

ההסתדרות הרפואית בישראל

**החברה הישראלית לחקר השינה**

**הכינוס השנתי ה – 16**

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**תמונת מצב ומגמות בצריכת תרופות שינה - האם אכן התקדמנו  
אסנת מרום, מחלקת ילדים, בית חולים כרמל**

**רקע-** לפי מחקרים רבים שבוצעו עד כה ידוע שיש חשיבות גבוהה מאוד לטפל באינסומניה, טיפול שעשוי הן לעזור לפרט בהפחתת תחלואה ושיפור התפקוד ואיכות החיים והן להיות טוב מבחינת עלות תועלת לכלל. מחקרים רבים הראו את היעילות של בנזודיאזפינים ו-Z בהקלת אינסומניה לטווח קצר, אולם רובם לא בדקו טיפול בתרופות אלו לתקופת זמן ארוכה מחצי שנה עד שנה. בשנים האחרונות פותחו תרופות שינה חדשות יותר, עם פוטנציאל התרגלות והתמכרות נמוך יותר, אך חסרים מחקרים המצביעים על תמונת מצב ככלל, ובארץ בפרט, כדי לתעד ולהבין את הרגלי השימוש בתרופות שינה, את מגמות השינוי בהרגלים אלו (עם פיתוחן של תרופות חדשות יותר), וחקר האפשרות של התרגלות לתרופות בשימוש לטווח ארוך.

**מטרת העבודה -** כימות ואפיון הרגלי צריכת תרופות שינה בקרב אוכלוסיית מבוטחי קופת חולים כללית (ארצית) והשוואה בין שתי תקופות זמן (שנת 2000 לעומת שנת 2010).  
בחינת צריכת תרופות שינה לתקופה של חצי שנה ומעלה על מנת לבדוק אם ישנה התרגלות (העלאת מינון).

**שיטות-** מחקר רטרוספקטיבי, שבוצע מתוך מאגר הנתונים של קופת חולים כללית ארצית, נאספו נתונים על כל מנפקי מרשמים עבור תרופות שינה מגיל 18 ומעלה בשנת 2000 ובשנת 2010, הנתונים רוכזו בעילום שם בגיליונות אקסל ו-SPSS ועברו עיבוד סטטיסטי תיאורי והשוואתי.

**תוצאות-** נכללו במחקר 222,274 איש עבור שנת 2000 ו-282,975 איש עבור שנת 2010. כ-6.2% מכלל מבוטחי כללית בשנת 2000, ו-6.8% בשנת 2010, צרכו תרופות שינה, כרבע מהם לתקופה של מעל חצי שנה. בשנת 2000 78% מצורכי תרופות שינה ניפקו מרשמים לתרופה מסוג אחד לעומת רק 54.8% בשנת 2010. בצריכת תרופות שינה למשך חצי שנה ומעלה רק 11% בשנת 2000 ו-9% בשנת 2010 עלו בכמות הכדורים, כלומר, במרבית הנחקרים לא נצפתה תופעה של התרגלות לתרופה. בשנת 2010 עלה השימוש בתרופות Z יחסית ל-2000 באופן משמעותי.

**מסקנות-** בהתבסס על נתונים אלו יתכן ויש לשקול מחדש את נטיית המערכת הרפואית לחשוש מטיפול תרופתי ארוך טווח לנדודי שינה.

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# **Cognitive Training Improves Sleep Quality and Cognitive Function among Older Adults with Insomnia**

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**Background:** Insomnia is a sleep disorder frequently observed in older persons. Along with the changes in sleep structure accompanying the ageing process, ageing is also associated with cognitive impairment. In view of the findings showing that sleep during the night is critical in the consolidation of previously acquired memory traces, we hypothesized that intensive new learning experience provided by systematic cognitive training will act as a catalyst to change sleep architecture and by doing so will improve sleep quality among older adults with insomnia. Furthermore, we posited that if that learning specifically targets cognitive function, older people with insomnia will also exhibit improved cognitive performance. Thus, the present study examined the impact of cognitive training on sleep quality and cognitive performance among older adults with insomnia.

