CHEST

Reboxetine Plus Oxybutynin for OSA Treatment

A 1-Week, Randomized, Placebo-Controlled, Double-Blind Crossover Trial

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BACKGROUND: The recent discovery that a combination of noradrenergic and antimuscarinic drugs improved upper airway muscle function during sleep and reduced OSA severity has revitalized interest in pharmacologic therapies for OSA.

RESEARCH QUESTION: Would 1 week of reboxetine plus oxybutynin (Reb-Oxy) be effective on OSA severity?

STUDY DESIGN AND METHODS: A randomized, placebo-controlled, double-blind, crossover trial was performed comparing 4 mg reboxetine plus 5 mg oxybutynin (Reb-Oxy) vs placebo in patients with OSA. After a baseline in-laboratory polysomnogram (PSG), patients underwent PSGs after 7 nights of Reb-Oxy and 7 nights of placebo to compare apnea-hypopnea index (AHI), which was the primary outcome. Response rate was based on the percentage of subjects with a $\geq$ 50% reduction in AHI from baseline. Secondary outcomes included Epworth Sleepiness Scale (ESS) score and psychomotor vigilance test (PVT) values. Home oximetry evaluated overnight oxygen desaturation index (ODI) throughout treatment.

RESULTS: Sixteen subjects aged 57 [51-61] years (median [interquartile range]) with a BMI of 30 [26-36] kg/m^2 completed the study. Reb-Oxy lowered AHI from 49 [35-57] events per hour at baseline to 18 [13-21] events per hour (59% median reduction) compared with 39 [29-48] events per hour (6% median reduction) with placebo ($P < .001$). Response rate for Reb-Oxy was 81% vs 13% for placebo ($P < .001$). Although ESS scores were not significantly lowered, PVT median reaction time decreased from 250 [239-312] ms at baseline to 223 [172-244] ms on Reb-Oxy vs 264 [217-284] ms on placebo ($P < .001$). Home oximetry illustrated acute and sustained improvement in the oxygen desaturation index on Reb-Oxy vs placebo.

INTERPRETATION: The administration of Reb-Oxy greatly decreased OSA severity and increased vigilance. These results highlight potential possibilities for pharmacologic treatment of OSA.

CLINICAL TRIAL REGISTRATION: ClinicalTrials.gov; No.: NCT04449133; URL: www.clinicaltrials.gov

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KEY WORDS: antimuscarinic and norepinephrine reuptake inhibitors; OSA; pharmacologic treatment; upper airway; vigilance

ABBREVIATIONS: AHI = apnea-hypopnea index; CYP = cytochrome P450; ESS = Epworth Sleepiness Scale; KSS = Karolinska Sleepiness Scale; NREM = non-rapid eye movement; ODI = oxygen desaturation index; PGI-S = Patient Global Impression of OSA-Severity; PSG = polysomnogram; PVT = psychomotor vigilance test; Reb-Oxy = reboxetine plus oxybutynin; REM = rapid eye movement; RT = reaction time; UA = upper airway

AFFILIATIONS: From the Istituto Auxologico Italiano (E. Perger, D. Rosa, S. Vicini, M. Marconi, L. Zanotti, C. Lombardi, and G. Parati), IRCCS, Sleep Disorders Center & Department of Cardiovascular,

Σχόλιο:

Αυτή η τυχαιοποιημένη,placebo-controlled, διπλή τυφλή μελέτη, απαντά στο ερώτημα εάν η χρήση συνδυασμού της reboxetine,ενός αναστολέα επαναπρόσληψης της νορεπινεφρίνης, και της oxybutynin, ενός αντιμουσκαρινικού παράγοντα, μπορεί να μειώσει τη βαρύτητα της αποφρακτικής υπνικής άπνοιας. Η μειωμένη νοραδρενεργική δραστηριότητα,θεωρείται ότι παίζει σημαντικό ρόλο στον μειωμένο τόνο των φαρυγγικών μυών, κυρίως στη διάρκεια του NREM ύπνου, ενώ η μουσκαρινική δραστηριότητα εμπλέκεται κυρίως στη μυική ατονία στο REM ύπνο.

Συμμετείχαν στην ανάλυση 16 ασθενείς, με μέση ηλικία τα 57 έτη και με πρόσφατη διάγνωση Αποφρακτικής Υπνικής άπνοιας (< 1 έτος) μέτριας ή σημαντικής βαρύτητας. Η ομάδα ελέγχου έλαβε 4mg reboxetine και 5 mg oxybutynin για μία εβδομάδα, ενώ όλοι οι ασθενείς υποβλήθηκαν σε μελέτη ύπνου πριν την έναρξη της αγωγής και την έβδομη ημέρα, καθώς και σε παρακολούθηση οξυμετρίας κατά το διάστημα της μελέτης.

Στην ομάδα που έλαβε την αγωγή παρατηρήθηκε μείωση του AHI κατά 59% σε σχέση με την αρχική τιμή, το 81% εμφάνισαν μείωση του AHI κατά >50%, ενώ παρατηρήθηκε και μείωση του δείκτη αποκορεσμών. Αντίθετα, δεν παρατηρήθηκε στατιστικά σημαντική διαφορά στην υπνηλία των ασθενών με βάση την EPSS.

Η μελέτη έχει περιορισμούς που αφορούν στο μικρό αριθμό ασθενών, τη μικρή διάρκειά της, καθώς και τον αποκλεισμό ασθενών με σοβαρές συννοσηρότητες. Τα αποτελέσματα,όμως, πιθανώς θα αποτελέσουν το έναυσμα για τη διενέργεια μεγαλύτερων και μεγαλύτερης διάρκειας μελετών σε σχέση με τη φαρμακευτική θεραπεία της αποφρακτικής υπνικής άπνοιας, η οποία θα μπορούσε να αποτελεί μία επιπλέον εναλλακτική θεραπεία σε ασθενείς που δεν δείχνουν ικανοποιητική συμμόρφωση στη χρήση της CPAP.

Επιλογή άρθρου – Σχολιασμός: Αθηνά Βλάχου

Sleep Disturbances Linked to Genetic Disorders

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KEYWORDS

• Sleep • Sleep disturbance • Sleep regulation • Genetics • Circadian clock

KEY POINTS

- Sleep is a very complex behavior, regulated by processes that have underlying genetical factors.
- However, up till now, no sleep genes are identified.
- Some sleep disturbances are inherited and have underlying genetic factors.
- Sleep disturbances are caused by the interplay of genetic, neurobiological, and environmental factors.

INTRODUCTION

The understanding of sleep remains elusive, it must have an important purpose, as it survived many evolutionary cycles. Genetic factors are surmised to regulate sleep as evidenced by the heritability of sleep traits, specific genetic polymorphisms of these traits, and existence of familial sleep disorders.[1]

Recent studies in human and animal models have uncovered some genetic factors underlying sleep disturbances. However, there are more questions than answers. Studying the genetic factors underlying sleep disturbance will aid in understanding the underlying mechanism of sleep. Identification of the first familial circadian phenotype (familial advanced sleep phase syndrome [FASPS]) in the late 1990s made it possible to begin genetic mapping and cloning of genes or mutations that have strong effects on human circadian timing, thus starting the quest for understanding the genetics of sleep.[2] In this review, an overview of genetical regulation of sleep and genetic factors underlying several sleep disturbances will be presented.

