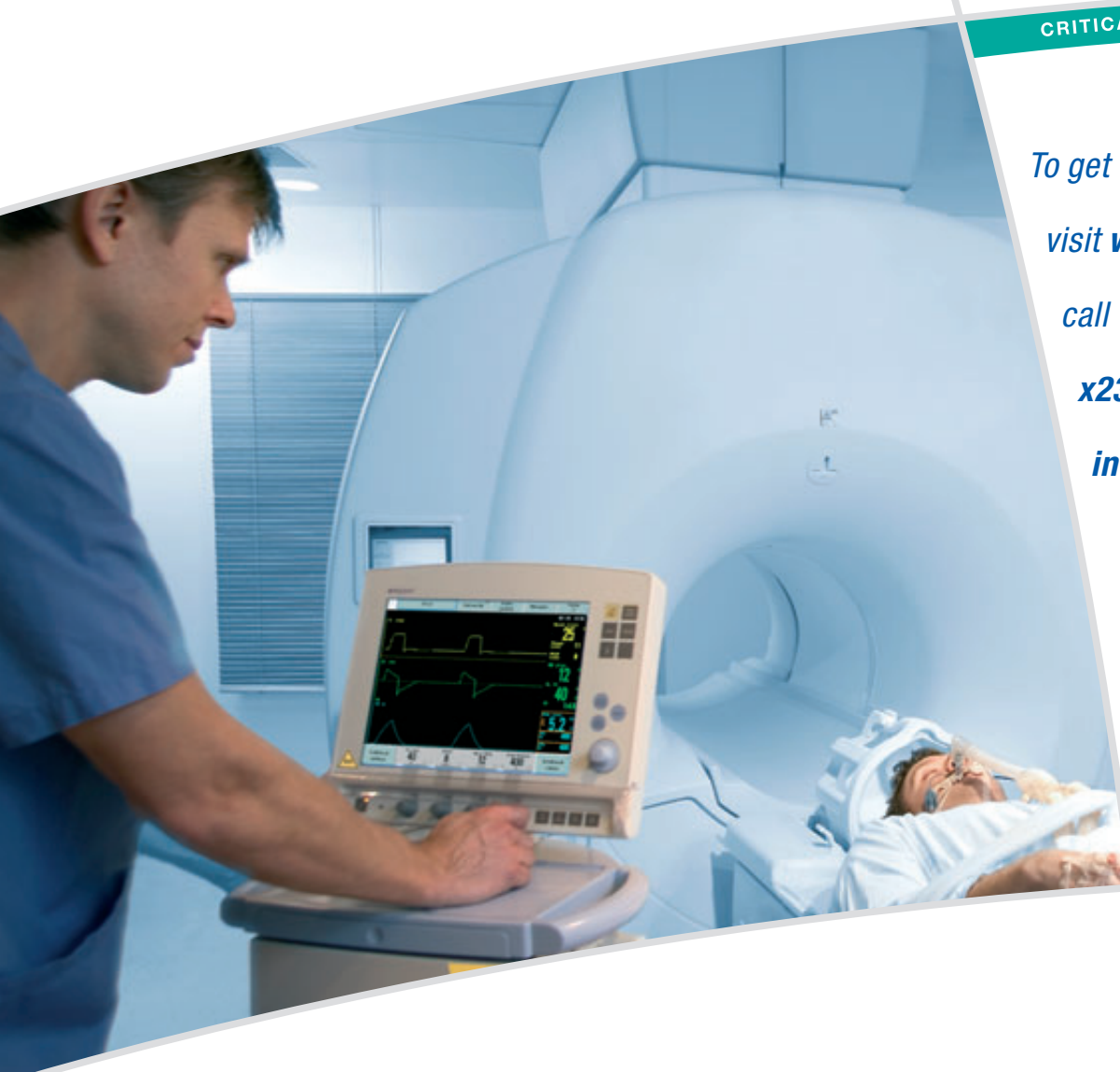
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