**Methods:** Fifty-one older adults with insomnia (22M/29F; mean age:  $72.13 \pm 5.1$ ) were randomized into two groups: a cognitive training group ( $n=34$ ) and an active control group ( $n=17$ ). The participants in the cognitive training group completed an eight-week, home-based, personalized, computerized cognitive training program, while the participants in the active control group completed an eight-week, home-based program involving computerized tasks that do not engage high-level cognitive functioning. Before and after training, all participants' sleep was monitored for one week by an actigraph and their cognitive performance was evaluated.

**Results:** Mixed models for repeated measures analysis showed between-group improvements for the cognitive training group on both sleep quality (sleep onset latency and sleep efficiency:  $F_{1,51}=5.49$ ,  $P<0.05$  ;  $F_{1,51}=6.86$ ,  $P<0.05$  , respectively) and cognitive performance (avoiding distractions, working memory, visual memory, general memory and naming:  $F_{1,36}=5.18$ ,  $P<0.05$  ;  $F_{1,35}=13.92$ ,  $P<0.001$ ;  $F_{1,35}=14.03$ ,  $P<0.001$  ,  $F_{1,35}=15.65$ ,  $P<0.001$ ;  $F_{1,35}=9.65$ ,  $P<0.01$  respectively). Moreover, hierarchical linear regressions analysis indicated correlation between the improvement in cognitive function and those in sleep quality.

**Conclusions:** Cognitive training may be beneficial in the initiation and maintenance of sleep among older adult insomniacs. Cognitive training may be used as a novel non-pharmacological alternative to improve the sleep quality of older adults suffering from insomnia. The present study constitutes pioneering work in this field among older adults with insomnia.

## **The link between Social Anxiety Disorder, treatment outcome and sleep difficulties among patients receiving CBGT**

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**Background and aims:** Sleep difficulties are very common in patients with anxiety disorders (AD). The findings of previous studies assessing the link between sleep disturbances and Social Phobia (SP) are limited and have been inconsistent. Additionally, very few studies reported the effect of Cognitive Behavioral Therapy for AD on co-occurring sleep problems. The aim of this current study was to examine the association between sleep disturbances and SP. Another aim was to explore the impact of Cognitive Behavioral Group Therapy (CBGT) for SP on co-occurring sleep difficulties. **Methods:** The data was obtained retrospectively from patient files receiving group CBGT for SP. The sample included 63 patients with SP (Mage = 30.42, SD = 6.92), 41 male and 22 female. 41 subjects completed the treatment. Before treatment onset patients completed the Liebowitz Social Anxiety Scale, Beck Depression Inventory, Pittsburgh Sleep Quality Index, and also completed several socio demographic questions. Upon completion of the treatment, the same measures were filled with the addition of the Sheehan Disabilities Scale. **Results:** The results of this current study suggest that: (a) subjective insomnia predicts SP severity even after controlling for depression severity and additional variables; (b) subjects with SP with co occurring clinical levels of subjective insomnia present a more severe clinical picture, both at treatment onset and termination; (c) although CBGT lead to reduction in SP and depression symptoms severity, it had no significant impact on co occurring sleep difficulties. **Conclusions:** Sleep difficulties predict SP severity regardless of depressive symptoms, and may be linked to a more severe clinical picture. Clinicians should be aware of these sleep difficulties co occurring with SP, and consider implementing specific therapeutic interventions to reduce their impact.

# **Sleep indices, chronic pain and cognitive state differences between opiate addicts following >10 years of protracted abstinence or of methadone maintenance treatment**