Genetic Factors of Sleep

Although mechanisms regulating sleep are conserved across species from flies to mammals, studies find that genes regulating sleep remain ambiguous. The probable cause may be that sleep is not one phenotype; there are variabilities in rapid eye movement (REM) and non-REM (NREM) sleep for instance. Diessler and colleagues found more than 300 sleep phenotypes in mice.[3] Sleep is a very complex behavior that is regulated by the circadian rhythm (process C) and homeostatic drive (process S). Process S keeps track of prior sleep-wake history and controls the homeostatic need for sleep, whereas process C sets the time-of-day that sleep preferably occurs.[4]

Circadian rhythm plays a role in sleep regulation, especially in sleep timing. In mammals, the circadian clock genes consist of activators CLOCK and BMAL1, repressors PER (period) and CRY (cryptochrome).[5] The mechanism consists of clock proteins that regulate their own transcription in an autoregulatory feedback loop.[1,6] The degradation of PER and CRY proteins is also regulated by the serine/threonine kinases, casein kinase 1δ (CK1δ) and CK1ε, the F-box proteins, FBXL3 and FBXL21. Several additional genes and feedback loops have been uncovered, increasing the complexity of the mammalian circadian clock gene network. In a second feedback loop, CLOCK and BMAL1 also regulate the transcription of genes for the nuclear receptors REV-ERBα and REV-ERBβ. A third feedback loop is mediated by

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Σχόλιο:

Ο ύπνος θεωρείται μια ιδιαίτερα σύνθετη συμπεριφορά, που ρυθμίζεται από τον κιρκάδιο ρυθμό και τον μηχανισμό ομοιόστασης. Αυτοί επηρεάζονται από γενετικούς, αλλά και περιβαλλοντικούς παράγοντες. Αν και πολλές διαταραχές ύπνου έχουν ως υποκείμενα αίτια γενετικές ανωμαλίες και παρότι ακόμα δεν έχουν ανακαλυφθεί γονίδια που ελέγχουν τον ύπνο, οι περισσότερες από αυτές τις διαταραχές καθορίζονται από την επίπτωση περιβαλλοντικών/βιολογικών και γενετικών παραγόντων και τη μεταξύ τους διάδραση. Η μελέτη και ταυτοποίηση των γενετικών παραγόντων που ευθύνονται για τις διάφορες διαταραχές ύπνου θα βοηθήσει στην ανακάλυψη και την καλύτερη κατανόηση των μηχανισμών του ύπνου. Το άρθρο αυτό παρουσιάζει μια περίληψη της γενετικής ρύθμισης του ύπνου και των γενετικών παραγόντων που κρύβονται πίσω από διάφορες διαταραχές ύπνου.

Επιλογή άρθρου – Σχολιασμός : Άγης Δέρβας

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Mindfulness is Associated with Better Sleep Quality in Young Adults by Reducing Boredom and Bedtime Procrastination

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Affiliations

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Abstract

Objective: Bedtime procrastination is a relatively new topic of research and has been found to compromise sleep. Researchers have studied the predictors, but only a few studies have focused on the ways to reduce bedtime procrastination. Mindfulness, a novel variable in this research area, may shed some light on how to decrease bedtime procrastination. This study examined a serial mediation model and hypothesized that the relationship between mindfulness and better sleep quality would be serially mediated by lower levels of boredom and bedtime procrastination.

Methods: This study employed a correlational approach and recruited a sample of 220 participants aged between 17 and 30 (M = 20.34 years, SD = 2.86). In the Qualtrics online survey, participants completed a series of questionnaires measuring mindfulness, boredom, bedtime procrastination, and sleep quality.

Results: The analyses provided support for our serial mediation model. Mindfulness predicted a lower level of boredom, which in turn predicted a lower level of bedtime procrastination and subsequently better sleep quality.

Conclusion: Our findings highlighted the role of mindfulness in curbing bedtime procrastination, setting a foundation for future research on the interventions for sleep issues associated with bedtime procrastination. We discussed the theoretical and practical implications of the findings.

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Σχόλιο:

Περίληψη

Η αναβλητικότητα έναρξης της ώρας του ύπνου είναι ένα σχετικά νέο θέμα έρευνας και έχει βρεθεί ότι επηρεάζει την ποιότητα του ύπνου. Οι ερευνητές έχουν μελετήσει τους προγνωστικούς παράγοντες αυτής της συσχέτισης, αλλά μόνο λίγες μελέτες έχουν επικεντρωθεί στους τρόπους μείωσης της αναβλητικότητας πριν τον ύπνο. Η ενσυνειδητότητα (Η μείωση του άγχους βασισμένη σε στοιχεία που προσφέρει η εντατική εκπαίδευση για να βοηθήσει άτομα με άγχος, άγχος, κατάθλιψη και πόνο), μια νέα μεταβλητή σε αυτόν τον ερευνητικό τομέα, μπορεί να ρίξει φως στο πώς να μειωθεί η αναβλητικότητα του ύπνου. Αυτή η μελέτη εξέτασε ένα σειριακό μοντέλο διαμεσολάβησης και υπέθεσε ότι η σχέση μεταξύ ενσυνειδητότητας και καλύτερης ποιότητας ύπνου θα διαμεσολαβούνταν σειριακά από χαμηλότερα επίπεδα πλήξης και αναβλητικότητας πριν τον ύπνο.

Μέθοδοι

Αυτή η μελέτη χρησιμοποίησε μια συσχετιστική προσέγγιση και στρατολόγησε ένα δείγμα 220 συμμετεχόντων ηλικίας μεταξύ 17 και 30 ετών (M = 20,34 ετών, SD = 2,86). Στην διαδικτυακή έρευνα της Qualtrics, οι συμμετέχοντες συμπλήρωσαν μια σειρά από ερωτηματολόγια που μετρούσαν την επίγνωση, την πλήξη, την αναβλητικότητα και την ποιότητα του ύπνου.

Αποτελέσματα

Οι αναλύσεις επιβεβαίωσαν το μοντέλο μιας σειριακής διαμεσολάβησης. Η ενσυνειδητότητα προέβλεψε χαμηλότερο επίπεδο πλήξης πριν τον ύπνο, το οποίο με τη σειρά του προέβλεπε χαμηλότερο επίπεδο αναβλητικότητας και ως αποτέλεσμα καλύτερη ποιότητα ύπνου.

Συμπεράσματα

Τα ευρήματά της έρευνας υπογράμμισαν τον ρόλο της ενσυνειδητότητας στον περιορισμό της αναβλητικότητας της ώρας του ύπνου, θέτοντας τα θεμέλια για μελλοντική έρευνα σχετικά με τις παρεμβάσεις για προβλήματα ύπνου που σχετίζονται με την αναβλητικότητα του ύπνου.

Επιλογή άρθρου – Σχολιασμός: Δημήτριος Κάντας

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Physical activity, sedentary behaviour and incidence of obstructive sleep apnoea in three prospective US cohorts

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Abstract

Background: Reduced physical activity and increased sedentary behaviour may independently contribute to the development of obstructive sleep apnoea (OSA) through increased adiposity, inflammation, insulin resistance and body fluid retention. However, epidemiological evidence remains sparse and is primarily limited to cross-sectional studies.

