Sleep memory processing: the sequential hypothesis.

Giuditta A(1).

AUTHOR INFORMATION: (1)Department of Biology, Federico II University Naples, Italy. According to the sequential hypothesis (SH) memories acquired during wakefulness are processed during sleep in two serial steps respectively occurring during slow wave sleep (SWS) and rapid eye movement (REM) sleep. During SWS memories to be retained are distinguished from irrelevant or competing traces that undergo downgrading or elimination. Processed memories are stored again during REM sleep which integrates them with preexisting memories. The hypothesis received support from a wealth of EEG, behavioral, and biochemical analyses of trained rats.

Further evidence was provided by independent studies of human subjects. SH basic premises, data, and interpretations have been compared with corresponding viewpoints of the synaptic homeostatic hypothesis (SHY). Their similarities and differences are presented and discussed within the framework of sleep processing operations. SHY’s emphasis on synaptic renormalization during SWS is acknowledged to underline a key sleep effect, but this cannot marginalize sleep’s main role in selecting memories to be retained from downgrading traces, and in their integration with preexisting memories. In addition, SHY’s synaptic renormalization raises an unsolved dilemma that clashes with the accepted memory storage mechanism exclusively based on modifications of synaptic strength. This difficulty may be bypassed by the assumption that SWS-processed memories are stored again by REM sleep in brain subnuclear quantum particles. Storing of memories in quantum particles may also occur in other vigilance states. Hints are provided on ways to subject the quantum hypothesis to experimental tests.

Insomnia among community dwelling elderly in Alexandria, Egypt.

Ayoub Al(1), Atta M, El Kady HM, Ashour A.

AUTHOR INFORMATION: (1)aGeriatric Health Specialty bMental Health Specialty, Family Health Department, High Institute of Public Health, Alexandria University, Alexandria, Egypt.

BACKGROUND: Insomnia is a common problem in the elderly population. Poor sleep quality is associated with decreased memory and concentration, increased risk of falls, cognitive decline, and higher rate of mortality. Inadequate sleep hygiene such as irregular sleep schedules, use of stimulants, and daytime naps may predispose to insomnia.

AIM: The aim of this study was to determine the prevalence of insomnia among community dwelling elderly in Alexandria and to assess some of the risk factors and comorbid conditions related to insomnia.

PARTICIPANTS AND METHODS: This is a cross-sectional study conducted among 380 elderly people taken from different clubs in Alexandria using a predesigned structured interview questionnaire. Data on sociodemographic characteristics, medical history, and personal and sleeping habits were collected. The Insomnia Severity Index was used to assess insomnia and the Depression Anxiety Stress Scale was used to measure
depression, anxiety, and stress.

RESULTS: One-third (33.4%) of the elderly suffered from insomnia. On logistic regression, the most independent factors that were significantly associated with insomnia were number of chronic diseases [odds ratio (OR)=7.25 for having e’5 diseases], being female (OR=2.37), anxiety (OR=1.91), watching television in bed before sleeping (OR=1.90), depression (OR=1.74), nocturia (OR=1.13), and daily sunlight exposure (OR=0.57).

CONCLUSION AND RECOMMENDATIONS: Insomnia is a common problem among the elderly in Alexandria. Female sex, chronic diseases, mental health problems, and bad sleep hygiene practice increase the risk for insomnia. Improving knowledge among the elderly about the prevalence and risk factors of insomnia could help the development of effective public health prevention and intervention programs for better sleep quality.


The relationship between self-reported sleep quality and reading comprehension skills.

Ellis SK(1), Walczyk JJ(2), Buboltz W(2), Felix V(1).

AUTHOR INFORMATION: (1) Houston Baptist College, United States. (2)Louisiana Tech University, United States. Inadequate sleep undermines many cognitive functions, including memory, concentration, and attention, which are vital in everyday activities. We hypothesized that poor quality or shorter sleep length may impair reading-related skills, resources, and outcomes, specifically verbal working memory span, verbal efficiency, and reading comprehension. Contrary to the hypotheses, neither short sleep length nor self-reported sleep quality were related to reading skills performance. However, longer sleep times were significantly related to lower verbal efficiency, and participants with the poorest sleep quality fared significantly better on the reading comprehension task than participants with moderate sleep quality. Given the paucity of research examining sleep and reading specifically, as well as these surprising data, more research in this area is warranted.