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**Background:** Although opiate addiction is known to be a chronic relapsing disorder, treated best with methadone maintenance (MMT), still, few patients (<10%) succeed to manage a protracted abstinence. **Aims:** To compare sleep indices, chronic pain and cognitive status between MMT patients and opiate addicts who succeeded  $\geq 10$  years of protracted abstinence. **Method:** 39 MMT patients treated  $\geq 10$  years, with negative urines for any drugs were compared to 99 protracted abstinent (PA) persons for  $\geq 10$  years. Addiction indices, psychiatric disorders, sleep quality (PSQI) and daily sleepiness EPPS, and Cognitive indices (Mini mental exam test (MMES) and Clock Drawing Test (CDT)) were compared. **Results:** Groups did not differ in age ( $53.5 \pm 7.8$ y) and education years ( $10.1 \pm 2.9$ ). Duration since MMT entry was  $14.3 \pm 3.2$  years among MMT patients and since started abstinence was  $17.0 \pm 5.0$  among PA ( $p=0.002$ ). MMT patients had higher proportion of female (35.9% vs. 19.2%,  $p=0.05$ ). MMT and PA groups did not differ by sera-positive hepatitis C (48.7% vs. 33.7%,  $p=0.1$ ) and HIV (5.1% vs. 2.0%,  $p=0.3$ ) rates. MMT patients had higher proportion of patients with any Axis I DSM-IV-TR psychiatric diagnosis (51.3% vs. 15.2%,  $p<0.0005$ ), with chronic pain (48.7% vs. 26.2%,  $p=0.02$ ), with poor sleep (PSQI $>5$ ) (64.1% vs. 38%,  $p=0.01$ ) and with impaired cognitive state as measured by (MMES $<27$ ) (23.8% vs. 7.5%,  $p=0.01$ ) and by CDT (60.7% vs. 32.5%,  $p=0.01$ ), with no differences in rate of daily sleepiness (EPPS $>7$ ) (51.3% vs. 62.5%,  $p=0.3$ ). Logistic regression characterized MMT patients as suffering more from Axis I psychiatric diagnosis, chronic pain, and characterized as having poor sleep and worse cognitive state. **Conclusion:** Treatment of chronic pain, may improve sleep quality and cognitive state. Axis I Psychiatric disorders may differentiate those who succeeded to

manage protracted abstinence. Future studies, in particular genetic ones, are needed in order to understand the differences between these two groups.

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# **Sublingual Flumazenil reverses hypnotic effects of therapeutic doses of Zolpidem and Brotizolam**

## **Facing the post-hypnotics morning somnolence with sublingual Flumazenil – The sleeping beauty**

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Supported by Coeruleus Ltd, Israel.

**Background:** Thirty percent of patients with insomnia treated with hypnotics experience residual morning drowsiness, which may reduce their daytime function and their ability to benefit from hypnotic treatment.

**Purpose:** To study the safety and efficacy (dose finding) of sublingual Flumazenil (GABA-A antidote) in reversing the residual hypnotic effect of sleeping pills in healthy volunteers (a proof of concept study).

Setting: A tertiary university hospital.

Design: A double blind, placebo controlled, randomized cross over study.

**Methods:** 20 healthy subjects slept for 1.5 hours following sleep induction (Zolpidem n=10; Brotizolam n=10). Upon awakening, they underwent a physical examination and neurocognitive tests including immediate word recall test (iWRT), Digit Symbol Substitution Test (DSST), and mood/performance questionnaires including visual analogue scale (VAS) to assess subjective alertness. They were then treated by Flumazenil (0.4mg; n=10 and 1.6 mg; N=10) or placebo (n=20) and were re-evaluated after 20min and 60 minutes. A week later, the same procedures and evaluations were performed again.

**Results:** All 20 volunteers (10 males, aged  $28.8 \pm 5.7$ ) completed the study without any adverse events. Flumazenil was superior to placebo by 59-93% ( $P < 0.05-0.001$ ) in improving performance in the various neurocognitive tasks. Subjects reported a significant improvement in vigilance on a VAS with Flumazenil compared to placebo, both 20min following administration ( $3.0 \pm 0.6$  vs  $1.3 \pm 0.6$ ,  $p < 0.02$ ) and 60min following administration of Flumazenil ( $4.7 \pm 0.6$  vs  $2.8 \pm 0.7$ ,  $p < 0.03$ ). A parallel improvement was seen in the iWRT for Flumazenil vs placebo 20min following administration ( $4.2 \pm 0.8$  vs  $1.3 \pm 0.9$  words,  $p < 0.005$ ) and 60min following administration ( $5.4 \pm 1.1$  vs  $1.2 \pm 1.2$  words,  $p < 0.02$ ).