Methods: We prospectively followed 50 332 women from the Nurses' Health Study (2002-2012), 68 265 women from the Nurses' Health Study II (1995-2013) and 19 320 men from the Health Professionals Follow-up Study (1996-2012). Recreational physical activity (quantified by metabolic equivalent of task (MET)-h per week) and sitting time spent watching TV and at work/away from home were assessed by questionnaires every 2-4 years. Physician-diagnosed OSA was identified by validated self-report. Cox models were used to estimate hazard ratios (HRs) and 95% confidence intervals for OSA incidence associated with physical activity and sedentary behaviour.

Results: During 2 004 663 person-years of follow-up, we documented 8733 incident OSA cases. After adjusting for potential confounders, the pooled HR for OSA comparing participants with ≥36.0 *versus* <6.0 MET-h per week of physical activity was 0.46 (95% CI 0.43-0.50; p_{trend}<0.001). Compared with participants spending <4.0 h per week sitting watching TV, the multivariable-adjusted HR was 1.78 (95% CI 1.60-1.98) for participants spending ≥28.0 h per week (p_{trend}<0.001). The comparable HR was 1.49 (95% CI 1.38-1.62) for sitting hours at work/away from home (p_{trend}<0.001). With additional adjustment for several metabolic factors, including body mass index and waist circumference, the associations with physical activity and sitting hours at work/away from home were attenuated but remained significant (p_{trend}<0.001), whereas the association with sitting hours watching TV was no longer statistically significant (p_{trend}=0.18).

Conclusions: Higher levels of physical activity and fewer sedentary hours were associated with lower OSA incidence. The potential mediating role of metabolic factors in the association between sedentary behaviour and OSA incidence may depend on the type of sedentary behaviour. Our results suggest that promoting an active lifestyle may reduce OSA incidence.

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Σχόλιο:

Η ελαττωμένη άσκηση και η καθιστική ζωή αποτελούν παράγοντες κινδύνου για εμφάνιση ΣΑΑΥ μέσω κυρίως : 1) αύξησης της εναπόθεσης λίπους, 2) συστηματικής φλεγμονής, 3) αύξησης της αντίστασης στην ινσουλίνη, 4) κατακράτησης υγρών. Σε αυτή την προοπτική μεγάλου μεγέθους μελέτη σε υγειονομικούς (50332 γυναίκες και 19920 άνδρες), μελετήθηκαν με ερωτηματολόγια κάθε 2-4 χρόνια, η φυσική δραστηριότητα σε MET-h/week (metabolic equivalents), καθώς και ο χρόνος παρακολούθησης τηλεόρασης και ο χρόνος καθιστικής εργασίας μακριά από το σπίτι. Η διάγνωση του ΣΑΑΥ έγινε μετά σχετική δήλωση του υγειονομικού (92% in lab PSG). Βρέθηκε ότι η ελαττωμένη άσκηση (διχοτόμηση σε <4 MET-h/week vs >/ 28 MET-h/week), overall adjusted for confounding, έδωσαν hazard ratios (Cox proportional hazards) = 0.46 (p for trend <0.001). Η παρακολούθηση τηλεόρασης και η καθιστική εργασία (διχοτόμηση σε <4ώρες vs.>/ 28 ώρες, έδωσαν HRs 1.78 και 1.49 αντίστοιχα. Οι μεταβολικοί παράγοντες (BMI και Waist Circum) τροποποίησαν την παρακολούθηση TV (p=0.18). Φαίνεται ότι ο συνδυασμός άσκησης έστω και μέτριας και ο ελαττωμένος χρόνος καθιστικής ζωής σχετίζονται με μικρότερη επίπτωση ΣΑΑΥ. Επίσης φαίνεται ότι η σχέση μεταξύ ΣΑΑΥ και καθιστικής ζωής επηρεάζεται από τον χαρακτήρα της καθιστικής συμπεριφοράς.

Επιλογή άρθρου – Σχολιασμός: Παναγιώτης Πανάγου

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COMMENTARY

Is bilevel PAP more effective than CPAP in treating hypercapnic obese patients with COPD and severe OSA?

Commentary on Zheng Y, Yee BJ, Wong K, Grunstein R, Piper A. A pilot randomized trial comparing CPAP vs bilevel PAP spontaneous mode in the treatment of hypoventilation disorder in patients with obesity and obstructive airway disease. *J Clin Sleep Med*. 2022;18(1):99–107. doi:10.5664/jcsm.9506

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Chronic hypercapnic respiratory failure, defined as awake resting $PaCO_2 \geq 45$ mm Hg with a normal pH, can occur in both chronic obstructive pulmonary disease (COPD) and obesity (ie, obesity hypoventilation syndrome or OHS). Nocturnal positive airway pressure (PAP) improves awake and sleep hypercapnia in both conditions. Evidence has emerged from clinical trials that in ambulatory patients with stable chronic hypercapnic COPD, nocturnal bilevel positive airway pressure with a backup rate (BPAP-spontaneous timed) with high inspiratory pressure and very low expiratory pressure, ie, high-intensity noninvasive ventilation, improves important clinical outcomes such as mortality and hospital readmissions.[1,2] Importantly, patients with significant obesity or suspected of having obstructive sleep apnea (OSA) were excluded from these clinical trials. In fact, clinical practice guidelines on the management of chronic stable hypercapnic COPD suggest continuous positive airway pressure (CPAP) as the treatment of choice, rather than the more costly and challenging-to-implement noninvasive ventilation, if OSA is considered to be the main contributor to the patient's chronic hypercapnia.[3]

Similarly, clinical trials in patients with OHS have excluded patients with COPD and have predominantly focused on ambulatory patients who have concomitant severe OSA (approximately 70% of patients with OHS have severe OSA). In these clinical trials of OHS and concomitant severe OSA, CPAP and noninvasive ventilation (either BPAP-spontaneous timed or volume-targeted pressure support) were equally effective compared to CPAP.[4,5] Therefore, clinical practice guidelines have recommended the use of CPAP in this group.[6] BPAP is recommended for patients with OHS who have mild or moderate OSA, nonobstructive sleep-dependent hypoventilation, or experience treatment failure with CPAP.[6]

The preceding recommendations for chronic hypercapnic respiratory failure were derived from studies using strict exclusion criteria that deliberately separated patients with OHS or severe OSA from those with COPD.[3,6] It is therefore not surprising that providers are frequently faced with a clinical conundrum: Are obesity and OSA the main contributor to the patient's chronic hypercapnia or COPD? And what form of PAP therapy is best suited for the obese hypercapnic patient with COPD and severe OSA (ie, overlap syndrome)? Although the exact prevalence of overlap syndrome is unknown, the clinical conundrum becomes more relevant because in 1 study of patients with moderate-to-severe COPD referred from a pulmonary rehabilitation facility, OSA prevalence was 66%.[7]

In this issue of the *Journal of Clinical Sleep Medicine,* Zheng and colleagues[8] rejected prior exclusion criteria and instead sought to describe the chronic hypercapnic patient with obesity, severe OSA, and COPD. The authors enrolled participants with daytime hypercapnia ($PaCO_2 > 45$ mm Hg), obesity (body mass index > 30 kg/m^2), and obstructive airways disease defined as forced expiratory volume in the first second over forced vital capacity ($FEV_1/FVC < 0.7$ presenting to a single-center outpatient sleep clinic. This single-blinded, randomized controlled trial with 2 parallel arms was designed to compare CPAP with BPAP-spontaneous-mode (BPAP-S) over 3 months. Thirty-two participants were randomized evenly to either CPAP or BPAP with polysomnography used to titrate PAP settings. The primary endpoint was improvement in awake $PaCO_2$. Following intergroup analysis, BPAP-S was demonstrated to be more effective than CPAP at reducing $PaCO_2$ (9.4 mm Hg, confidence interval = 4.3–15 mm Hg, $P = .001$). The mean baseline $PaCO_2$ was 5 mm Hg higher in those randomized to BPAP-S. This difference is clinically relevant, and it may have not reached statistical significance due to the small sample size. Patients in the BPAP group had more opportunity to normalize (or regress to the mean) than patients randomized to CPAP. With that said, BPAP-S remained superior to CPAP after adjusting for baseline differences in $PaCO_2$ between groups.