Slow wave activity as the default mode of the cerebral cortex.

Sanchez-Vives MV(1,)(2), Mattia M(3).

AUTHOR INFORMATION: (1) Institut d’Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain. Email: msanche3@clinic.ub.es. (2)Institució Catalana de Recerca i Estudis Avançats (ICREA), Barcelona, Spain. (3)Istituto Superiore di Sanità (ISS), Rome, Italy.

The function of sleep remained one of largest enigmas of neuroscience for most of the 20th century. However in recent years different evidence has accumulated in support of a critical role of sleep on functions such as replay and memory consolidation. In particular slow wave sleep, and its underlying cortico-thalamo-cortical activity, slow oscillations, could be critical not only for memory but also for the maintenance of the brain’s structural and functional connectivity. In this article we ask: why slow oscillations? To answer this question we put forward the idea that slow oscillations are the default activity of the cortical network based on both experimental and theoretical evidence. We go on to discuss why slow oscillations emerge from the cortical circuits and what are the dynamic advantages of this activity pattern, such as the resilience to perturbances and the facilitation of transitions between a disconnected (e.g. deep sleep) brain and a connected, awake brain.


Sleep and memory in the making. Are current concepts sufficient in children?

Peigneux P(1).

AUTHOR INFORMATION: (1)UR2NF, Neuropsychology and Functional Neuroimaging Research Unit at CRCN -Centre de Recherches Cognition et Neurosciences and UNI - ULB Neurosciences Institute, Universite Libre de Bruxelles, Belgium. Email:philippe.peigneux@ulb.ac.be.
Memory consolidation is an active process wired in brain plasticity. How plasticity mechanisms develop and are modulated after learning is at the core of current models of sleep-dependent memory consolidation. Nowadays, two main classes of sleep-related memory consolidation theories are proposed, namely system consolidation and synaptic homeostasis. However, novel models of consolidation emerge, that might better account for the highly dynamic and interactive processes of encoding and memory consolidation. Processing steps can take place at various temporal phases and be modulated by interactions with prior experiences and ongoing events. In this perspective, sleep might support (or not) memory consolidation processes under specific neurophysiological and environmental circumstances leading to enduring representations in long-term memory stores. We outline here a discussion about how current and emergent models account for the complexity and apparent inconsistency of empirical data.

Additionally, models aimed at understanding neurophysiological and/or cognitive processes should not only provide a satisfactory explanation for the phenomena at stake, but also account for their ontogeny and the conditions that disrupt their organisation. Looking at the available literature, this developmental condition appears to remain unfulfilled when trying to understand the relationships between sleep, learning and memory consolidation processes, both in healthy children and in children with pathological conditions.


**Building phonetic categories: an argument for the role of sleep.**

**Earle FS(1), Myers EB(2).**

**Author information:** (1) Department of Speech, Language, and Hearing Sciences, University of Connecticut, Storrs, CT, USA. (2) Department of Speech, Language, and Hearing Sciences, University of Connecticut, Storrs, CT, USA; Department of Psychology, University of Connecticut, Storrs, CT, USA; Haskins Laboratories, New Haven, CT, USA.

The current review provides specific predictions for the role of sleep-mediated memory consolidation in the formation of new speech sound representations. Specifically, this discussion will highlight selected literature on the different ideas concerning category representation in speech, followed by a broad overview of memory consolidation and how it relates to human behavior, as relevant to speech/perceptual learning. In combining behavioral and physiological accounts from animal models with insights from the human consolidation literature on auditory skill/word learning, we are in the early stages of understanding how the transfer of experiential information between brain structures during sleep manifests in changes to online perception. Arriving at the conclusion that this process is crucial in perceptual learning and the formation of novel categories, further speculation yields the adjacent claim that the habitual disruption in this process leads to impoverished quality in the representation of speech sounds.