**Conclusions:** This study proves the concept that sublingual administration of Flumazenil is safe and effective in reversing the hypnotic effects of both Zolpidem and Brotizolam, assessed both subjectively and objectively by performance tasks. There are numerous potential applications for this concept, particularly when the residual hypnotic effect is undesired. It may allow better treatment and improvement in sleep-wake rhythm in insomniac patients. However, further research is required before this concept progresses to clinical useage.

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# Relationships between Creativity and Between Sleep Structure, Pattern & Quality, Among Visual Arts Students

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**Background:** Creativity has been associated with distinct sleep characteristics. Aiming to further explore the relationships between creativity and sleep, it was hypothesized that creativity and the practice of visual arts are associated with altered sleep structure, patterns and quality.

**Methods:** Fourteen visual arts and 16 social sciences students, ages 20-29, participated in a comparative naturalistic study. Sleep patterns were monitored by actigraphy, and sleep structure was assessed by home monitored polysomnography (PSG). Students completed the Torrance Tests of Creative Thinking (TTCT), the Pittsburgh Sleep Quality Index (PSQI) and the Munich ChronoType Questionnaire (MCTQ) to assess creativity, sleep quality and chronotype, respectively. Creativity and sleep measures were correlated for the entire sample, and group comparisons were performed.

**Results:** Increased VERBAL creativity was associated with long sleep duration based on self report ( $p=0.02$ ) and (albeit not significantly) actigraphy ( $p=0.07$ ), and with late sleep midpoint before workdays, indicating late chronotype ( $p=0.04$ ). Increased VISUAL creativity was associated with poor self reported sleep quality ( $p=0.04$ ). Specifically, measures of visual elaboration were associated with sleep disturbance and daytime dysfunction (both  $p=0.03$ ), and measures of visual originality tended to be associated with daytime dysfunction ( $p=0.06$ ). Creativity was not related to sleep structure. Compared to the social sciences, visual arts students tended towards a lower percentage of stage 3 sleep ( $p=0.07$ ). They exhibited longer sleep duration based on actigraphy ( $p=0.01$ ), later chronotype, based on sleep midpoint before workdays ( $p=0.03$ ) and self assessment ( $p=0.03$ ), and increased self reported sleep disturbance ( $p=0.01$ ) and daytime dysfunction ( $p=0.05$ ).

**Conclusion:** While VERBAL creativity was associated with objective and subjective aspects of sleep patterns, VISUAL creativity was associated with subjective aspects of sleep quality. This study establishes that aspects of creativity and the practice of visual arts constitute predispositions underlying poor sleep quality among young adults.

# **Longer Sleep Duration is Associated with Increased Morning Pain Sensitivity in Healthy Young Men**

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**Introduction and objectives:** Experimental sleep deprivation protocols have demonstrated increased sensitivity to evoked pain in healthy subjects following total or partial sleep deprivation. Yet these controlled laboratory protocols have low ecological validity, and do not assess time-of-day effects. This study aimed to assess relationships between habitual sleep duration based on objective and subjective measurements in the natural environment, and sensitivity to experimental pain (cold pain threshold) in healthy young subjects, in the morning, afternoon and evening. It was hypothesized that increased sleep duration would be related to decreased sensitivity to pain, particularly in the morning.

**Materials and methods:** Forty-eight healthy young men underwent experimental pain testing for cold (cold bath) pain threshold in seconds (CT-sec), in the morning, afternoon and evening, in a randomized order repeated measures design. Scores were standardized to a logarithmic scale. Sleep duration was assessed by actigraphy for seven days prior to testing and by self-report. Repeated measures ANOVA with sleep duration as a covariate for each time point were computed.

**Results:** Sleep duration affected log of CT-sec in the morning ( $p < 0.02$ ) but not in the afternoon or evening. Increased sleep duration was associated with decreased CT-sec in the morning, indicating increased sensitivity to pain. Wilks' lambda multivariate effect of time was ( $F_{(2,44)} = 4.4$ ,  $p = 0.017$ ,  $F_{(2,45)} = 4.7$ ,  $P = 0.013$ ,  $F_{(2,42)} = 4.1$ ,  $p = 0.023$ , consecutively) when controlling for actigraph, PSQI and MCTQ sleep duration. The log of CT-sec in the morning significantly differed from that in the evening ( $p < 0.02$ ) after Bonferroni adjustment for multiple comparisons when accounting for sleep duration.