Although reduction in $PaCO_2$ was greater with BPAP-S, there was still a significant improvement in hypercapnia by both CPAP ($P < .05$) and BPAP-S ($P < .01$). In fact, 8 of 16 participants (50%) in the CPAP arm and 10 of 16 participants

(62.5%) in the BPAP-S arm corrected to eucapnia by the end of 3 months. BPAP-S also demonstrated greater improvement in health-related quality of life and spirometry indices of FEV_1 and FVC. Notably, no significant difference was observed in potential confounders of adherence, weight, and need for nocturnal supplemental oxygen. Adherence is of particular importance, as it has been consistently demonstrated that better adherence to PAP therapy is associated with stronger control of respiratory failure in OHS[9] and chronic hypercapnic COPD.[10] Although improvement in $PaCO_2$ is a common endpoint used in studies of patients with chronic hypercapnic respiratory failure, it remains unclear if the benefit of PAP is mediated directly through $PaCO_2$ reduction or whether $PaCO_2$ is a marker for other PAP benefits (ventilation/perfusion matching, respiratory muscle rest during sleep, improving airway obstruction, improvement in hypoxemia).[3]

All participants were naïve to PAP therapy and after an initial diagnostic polysomnography, each participant underwent a second polysomnography to titrate their PAP settings. The mean titrated CPAP setting was 12.7 cm H_2O. This value is comparable to the mean CPAP setting of 10.7 cm H_2O used in the Pickwick trial, the largest randomized controlled trial with the longest follow-up in patients with OHS comparing CPAP and noninvasive ventilation (ie, volume-targeted pressure support with a backup respiratory rate).[4] Mean titrated settings in the BPAP arm were inspiratory PAP (IPAP) 15.8 cm H_2O and expiratory PAP (EPAP) 9.7 cm H_2O. This driving pressure of 6 cm H_2O (difference between IPAP and EPAP) is substantially lower than most "high-intensity" chronic hypercapnic COPD trials,[11,12] and lower than the mean inspiratory and expiratory pressures of 19.7 cm H_2O and 8.2 cm H_2O, respectively, used in the Pickwick trial.[4] It is important to acknowledge that there is significant variability in how BPAP is titrated in sleep laboratories. In the Pickwick trial[4] and the study by Zheng et al,[8] EPAP was titrated to relieve obstructive apneas. Once the upper airway was splint open, IPAP was increased to improve obstructive hypopneas, flow limitation, and hypoxemia. This strategy leads to lower EPAP settings and, thereby, allows for higher levels of driving pressure or pressure support (difference between IPAP and EPAP) compared to a strategy in which EPAP is increased to relieve obstructive apneas, hypopneas, and flow limitation. The discrepancy in the level of pressure support or driving pressure between the current study and the Pickwick trial cannot be explained by the severity of OSA, given that mean apnea-hypopnea indices were fairly similar between the 2 studies. Although we agree with the authors' acknowledgment that the optimal pressure target remains unclear for their study population, it is conceivable that a higher level of pressure support would have led to an even more significant reduction in $PaCO_2$ in the BPAP group compared to CPAP. However, it is important to consider that higher levels of pressure support during BPAP-S titration can induce central apneas, which is why the Pickwick trial and clinical trials of hypercapnic COPD used modes of BPAP or noninvasive ventilation that included a backup respiratory rate (BPAP-ST).

Without question, the most significant contribution from Zheng and colleagues[8] is the recognition and study of a cohort previously not reported in the literature and frequently excluded from clinical trials. By the presence of obstructive lung disease and OSA, nearly every study participant (31/32) met the criteria for overlap syndrome. The authors then added obesity and chronic hypercapnia to form a heterogeneous group that may be best described as "OHS with COPD." Compared to prior studies of patients with OHS, the study participants weighed less but had worse lung function (FEV_1). Similarly, compared to patients with chronic hypercapnic COPD, the study population had better lung function but was substantially more obese and had severe OSA. The result is a patient with chronic hypercapnia we recognize from routine clinical practice, but unfortunately we lack evidence-based strategies for management. Prior studies of OHS have demonstrated that poorer lung function is associated with failure to respond to CPAP.[13] In interpreting their results, Zheng and colleagues[8] attributed the superiority of BPAP-S over CPAP to the additive effects of obstructive lung disease to chronic respiratory failure.

Despite the study's strengths, limitations are recognized and several questions remain unanswered. The most apparent limitations are the short follow-up period (3 months) and small sample size (32 patients). It remains unclear if the larger improvement in $PaCO_2$ in the BPAP-S arm would have persisted during a follow-up period greater than 3 months. The study was underpowered to assess clinically meaningful outcomes, such as mortality, health care utilization, and cardiovascular events. Likewise, many treatment effects were found in within-group analysis, as their study was likely too small to detect treatment effects between groups. To their credit, Zheng and colleagues[8] appropriately designated their work a "pilot study," given the small number of participants. The inclusion of laborious neurocognitive testing is admirable, but valuable clinical markers for dyspnea and exercise tolerance (ie, 6-minute walking test) are unfortunately missing from this work. All participants received standard medical care for COPD, but no baseline data were collected regarding pulmonary therapeutics. Furthermore, it is unknown if participants received exercise training or changes to their medical regimen. Importantly, no participant experienced an exacerbation requiring hospitalization during the study.

The timing of initiating PAP therapy for patients with chronic hypercapnia remains unclear. In the study by Zheng and colleagues,[8] all patients presented to an outpatient sleep clinic with a presumably stable daytime hypercapnia (normal pH), as no data were collected for last hospitalization. Guidelines for chronic hypercapnic COPD recommend a 2- to 4-week recovery period following hospitalization for COPD exacerbation before assessing for noninvasive ventilation to confirm that chronic hypercapnia is persistent (eg, $PaCO_2 \geq 52$ mm Hg).[3] This recommendation is derived from the fact that 21% of patients with COPD recruited for the Home Oxygen Therapy-Home Mechanical Ventilation (HOT-HMV) trial were excluded because the hypercapnia on discharge resolved after 2 to 4 weeks.[1] Conversely, the guidelines for OHS suggest hospitalized patients with OHS be continued on PAP therapy following hospital discharge until they undergo polysomnography, ideally within the first 3 months of discharge.[6] This recommendation is driven by a mortality difference at 3 months postdischarge between patients with OHS discharged without PAP (16.8%) and with PAP (2.3%).[14] Last, although BPAP-S

outperformed CPAP, there was no economic analysis performed between arms. Guidelines for OHS and chronic hypercapnic COPD both recognize cost and feasibility as significant reasons to recommend CPAP over BPAP when severe OSA is present.[3,6]

The 2020 guidelines for chronic hypercapnic COPD concluded with an appeal for more generalizable studies with less-restrictive inclusion criteria.[3] Zheng and colleagues answered that call by embracing the heterogeneity of our patients with pulmonary and sleep disorders. Although their work is small in participants and short in follow-up, the authors should be commended for challenging prior study designs to identify such a unique cohort. Future studies should follow their lead by acknowledging the many gray areas in sleep medicine.