**Complex associative memory processing and sleep: a systematic review and meta-analysis of behavioural evidence and underlying EEG mechanisms.**

**Chatburn A, Lushington K, Kohler MJ.**

The beneficial influence of sleep on memory consolidation is well established; however, the mechanisms by which sleep can dynamically consolidate new memories into existing networks for the continued environmental adaptation of the individual are unclear. The role of sleep in complex associative memory is an emerging field and the literature has not yet been systematically reviewed. Here, we systematically review the published literature on the role of sleep in complex associative memory processing to determine (i) if there is reasonable published evidence to support an active role for sleep facilitating complex associative processes such rule and gist extraction and false memory; (ii) to determine which sleep physiological events and states impact these processes, and to quantify the strength of these relationships through meta-analysis. Twenty-seven studies in healthy adults were identified which combined indicate a moderate effect of sleep in facilitating associative memory as tested behaviourally. Studies which
have measured sleep physiology have reported mixed findings. Significant associations between sleep electrophysiology and outcome appear to be based largely on mode of acquisition. We interpret these findings as supporting reactivation based models of associative processing.


**Effect of acupuncture on patients with insomnia: study protocol for a randomized controlled trial.**

**Han KH, Kim SY, Chung SY(1).**

**AUTHOR INFORMATION:** (1) Department of Hwabyung/Stress Clinic, Kyung Hee University Korean Medicine Hospital at Gangdong, 149, Sangil-Dong, Gangdong-gu, Seoul, Korea. ovepwr@khu.ac.kr.

**BACKGROUND:** Hypnotic drugs tend to be the dominant form of treatment of insomnia, but these come with a number of reported side effects. Acupuncture has been studied as an alternative, resulting in a rising need for methodological research towards verifying its efficacy as insomnia treatment.

**METHODS/DESIGN:** We describe a proposal for a single-center, patient-assessor-blinded, randomized controlled trial with two parallel arms. A total of 38 patients complete screening tests at the first visit, are registered into the clinical trial, and then randomly assigned to the experimental or sham control groups (19 patients for each group). All subjects are clinical insomnia patients who score a 6 or above on the Pittsburgh Sleep Quality Index (PSQI) and meet all inclusion criteria. All subjects are treated with acupuncture and intradermal acupuncture (IDA) three times during the first week. Five sham acupoints are used in the control group. In the experimental group, five real acupoints (PC6, SP6, HT7, KI6, and BL62) are used unilaterally in turn. Sham acupoints are over 1 cm away from each real acupoint. The primary outcomes are the scores on the Insomnia Severity Index (ISI) and PSQI. Secondary outcomes are the sleep log, the Beck Depression Inventory (BDI), the State-Trait Anxiety Inventory (STAI), the World Health Organization Quality of Life Abbreviated Version (WHOQOL-BREF), the Korean-Auditory Verbal Learning Test (K-AVLT), the Digit Span Test (DS), Event Related Potentials (ERPs) and heart rate variability (HRV) to assess emotional states, sleep quality, cognitive functioning, and elecro-physiological changes. Subjects are assessed at three time points: baseline, post-treatment and follow-up. The duration of the clinical trial is 18 days.

**DISCUSSION:** To study the enhancement of the effectiveness of acupuncture for insomnia, we test the intradermal acupuncture method, which is performed continuously on the subject's skin and stimulated at home by the subject every night. In the trial, objective measurements including ERPs and HRV are used to evaluate states of cognition and autonomic nervous system functioning and subjective self-report questionnaires assess insomnia symptoms. 'Sham' acupuncture points provided by STRICTA are used for the control group.


**Adaptive servo-ventilation for the treatment of central sleep apnea in congestive heart failure: what have we learned?**

**Brown LK(1), Javaheri S.**

**AUTHOR INFORMATION:** (1) aDepartment of Internal Medicine, University of New Mexico School of Medicine, Albuquerque, New Mexico bUniversity of Cincinnati College of Medicine, Cincinnati, Ohio, USA.

**PURPOSE OF REVIEW:** Positive airway pressure devices for the noninvasive treatment of sleep disordered breathing are being marketed that have substantially expanded capabilities. Most recently, adaptive servo-ventilation devices have become available that are capable of measuring patient ventilation continuously and use that information to adjust expiratory positive airway pressure and pressure support levels to abolish central and obstructive apneas and hypopneas, including central sleep-disordered breathing of the Hunter-Cheyne-Stokes variety. Patients with congestive heart failure are particularly prone to developing central sleep apnea and/ or Hunter-Cheyne-Stokes breathing, and studies have shown that suppression of these abnormal breathing patterns may improve cardiac function and, ultimately, mortality.