**Conclusions:** Findings show for the first time that habitual longer sleep duration and later wake-time are associated with increased sensitivity to pain. Pending further investigation, it may be claimed that a U shaped relationship characterizes sleep duration and pain, with short and long sleepers demonstrating increased sensitivity to painful stimuli.

# **The Relationship between Objectively Measured Sleepiness and Driving Ability**

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**Introduction:** The complex task of driving requires driver vigilance, attention and ability to perceive, comprehend, react and adapt. While it appears self-evident that most, if not all, of these functions are affected by fatigue and drowsiness, little direct, concrete proof exists. Therefore, the aim of the present study was to examine the relationship between objectively measured sleepiness and driving ability.

**Methods:** Twelve adults (mean age  $24.5 \pm 1.4$  years: 6 males, 6 females) participated in the study. During the entire study period (24 hours of continuous awakening) participants were tested every three hours with a battery of computerized tests (Vienna Test System) known to significantly correlate with accident involvement and with the Pupillographic Sleepiness Test (PST) that objectively measures sleepiness. The PST consists of an 11-minute recording by infrared video pupillography of the sitting participant's pupil diameter, followed by automated data analysis. Spontaneous pupillary oscillations provide objective and quantitative measures of tonic central nervous activation, which is a precondition for higher level mental performance. In sleepy subjects the pupil shows spontaneous oscillations with a predominantly low frequency component and amplitudes reaching several millimeters.

**Results:** Analysis revealed significant difference between day and night tests in mean motor reaction time [ $t(11)=3.61$ ;  $p<0.01$ ], in distribution reaction time [ $t(11)=2.89$ ;  $p<0.05$ ], and in the percentage of wrong responses [ $t(11)=-1.80$ ;  $p<0.001$ ]. Likewise, analysis revealed a significant correlation between PST Index and mean motor reaction time ( $r=0.94$ ;  $p<0.01$ ), between PST Index and distribution reaction time ( $r=0.84$ ;  $p<0.05$ ), and between PST Index and percentage of wrong responses ( $r=0.80$ ;  $p<0.005$ ).

**Conclusion:** The results suggest that driving ability is directly and highly related to fatigue and sleepiness. This exploratory study can shed light on the role fatigue plays in decreased driving skills and increased road accidents.

# **Comparison Between Adenotonsillectomy and Adenoidectomy in the Treatment of Obstructive Sleep Apnea in Children**

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**Background:** Adenotonsillectomy is the first line of treatment of pediatric obstructive sleep apnea syndrome (OSAS). Compared to adenoidectomy alone, adenotonsillectomy is associated with a higher cost, complications and even mortality. The most serious complication is bleeding. However, no study has investigated OSAS outcome of adenotonsillectomy versus adenoidectomy alone.

**Objectives:** To compare the outcome of adenoidectomy to adenotonsillectomy in regards to the resolution of OSAS.

**Methods:** All 471 children diagnosed with OSAS at the Dana Children's Hospital between 2007-2010 were reevaluated. A comparison was made between: 1) children who underwent adenoidectomy (group A, n=98), 2) children who underwent adenotonsillectomy (group AT, n=227), and 3) children who were not operated (no surgery-NS, n=69). Outcome measure included: 1) recurrent or unresolved OSAS by a validated questionnaire (the Pediatric Sleep Questionnaire, PSQ), 2) persistent or recurrent snoring, 3) repeat surgery.

**Results:** A borderline difference was found for residual or recurrent OSA based on the PSQ scores between the adenoidectomy, adenotonsillectomy and the no surgery groups (residual rate = 17.3%, 14.1%, 26.1% respectively,  $p=0.067$ ). When overweight children were excluded, the difference between groups A (n=91) and TA (n=209) compared to NS (n=63) was significant (residual rate = 17.6%, 12.4%, 27.0% respectively,  $p=0.02$ ). However, there was no difference between A and AT. Compared to patients who underwent adenotonsillectomy, children who underwent adenoidectomy alone had a higher rate of continued or repeat snoring post-surgery (47.4% vs. 19.1%,  $p<0.001$ ) and repeat intervention (27.4% vs. 6.7%,  $p<0.001$ ). BMI, tonsil size, or AHI, had no effect on residual or recurrent OSA.