CITATION

Nowalk NC, Neborak JM, Mokhlesi B. Is bilevel PAP more effective than CPAP in treating hypercapnic obese patients with COPD and severe OSA? *J Clin Sleep Med.* 2022; 18(1):5–7.

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DISCLOSURE STATEMENT

All authors have seen and approved this manuscript. The authors report no conflicts of interest.

Σχόλιο:

Το άρθρο αυτό συνιστά μια έγκυρη πληροφόρηση για τη χρήση CPAP ή BiPAP σε περίπτωση συνδυασμού αποφρακτικής υπνικής άπνοιας, συνδρόμου παχυσαρκίας-υπαερισμού και ΧΑΠ.

Περιέχει όλες τις βασικές οδηγίες και πληροφορίες σύμφωνα με τις διεθνείς οδηγίες και επιπλέον αποκαλύπτει πόσο πολύπλοκο είναι το θέμα σε περίπτωση που έχουμε συνδυασμό παθήσεων και αιτίων υπερκαπνίας.

Παρατίθεται αυτούσιο.

Επιλογή άρθρου – Σχολιασμός: Μάνος Βαγιάκης

Future Treatment of Sleep Disorders

Syndromic Approach Versus Management of Treatable Traits?

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KEYWORDS

• Sleep disorders • Sleep medicine • Obstructive sleep apnea • Endotype • Phenotype
• Precision medicine • Treatable trait • Fallacy

KEY POINTS

- Sleep medicine is cataloged according to a conventional disease classification system. Disease models are rooted in the pathophysiology of sleep. Polysomnography and other tests are used to demonstrate pathophysiological mechanisms underlying the currently known sleep disorders.
- Although many patients with sleep disorders may be adequately managed by this pathophysiological approach, therapeutic results are insufficient in some subjects, the causes of which lie in nonspecificity of symptoms, coincidental association between symptoms and pathophysiological endotype, as well as co-occurrence of two or more pathologic mechanisms affecting sleep.
- As co-occurrence of different pathogenetic mechanisms may produce phenotypes that are at odds with the idealized description of classic sleep disorders, the result of standard therapeutic interventions may be disappointing.
- The mechanisms underlying the expression of certain traits may be a substrate for targeted treatment. Treatable traits are characterized by biomarkers with predictive value as to beneficial treatment response.
- The challenge for the future is to gradually embrace the principles of systems medicine and to shift gear toward managing treatable traits in sleep disorders surpassing the limits of the traditional nosologic approach.

INTRODUCTION

Over the past decades, sleep medicine has evolved as a novel discipline in health care. The development of relevant medical specialties has invariably been preceded by major scientific advances in particular areas of interest. Medical and surgical specialties have traditionally been organized on anatomic or organ-based models in line with growing insight in organ-system physiology and pathology. The taxonomy of human disease dates back to the nineteenth century and is largely ascribed to the work of Sir William Osler, one of the founding fathers of modern medicine.[1] The classification of diseases by connecting the affected organ system with physiologic, anatomic, and histologic findings has been called the "Oslerian paradigm."[2] Syndromic patterns and nosologic entities are the building blocks of the Oslerian taxonomy that still prevails in the contemporary classification of human diseases.

Later in medical history, cross-sectional disciplines have emerged that are rooted in common

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Σχόλιο:

Το άρθρο αυτό είναι μια ωραία ανασκόπηση για τις παθήσεις των οφθαλμών που συσχετίζονται με την αποφρακτική υπνική άπνοια.

Τέτοιες είναι το γλαύκωμα, η μη αρτηριτικη ισχαιμική οπτική νευροπάθεια, η κεντρική ορώδης χοριοαμφιβληστροειδοπάθεια και η διαβητική αμφιβληστροειδοπάθεια.

Είναι ενδιαφέρουσα η παράθεση της βιβλιογραφίας η οποία εντάσσει τον οφθαλμό στα όργανα τα οποία επηρεάζονται από την αποφρακτική υπνική άπνοια.

Επιλογή άρθρου – Σχολιασμός: Μάνος Βαγιάκης

Sleep Disturbance in Pregnancy

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KEYWORDS

• Sleep disturbances • Sleep complaints • Pregnancy

KEY POINTS

- During pregnancy, alteration of sleep occurs related to the anatomic and physiologic changes in gestation.
- Sleep disturbances are common in pregnant women and can be due to the changes in pregnancy and/or the existing or aggravated sleep disorders.
- Poor sleep quality, insufficient sleep, and sleep disorders particularly obstructive sleep apnea contribute to adverse maternal and fetal outcomes.
- Screening and treatment of sleep disorders are important and may improve pregnancy outcomes.
- Promoting good sleep for healthy pregnancy should be integrated into routine antenatal care.

INTRODUCTION

Pregnancy is a vulnerable time for both the mother and fetus. Sleep as part of body and mind restoration plays an important role in maternal and fetal health. Inevitably, alteration in sleep occurred continuously throughout pregnancy due to the physiologic and hormonal changes.[1,2] Moreover, sleep disorder such as obstructive sleep apnea (OSA) can be aggravated or developed during this time.[3] Evidence had shown that OSA leads to several adverse outcomes including preeclampsia, gestational hypertension, gestational diabetes, preterm delivery, and stillbirth.[4] Short sleep duration and poor sleep quality could also lead to perinatal depression and gestational diabetes.[5,6] Socioeconomic status may contribute to the sleep loss in pregnant women as the mother's sleep is not protected.[7–9]

SLEEP CHANGES DURING PREGNANCY

Hormonal and physical changes in pregnancy cause alterations in sleep duration and architecture.[1,2] Total sleep time increases during the 1st trimester than nonpregnant period, thereafter it progressively decreases and is significantly reduced toward the 3rd trimester.[1,2] Deep sleep and REM sleep are reduced after the 1st trimester.[1,2] However, preeclamptic women had higher slow wave sleep than normal pregnant women (43 ± 3 vs $21 \pm 2\%$, $P < .001$).[10] Possible explanations for the increase in slow wave sleep might be related to cerebral edema and cytokine release (ie, tumor necrosis factor-α, interleukin-6, IL-6, and interleukin-8, IL-8) associated with preeclampsia.[10,11] Subjective perception of poor sleep quality was highly reported during the 3rd trimester in association with the changes in sleep macrostructure.[12] Izci -Balserak, et al. studied the changes in sleep architecture and EEG spectral analysis during early and late pregnancy.[13] It showed that pregnant women had shorter sleep duration, poorer sleep efficiency, more awakening, and higher N2 sleep with less slow wave and REM sleep, compared to nonpregnant counterpart.[13] Additionally, these changes subsequently worsened from early to late pregnancy.[13]

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Σχόλιο:

Αλλαγές στη διάρκεια και στην αρχιτεκτονική του ύπνου συμβαίνουν συνεχώς κατά την εγκυμοσύνη, ως αποτέλεσμα φυσιολογικών και ορμονικών μεταβολών. Όσο προχωράει η εγκυμοσύνη, η συνολική διάρκεια και η αποδοτικότητα ύπνου σταδιακά μειώνονται, ενώ η έγκυος παρουσιάζει περισσότερες αφυπνίσεις και μικρότερα ποσοστά ύπνου βραδέων κυμάτων και σταδίου REM.