RECENT FINDINGS: Over the last approximately 18 months, increasing numbers of studies have appeared demonstrating improvement in cardiac function and other important outcomes after both acute application of adaptive servo-ventilation as well as 3 to 6 months of use in patients with congestive heart failure and central sleep apnea/Hunter-Cheyne-Stokes breathing. Several of these studies are randomized controlled trials and several include assessment of cardiac event-free survival showing an advantage to treating with adaptive servo-ventilation.

SUMMARY: As an adjunct to optimal pharmacological management, adaptive servo-ventilation shows considerable promise as a means to improve outcomes in patients with congestive heart failure complicated by central sleep apnea/Hunter-Cheyne-Stokes breathing. Larger randomized controlled trials will be necessary to demonstrate the ultimate role of this therapeutic modality in such patients.


Plasma brain-derived neurotrophic factor and reverse dipping pattern of nocturnal blood pressure in patients with cardiovascular risk factors.

Kadoya M(1), Koyama H(1), Kanzaki A(1), Kurajoh M(1), Hatayama M(1), Shiraishi J(1), Okazaki H(1), Shoji T(1), Moriwaki Y(1), Yamamoto T(1), Inaba M(2), Namba M(1).

AUTHOR INFORMATION: (1)Department of Internal Medicine, Division of Diabetes, Endocrinology and Metabolism, Hyogo College of Medicine, Nishinomiya, Hyogo, Japan. (2) Department of Endocrinology, Metabolism and Molecular Medicine, Osaka City University Graduate School of Medicine, Osaka, Japan.

CONTEXT: Basic studies have shown that brain-derived neurotrophic factor (BDNF) has critical roles in the survival, growth, maintenance, and death of central and peripheral neurons, while it is also involved in regulation of the autonomic nervous system. Furthermore, recent clinical studies have suggested potential role of plasma BDNF in the circulatory system.

OBJECTIVE: We investigated the mutual relationships among plasma BDNF, patterns of nocturnal blood pressure changes (dippers, non-dippers, extra-dippers, and reverse-dippers), and cardiac autonomic function as determined by heart rate variability (HRV).

DESIGN: This was a cross-sectional study of patients registered in the Hyogo Sleep Cardio-Autonomic Atherosclerosis (HSCAA) Study from October 2010 to November 2012.

PATIENTS: Two-hundred fifty patients with 1 or more cardiovascular risk factor(s) (obesity, smoking, presence of cardiovascular event history, hypertension, dyslipidemia, diabetes mellitus, chronic kidney disease) were enrolled.

RESULTS: Plasma BDNF levels (natural logarithm transformed) were significantly (\(p = 0.001\)) lower in reverse-dipper patients (7.18±0.69 pg/ml, mean ± SD, \(n = 36\)) as compared to dippers (7.86±0.86 pg/ml, \(n = 100\)). Multiple logistic regression analysis showed that BDNF (odds ratios: 0.417, 95% confidence interval: 0.228-0.762, \(P = 0.004\)) was the sole factor significantly and independently associated with the reverse-dippers as compared with dippers. Furthermore, plasma BDNF level was significantly and positively correlated with the time-domain (SDNN, SDANN5, CVRR) and frequency-domain (LF) of HRV parameters. Finally, multiple logistic regression analyses showed that the relationship between plasma BDNF and the reverse-dippers was weakened, yet remained significant or borderline significant even after adjusting for HRV parameters.

CONCLUSIONS: Low plasma BDNF was independently associated with patients showing a reverse-dipper pattern of nocturnal blood pressure, in which an imbalance of cardiac autonomic function may be partly involved.


Circulation time measurement from sleep studies in patients with obstructive sleep apnea.

Kwon Y(1), Khan T(2), Pritzker M(3), Iber C(4).

AUTHOR INFORMATION: (1)Hennepin County Medical Center, Minneapolis, MN ; University of Minnesota, Minneapolis, MN. (2)Medical College of Wisconsin, Milwaukee, WI. (3)Hennepin County
INTRODUCTION: Lung to finger circulation time (LFCT) can be estimated from polysomnography (PSG) in the presence of an apneic event by using oxygen as an indicator and a finger as the site of detection. The purpose of this study was to refine the methodology of LFCT measurement and to compare LFCT in patients with obstructive sleep apnea (OSA) with and without heart failure (HF).