**Conclusions:** These results suggest that adenoidectomy alone may be sufficient for improvement of OSA in a significant portion of children with OSA. Watchful waiting was also found useful, however significantly less compared to surgical intervention. Such a strategy is expected to yield decreased morbidity and mortality related to tonsillectomy.

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## שינה ומאפייני מזג של ילדים צעירים: שאלה של ויסות?

מורן סמואל – אוניברסיטת חיפה (תיזה בהנחיית פרופ' ענת שר)

מטרת המחקר הייתה לבחון את הקשר בין מזג ושינה בפרספקטיבה התפתחותית ותוך התמקדות במושג הוויסות, בקבוצת הגיל 4-5 שנים, שלב בו מצופה שילדים כבר שכללו יכולות ויסות עצמי (Kopp, 1982; Thompson, 1994) ושנתם אמורה להיות מגובשת ומסודרת (Acebo et al, 2005; Dahl, 1996; Johnson & McMahon, 2008). ההשערות המרכזיות במחקר טוענות לקשר בין קשיים בויסות התנהגותי לבין בעיות הקשורות בהשכבה ובשינה של הילד.

המחקר כלל 30 ילדים בגילאי 4-5 שנים, משכבה סוציאקונומית בינונית ומעלה. הגיל הממוצע היה 4 שנים ועשרה חודשים (ס"ת 0.42), 15 בנים ו-15 בנות. כל הילדים לקחו חלק במחקר קודם שעסק בשינה והתפתחות מוטורית בשנת החיים הראשונה (Cohen, Atun-Einy & Scher, 2012). לצורך המחקר הנוכחי נעשה שימוש במידע מגיל 11 חודשים, וגל נוסף של נתונים אשר נאספו באמצעות שאלוני שינה ושאלוני מזג, וויסות והתנהגות<sup>1</sup>. האימהות מילאו יומן שינה והצמידו אקטיגרף (Ambulatory Monitoring inc., Ardsley, N.Y) לקרסול הילד למשך שלושה לילות באמצע השבוע.

נמצא קשר בין דיווח על בעיות השכבה לבין ציון במדד האינהיביציה של ה-BRIEF ( $r=.44, p=0.01$ ). מעורבות הורית גבוהה בהרדמה נמצאה קשורה למשך הזמן שלקח לילד להירדם ( $r=.35, p=0.05$ ) וכן נמצא הבדל ביכולות הויסות ההתנהגותי בין קבוצת ההורים שהמעורבות שלהם בהשכבה הייתה בינונית-גבוהה לבין קבוצת ההורים שהמעורבות שלהם הייתה נמוכה-בינונית ( $t=1.993, p=0.05$ ). נמצא קשר בין יכולות טובות בממד המזג "שליטה וויסות" לבין (א) התעוררויות בלילה ע"פ האקטיגרף ( $r=.46, p=0.02$ ), ו(ב) תנועות מוטוריות גבוהה ב-10 הדקות לפני השינה ( $r=.54, p=0.003$ ). ההשוואה בין מאפייני השינה בגיל 11 חודשים לגילאי 4-5 שנים, הצביעה על הבדל מובהק בזמן עד הירדמות ובתנועות בלילה ( $F(8,20)=22.47, p<0.001, \eta^2=0.90$ ), כך שהתינוקות נרדמו תוך פרק זמן קצר יותר והתנועות שלהם בלילה הייתה גבוהה יותר.

ממצאי המחקר הדגימו את הקשר בין יכולות הויסות ההתנהגותי של הילד לבין בעיות בהשכבה ובשינה, וזאת על בסיס של שילוב בין מספר מקורות מידע, כולל מדידה אובייקטיבית של השינה. הדיון בוחן את הגורמים והתהליכים הנמצאים בבסיס יחסי הגומלין בין שני המשתנים, ואת זיקתם להתנהגות ולהתפתחות, ומדגיש כי הדיאלוג ההתנהגותי המתקיים בין ההורה לבין הילד בהקשר של השינה מתבסס בו זמנית על תפיסותיו והתנהגותו של ההורה ומאפייניו והתנהגותו של הילד.