Οι περισσότερες έγκυες γυναίκες παραπονιούνται για τουλάχιστον ένα ενόχλημα κατά τον ύπνο τους, κυρίως κατά το 3^{ο} τρίμηνο. Τέτοια κοινά προβλήματα μπορεί να επικαλύπτουν συμπτώματα ενδεχομένως προϋπαρχουσών υπνικών διαταραχών. Διάφορες διαταραχές ύπνου μπορούν συνεπώς να εμφανιστούν ή να επιδεινωθούν στην περίοδο αυτή.

Η υπερβολική ημερήσια υπνηλία είναι συχνή, σε ποσοστό 32-45%, και μπορεί να σχετίζεται με διάφορους παράγοντες, όπως μεταβολές στα επίπεδα ορμονών και διακοπές του φυσιολογικού ύπνου εξαιτίας συχνουρίας, συσπάσεων της μήτρας, εμβρυϊκών κινήσεων, συμπτωμάτων παλινδρόμησης κ.ά. Η επίπτωση του ροχαλητού αυξάνει περίπου 3 φορές και κυμαίνεται από 14 έως 48% σε υγιείς εγκύους και μπορεί να φτάσει το 70% σε εκείνες με παράγοντες κινδύνου, όπως παχυσαρκία, διαβήτη κυήσεως και υπέρταση. Το συχνό ροχαλητό κατά την εγκυμοσύνη αναφέρεται ως προγνωστικός παράγοντας ΣΑΥ και κακής έκβασης της κύησης.

Στατιστικά δεδομένα και στοιχεία από κλινικές μελέτες δεν υπάρχουν πολλά, αλλά είναι γνωστό πως η αποφρακτική υπνική άπνοια μπορεί να οδηγήσει σε κακή έκβαση εγκυμοσύνης, αυξάνοντας τον κίνδυνο για προεκλαμψία, υπέρταση/διαβήτη κυήσεως, πρόωρο τοκετό και αποβολή. Μικρή διάρκεια και κακή ποιότητα ύπνου μπορούν επίσης να οδηγήσουν σε επιλόχεια κατάθλιψη και διαβήτη κυήσεως.

Το άρθρο αναλύει στη συνέχεια δεδομένα σχετικά με την αϋπνία, τις παραϋπνίες, την παράδοξη κινητικότητα κατά τον ύπνο και το σύνδρομο ανήσυχων άκρων, δίνοντας έμφαση στις αναπνευστικές διαταραχές κατά τον ύπνο και καταλήγει με μια αναφορά στις φαρμακευτικές και μη-φαρμακευτικές θεραπευτικές επιλογές, καθώς και στις επιπτώσεις των διαταραχών ύπνου στην υγεία της μητέρας και του εμβύου.

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Music-based Intervention for Improving Sleep Quality of Adults without Sleep Disorder: A Systematic Review and Meta-analysis

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ABSTRACT

Background: Listening to music is often used as a self-help intervention to improve sleep quality, but its efficacy among individuals without sleep disorder remains unclear.

Methods: A search was performed on five databases to identify for studies that examined the use of music-based intervention to improve sleep quality among individuals without sleep disorder. Random-effects meta-analysis was performed, and the certainty of evidence was evaluated using GRADE (Grading of Recommendations Assessment, Development and Evaluation).

Results: Twenty-two articles which recruited 1,514 participants were included for review. Meta-analysis of six studies including 424 participants did not find an improvement in sleep quality among recipients of music-based intervention compared to those with standard care (mean difference: −0.80; 95% CI: −2.15 to 0.54, low-quality evidence). Subgroup analysis showed a clear improvement in sleep quality when interventions were administered for at least 3 weeks (−2.09; −3.84 to −0.34, n = 3). No difference in terms of sleep onset latency (standardized mean difference (SMD) −0.32; 95% CI −0.88 to 0.25, n = 4, very-low quality evidence) and sleep efficiency (SMD: −0.59; 95% CI −3.15 to 1.97, n = 2, very-low quality evidence) were observed. The effect of music-based intervention on anxiety, depression and quality of life were mixed with suggestions of possible benefits.

Conclusion: Music-based intervention in addition to standard care appears to be a promising strategy to improve sleep quality when delivered for 3 week or longer. However, effects are inconsistent across studies and larger randomized controlled studies reporting long-term outcomes are needed before it can be recommended for routine use.

PROSPERO registration: CRD42018081193

Introduction

Sleep is a critical need for every individual to safeguard our overall health and wellbeing (Altevogt & Colten, 2006). Evidence suggests that the global prevalence of insomnia is around 6% to as high as 18%, depending on the criteria used (Ohayon, 2002), with higher prevalence among older adults, females and those with mental health disorders (Hertenstein et al., 2019; Patel et al., 2018; Zhang &

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Supplemental data for this article can be accessed on the publisher's website.

Σχόλιο:

<u>Background</u>: Η ακρόαση μουσικής χρησιμοποιείται συχνά για την βελτιστοποίηση της ποιότητας του ύπνου σε ασθενείς με προβλήματα του ύπνου. Παρόλα αυτά η αποτελεσματικότητα της σε υγιείς ασθενείς δεν έχει διερευνηθεί ενδελεχώς.

<u>Μέθοδοι</u>: ΄Εγινε έλεγχος για μελέτες σε πέντε βάσεις δεδομένων ώστε να ανευρεθούν άρθρα σχετικά με την επίπτωση της μουσικοθεραπείας σε υγιείς. Πραγματοποιήθηκε μετά-ανάλυση και χρησιμοποιήθηκε το σύστημα GRADE για την κατηγοριοποίηση της σημαντικότητας. Η μουσική συμπεριελάμβανε οποιοδήποτε πρωτόκολλο που περιλάμβανε μουσική και συστατικά μουσικής όπως ζωντανή μουσική, παίξιμο ενός οργάνου, τραγούδι η επαναλαμβανόμενη μουσική μέσω playlist σύμφωνα με το πρωτόκολλο που ακολουθήθηκε από τον Sihvonen (Sihvonen et al., Lancet Neurol. 2017 Aug). Η μουσική είτε παιζόταν από έναν μουσικό θεραπευτή ή έμμεσα από το προσωπικό της κλινικής ή από αυτοματοποιημένο σύστημα.

<u>Αποτελέσματα</u>: βρέθηκαν 22 άρθρα που περιελάμβαναν συνολικά 1514 ασθενείς. Μια μετά-ανάλυση 6 μελετών περίπου 424 ασθενών δεν βρήκε κάποια βελτίωση με την ακρόαση μουσικής σε σχέση με την κύρια θεραπεία (μέση διαφορα-0,8 95 % CI -2,15 μέχρι 0,54). Ανάλυση υποομάδων έδειξε βελτίωση της ποιότητας του ύπνου όταν η μουσικοθεραπεία γινόταν τουλάχιστον για 3 βδομάδες(-2,09 CI -3,84 μέχρι -0,34). Δεν παρατηρήθηκε καμία διαφορά στον χρόνο έναρξης του ύπνου (-0,32 95% CI -0,88 μέχρι 0,25) και της αποτελεσματικότητας του ύπνου (-0,59 95% CI-3,15 μέχρι 1,97). Η στατιστική σημαντικότητα για τα ανωτέρω αποτελέσματα ήταν μικρή. Οι επιδράσεις της μουσικής στο άγχος, την κατάθλιψη και την ποιότητα ζωής ήταν μικτά.

<u>Συμπέρασμα</u>: Η προσθήκη της μουσικοθεραπείας στην στάνταρ θεραπευτική στρατηγική φαίνεται να έχει κάποιο όφελος ειδικά αν χρησιμοποιηθεί για πάνω από 3 βδομάδες. Παρ όλα αυτά τα αποτελέσματα είναι ακόμα ενδεικτικά και χρειάζονται μεγάλες τυχαιοποιημένες μελέτες πριν η χρήση της γίνει πιο εκτεταμένη.

<u>Σχόλιο</u>: Φαίνεται ότι η μουσικοθεραπεία βοηθά εκτός από τους νοσούσες και τους υγιείς κάτι που θέλει περαιτέρω διερεύνηση.

Επιλογή άρθρου – Σχολιασμός: Δημήτριος Κάντας

Association between depression and sleep apnoea: a Mendelian randomisation study

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Abstract

Background Studies have reported a close relationship between depression and sleep apnoea, yet it is unknown whether these are causally related. Thus, we aimed to determine whether depression is associated with the aetiology of sleep apnoea.

Methods We used publicly available genetic summary data from two large consortia: the Psychiatric Genomics Consortium, with data from 36 single-nucleotide polymorphisms (SNPs) closely associated with major depressive disorder (MDD), and the UK Biobank, including 456736 patients with sleep apnoea and 766964 controls. F Mendelian randomisation (MR) analysis, we used the inverse-variance weighted method, weighted median MR-Egger regression, MR pleiotropy residual sum and outlier test to retrieve summary data. Analyses were performed using the "TwoSampleMR" package in R.

Results Out of the 36 SNPs associated with MDD, we found statistically significant evidence of a potential causal effect of MDD on the risk of sleep apnoea (OR 1.004, 95% CI 1.001–1.006; p=0.001). Similar results were obtained using the MR-Egger and weighted median methods. Additionally, we found no heterogeneity or pleiotropy.

Conclusions Our findings suggest that depression slightly increases the risk of sleep apnoea. Further investigation of the potential biological mechanisms is necessary.

Σχόλιο:

Η κατάθλιψη και το ΣΑΑΥ είναι δύο νοσήματα με συνεχή αύξηση του επιπολασμού των, με αποτέλεσμα διεθνή ανησυχία, όμως δεν έχει βρεθεί αιτιολογική συσχέτιση αιτίου -αιτιατού.

Στη μελέτη χρησιμοποιήθηκαν δύο μεγάλες βάσεις δεδομένων, η Phychiatric Genomics consortium, που είχε δεδομένα από 36 SNPs (single nucleotide polymorphisms) σε ασθενείς με μείζονα κατάθλιψη και η UK Biobank με δεδομένα από 456736 ασθενείς με ΣΑΑΥ και 766964 controls.

Για την αιτιολογική συσχέτιση χρησιμοποιήθηκε η τεχνική Mendelian randomisation (MR), που μετρά τη διακύμανση γονιδίων για να βρεί την αιτιατή σχέση μιας έκθεσης ή ενός αποτελέσματος. Το πλεονέκτημα της τεχνικής είναι οτι ελαττώνει σημαντικά το reverse causation και confounding που αποτελούν βασικά εμπόδια στην ασφαλή εξαγωγή συμπερασμάτων.

Βρέθηκε πιθανή αιτιολογική συσχέτιση μεταξύ κατάθλιψης και ΣΑΑΥ, OR=1.004, 95% CI=1.001-1.006), p=0.001.Επίσης για τον αποκλεισμό του horizontal pleiotropy (exclusion restriction assumption), χρησιμοποιήθηκαν οι τεχνικές Weighted median και MR Egger με παρόμοια αποτελέσματα (OR=1.004,p=0.019, OR=1.004, p=0.511).

Συμπερασματικά η κατάθλιψη ελαφρώς αυξάνει τον κίνδυνο για ΣΑΑΥ με πιθανούς μηχανισμούς:

1. τα κατασταλτικά αντικαταθλιπτικά προκαλούν ελάττωση του μυικού τόνου των διαστολέων του φάρυγγα με αποτέλεσμα να αυξάνεται το wake up threshold και η διάρκεια και ο αριθμός των απνοιών.

2. προκαλούν αύξηση του βάρους

3. ασθενείς με κατάθλιψη έχουν διαταραχές στον ιππόκαμπο, anterior cingulate gyrus, amygdala και frontal complex, διαταραχές που υπάρχουν παρομοίως και στο ΣΑΑΥ.

4. στην κατάθλιψη υπάρχουν νευροενδοκρινικές και μεταβολικές διαταραχές που όμως σχετίζονται με το ΣΑΑΥ, ΄όπως γλυκοκορτικοειδή, adipokines, leptin, insulin και inflammatory signalling.

Επιλογή άρθρου – Σχολιασμός: Παναγιώτης Πανάγου

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Special Article

SPECIAL ARTICLE

Video-polysomnography procedures for diagnosis of rapid eye movement sleep behavior disorder (RBD) and the identification of its prodromal stages: guidelines from the International RBD Study Group

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Abstract

Video-polysomnography (v-PSG) is essential for diagnosing rapid eye movement (REM) sleep behavior disorder (RBD). Although there are current American Academy of Sleep Medicine standards to diagnose RBD, several aspects need to be addressed to achieve harmonization across sleep centers. Prodromal RBD is a stage in which symptoms and signs of evolving RBD are present, but do not yet meet established diagnostic criteria for RBD. However, the boundary between prodromal and definite RBD is still unclear. As a common effort of the Neurophysiology Working Group of the International RBD Study Group, this manuscript addresses the need for comprehensive and

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Σχόλιο:

Η βίντεο-πολυυπνογραφία είναι απαραίτητη για την διάγνωση της RBD διαταραχής. Η διαταραχή της συμπεριφοράς στον ύπνο REM χαρακτηρίζεται από κινήσεις , τινάγματα και/ή φωνήσεις κατά τον ύπνο REM που συχνά συσχετίζεται με ονειρικό περιεχόμενο. Σύμφωνα με τη παρούσα γνώση , η διαταραχή αυτή μπορεί να εμφανίζεται σαν μεμονομένο RBD (ή ιδιοπαθές RBD) , το οποίο αναγνωρίζεται σαν πρόδρομο στάδιο των α-συνουκλεινοπαθειών ή μπορεί να σχετίζεται με άλλες παθήσεις όπως ν. Parkinson, άνοια με σωμάτια Lewy, με ατροφία πολλαπλών συστημάτων ή ναρκοληψία. Παρότι υπάρχουν ήδη οδηγίες για την διάγνωση του από την Αμερικανική Ακαδημία της Ιατρικής Ύπνου, υπάρχουν ακόμη αρκετά σημεία που χρήζουν διευκρινίσεων ώστε να πετύχουμε εναρμόνιση μεταξύ των κέντρων ύπνου. Το πρόδρομο είναι μία κατάσταση στην οποία τα συμπτώματα και τα κλινικά σημεία είναι παρόντα αλλά κατά την μελέτη ύπνου δεν πληρούνται τα διαγνωστικά κριτήρια. Επίσης το όριο μεταξύ πρόδρομης μορφής και αδιαμφισβήτητο RBD δεν είναι ακόμη ξεκάθαρο. Η προσπάθεια της ομάδας Νευροφυσιολογίας της διεθνούς ομάδας εργασίας RBD αντανακλά την ανάγκη για οριστικές κατευθυντήριες οδηγίες διάγνωσης RBD και ανίχνευσης της πρόδρομης μορφής RBD. τις τεχνικές ρυθμίσεις της βίντεο-πολυυπνογραφίας.