<sup>1</sup> ISQ- Infant Sleep Questionnaire (Morrell, 1999); PIBBS- The Parental Interactive Bedtime Behavior Scale (Morrell & Cortina-Borja, 2002); CBQ- Child Behavior Questionnaire (Rothbart, 2001) ; SDQ – The Strength and Difficulty Questionnaire (Goodman, 2001) ; BRIEF- Behavior Rating inventory of Executive Function (Gioia et al, 2000)

## **Validation of actigraphy with continuous Video-EEG in children with epilepsy**

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The institution at which the work was performed: The Hospital for Sick Children, University of Toronto.

**Study Objectives:** The relationship between epilepsy and sleep is bidirectional as seizures disrupt sleep and coexisting sleep disorders have detrimental effects on seizure control and quality of life for both the children and their families. Previous research has reported on sleep disturbance in children with epilepsy primarily by subjective parental reports. Actigraphy may provide a more accurate objective evaluation of sleep, but to date the validity of this sleep measure for children with epilepsy has not been assessed. The primary objective of this study is to validate the use of actigraphy as a tool in studying sleep patterns in children with epilepsy.

**Design:** This is a prospective study of children with epilepsy, comparing sleep and wake epochs recorded for 24 hours simultaneously by actigraphy and by continuous video-electroencephalography (VEEG) monitoring.

**Setting:** VEEG in-patient monitoring unit. Participants: 27 patients age 2-18 years with medically refractory epilepsy. Intervention: 24 hours simultaneous VEEG and actigraph recording.

**Measurements and Results:** Epoch by epoch analysis indicated an overall sleep agreement (sensitivity) of 95% and overall wake agreement (specificity) of 91%. Examining night epochs only revealed relatively high sleep agreement (95%) with low wake agreement (42%). However, strong correlations were found between actigraph and VEEG sleep variables including night sleep period ( $r=0.99$ ), night sleep time ( $r=0.96$ ), duration of night wake time ( $r=0.93$ ) and number of significant wakings during the night ( $r=0.81$ )

**Conclusions:** The study results validate that actigraphy is a reliable clinical and research objective tool for evaluating sleep and wakefulness in children with epilepsy.



## **Role of Orexin in Respiratory and Sleep Homeostasis during Upper Airway Obstruction**

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**Study Objectives:** Chronic upper airway obstruction (UAO) elicits a cascade of complex endocrine derangements that affect growth, sleep, and energy metabolism. We hypothesized that elevated hypothalamic orexin has a role in maintaining ventilation during UAO, while at the same time altering sleep-wake activity and energy metabolism. Here, we sought to explore the UAO-induced changes in hypothalamic orexin and their role in sleep-wake balance, respiratory activity and energy metabolism.

**Interventions:** The tracheae of 22-day-old Sprague-Dawley rats were surgically narrowed; UAO and sham-operated control animals were monitored for 7 weeks. We measured food intake, body weight, temperature, locomotion, and sleep/wake activity; magnetic resonance imaging was used to quantify subcutaneous and visceral fat tissue volumes. In week 7 the rats were sacrificed and levels of hypothalamic orexin, serum leptin, and corticosterone were determined. The effect of dual orexin receptor antagonist (almorexant 300 mg/kg) on sleep and respiration was also explored.

**Measurements and Results:** UAO increased hypothalamic orexin mRNA and protein content by 64% and 65%, respectively. UAO led to 30% chronic sleep loss, excessive active phase sleepiness, decreased body temperature, increased food intake, reduction of the abdominal and subcutaneous fat tissue volume, and growth retardation. Administration of almorexant normalized sleep but induced severe breathing difficulties in UAO rats while it had no effect on sleep or on breathing of control animals.

**Conclusions:** In UAO animals, enhanced orexin secretion, while crucially important for respiratory homeostasis maintenance, is also responsible for chronic partial sleep loss, as well as considerable impairment of energy metabolism and growth.

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