1) **συγκεκριμένα σημεία της διάγνωσης του REM ύπνου**
2) **εναρμόνιση του scoring του REM ύπνου χωρίς ατονία**
3) **τις σταθερές μεθόδους αναλύσεων των δεδομένων από την ακουστική και βίντεο- καταγραφή κατά την πολυυπνογραφία και την ταξινόμηση κινήσεων και φωνήσεων**
4) **την αποσαφήνιση των κατευθυντηρίων οδηγιών της βιντεο-πολυυπνογραφίας για την διάγνωση του RBD και την ανίχνευση του πρόδρομου RBD .**

Τελικός στόχος είναι αυτές οι κατευθυντήριες οδηγίες να οδηγήσουν σε πιο ομοιογενείς οδηγίες και αντικειμενικές μεθόδους ώστε να δοθεί η ευκαιρία να αποκτήσουμε περισσότερες πληροφορίες μέσα από εναρμονισμένες πολυκεντρικές μελέτες.

Επιλογή άρθρου – Σχολιασμός: Ευαγγελία Φλώρου

Sleep and Breathing
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SLEEP BREATHING PHYSIOLOGY AND DISORDERS • ORIGINAL ARTICLE

Metabolic outcomes in adults with type 2 diabetes and sleep disorders

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Abstract

Purpose Insomnia is frequently co-morbid with obstructive sleep apnea (OSA); the effect of insomnia or co-morbid insomnia and OSA (OSA + I) on associated metabolic outcomes in adults with type 2 diabetes (T2D) remains unclear. This study in adults with T2D compared metabolic outcomes among persons with OSA, insomnia, or OSA + I.

Methods This study analyzed baseline data from the Diabetes Sleep Treatment Trial of persons recruited for symptoms of OSA or poor sleep quality. Home sleep studies determined OSA presence and severity. Insomnia was evaluated using the Insomnia Severity Index. Height and weight to calculate body mass index (BMI) and blood for laboratory values were obtained. Multivariate general linear models were used to examine the impact of the type of sleep disorder and sociodemographic, lifestyle, and sleep risk factors on metabolic outcomes.

Results Participants ($N=253$) were middle-aged (56.3 ± 10.5 years), white (60.5%), obese (mean BMI of 35.3 ± 7.1 kg/m^2), and male (51.4%) with poor glucose control (mean HbA1c of 8.0 ± 1.8%). Most participants had OSA + I (42.7%) or insomnia only (41.0%). HbA1c and BMI differed among the sleep disorder groups. In addition, in the adjusted models, having insomnia only, compared to OSA only, was associated on average with higher HbA1c levels ($b=1.08\pm0.40$, $p<0.007$) and lower BMI ($b=-7.03\pm1.43$, $p<0.001$).

Conclusions Findings suggest that insomnia frequently co-exists with OSA, is independently associated with metabolic outcomes in adults with T2D, and should be considered in investigations of the effects of OSA in persons with T2D.

Trial registration Diabetes-Obstructive Sleep Apnea Treatment Trial (NCT01901055), https: Clinicaltrials.gov/ct2/show/NCT01901055; Registration date: July 17, 2013.

Keywords Diabetes · Obstructive sleep apnea · Insomnia · Metabolic risk factors

Introduction

Insomnia and obstructive sleep apnea (OSA) are common among adults with type 2 diabetes (T2D) with an estimated prevalence of 25% and 50–70%, respectively [1–4]. Insomnia is characterized by difficulties falling asleep, difficulties with maintaining sleep including frequent awakenings or the inability to return to sleep after awakenings, and/or unwanted early awakenings resulting in significant distress or functional impairments [5]. OSA is characterized by intermittent apneas and hypopneas during sleep caused by upper airway obstruction [6]. Insomnia and OSA are independent risk factors for metabolic diseases. Both disorders result in inflammation, oxidative stress, impaired glucose tolerance, and insulin resistance [7–11].

There is emerging evidence that insomnia is frequently co-morbid with OSA [12]; however, the differences in demographic, behavioral and sleep risk factors, and associated metabolic outcomes between adults with T2D and OSA, insomnia, or co-morbid insomnia and OSA (OSA + I) remain unclear and understudied. A greater understanding of the characteristics of adults with these sleep disorders and their metabolic consequences may direct better T2D management

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Σχόλιο:

Η αϋπνία συχνά συνυπάρχει με την αποφρακτική άπνοια ύπνου (OSA). Το αποτέλεσμα της αϋπνίας ή της συνύπαρξης αϋπνίας και OSA (OSA+I) σχετικά με τα μεταβολικά αποτελέσματα σε ενήλικες με διαβήτη τύπου 2 (T2D) παραμένει ασαφές.

Σε αυτή τη μελέτη συνέκριναν τα μεταβολικά αποτελέσματα σε ενήλικες με T2D μεταξύ ατόμων με OSA, αϋπνία ή OSA+I. Οι μελέτες ύπνου στο σπίτι προσδιόρισαν την παρουσία και τη σοβαρότητα του OSA. Η αϋπνία αξιολογήθηκε χρησιμοποιώντας το δείκτη σοβαρότητας της αϋπνίας. Το ύψος και το βάρος για τον υπολογισμό του δείκτη μάζας σώματος (BMI) και εργαστηριακές εξετάσεις αίματος.

Χρησιμοποιήθηκαν πολυμεταβλητά γενικά γραμμικά μοντέλα για να εξετάσουν την επίδραση του τύπου της διαταραχής ύπνου και των κοινωνικοδημογραφικών παραγόντων κινδύνου, του τρόπου ζωής και του ύπνου στα μεταβολικά αποτελέσματα.

Οι συμμετέχοντες (N=253) ήταν μεσήλικες (56,3±10,5 έτη), λευκοί (60,5%), παχύσαρκοι (μέσος BMI 35,3±7,1 kg/m2), και άνδρες (51,4%) με κακό έλεγχο γλυκόζης (μέση τιμή HbA1c 8,0±1,8%). Οι περισσότεροι συμμετέχοντες είχαν OSA+I (42,7%) ή μόνο αϋπνία (41,0%).

Επιπλέον, στα προσαρμοσμένα μοντέλα, έχοντας μόνο αϋπνία, σε σύγκριση με το OSA

μόνο, συσχετίστηκε κατά μέσο όρο με υψηλότερα επίπεδα HbA1c (b=1,08±0,40, p<0,007) και χαμηλότερο BMI (b= -7,03±1,43, p<0,001).

Τα ευρήματα υποδεικνύουν ότι η αϋπνία συχνά συνυπάρχει με το OSA, συνδέεται ανεξάρτητα με το μεταβολισμό σε ενήλικες με T2D και θα πρέπει να ληφθούν υπόψιν στις έρευνες των επιπτώσεων του OSA σε άτομα με T2D.

Επιλογή άρθρου – Σχολιασμός: Κυριακή Χολίδου