METHODS: In a retrospective manner, 10 LFCT measurements per patient were made from the PSG in 171 consecutive patients with a diagnosis of OSA who were divided into two groups: (a) those with a clinical history of underlying HF (N = 42) and (b) those without HF (N = 129). Mean values were compared between the two groups. We also examined associations of LFCT with various factors in each group and the combined group separately using multiple regression analysis.

RESULTS: Gender and age were significantly associated with LFCT in patients with OSA alone. Use of ß-blockers was associated with LFCT in the group with OSA with HF. Among the entire cohort, HF, ß-blocker, gender, and age were found to be significantly associated with LFCT. The presence of HF was the strongest predictor of a prolonged LFCT (adjusted mean LFCT: OSA only = 18.5 [95% CI:17.2-19.7 sec] vs. OSA with HF = 26.1 [95% CI: 24.3-28.0 sec], p < 0.0001).

CONCLUSION: LFCT can be reliably measured and is prolonged in patients with OSA and underlying HF. LFCT based on PSG may be a useful marker for detection of coexisting HF in patients with OSA.

Adaptive servo-ventilation therapy improves long-term prognosis in heart failure patients with anemia and sleep-disordered breathing.


AUTHOR INFORMATION: (1)Department of Cardiology and Hematology, Fukushima Medical University. Sleep disordered breathing (SDB) and anemia influences the progression of chronic heart failure (CHF). Adaptive servo-ventilation (ASV) is an effective therapeutic device for treatment of CHF; however, the impacts of ASV on CHF patients with or without anemia remain unclear. A total of 139 patients with CHF and SDB were divided into two groups: those treated with ASV (n = 53) and without ASV (n = 86). All patients were prospectively followed after discharge with the endpoints of cardiac death or progressive heart failure requiring rehospitalization. There were 65 patients (47%) with anemia among all subjects. The anemia hypopnea index was improved, and plasma BNP and high sensitive C-reactive protein levels were decreased in both groups with and without anemia by ASV therapy. The Kaplan-Meier survival curve demonstrated that the cardiac event-free rate in patients with ASV was significantly higher than in those without ASV in the anemia group (P = 0.008). However, in the non-anemia group, the cardiac event-free rate was similarly high in patients both with and without ASV (P = 0.664). Multivariate Cox proportional hazard analysis demonstrated that ASV use was an independent predictor of cardiac events in the anemia group (P = 0.0308), but not in the non-anemia group. ASV treatment for CHF and SDB has more favorable impacts in patients with anemia than in those without anemia.

Positive airway pressure in patients with coronary artery disease and obstructive sleep apnea syndrome.


AUTHOR INFORMATION: (1)Ferrarotto Hospital, University of Catania bCannizzaro Hospital cETNA Foundation, Catania, Italy.

AIMS: We designed a prospective nonrandomized study aiming at assessing the impact of continuous positive airway pressure (CPAP) after a new diagnosis of obstructive sleep apnea syndrome (OSAS) in patients with coronary artery disease (CAD).

METHODS: Consecutive patients referred to coronary
angio-raphy underwent an overnight sleep study during their hospital stay. Among those with angiographically confirmed CAD and a new diagnosis of moderate or severe OSAS, we compared the 3-year major adverse cardiac or cerebrovascular event (MACCE)-free survival stratified by CPAP at discharge.

RESULTS: Of 496 patients undergoing an overnight sleep study, 129 had angiographically confirmed CAD and presented with moderate or severe OSAS. The incidence of 3-year MACCE was significantly lower in the CPAP-treated group (n = 17) than in the untreated group (n = 112; 12 vs. 44%, P = 0.02). After adjusting for differences in baseline characteristics, CPAP was significantly associated with a decreased risk of MACCE [adjusted hazard ratio 0.18, 95% confidence interval (CI) 0.04-0.78, P = 0.02]. Among men, CPAP was associated with a significant 3-year risk reduction in MACCE (adjusted hazard ratio 0.12, 95% CI 0.02-0.87, P = 0.04), whereas no significant benefit of CPAP was seen in women (adjusted hazard ratio 2.1, 95% CI 0.10-41.6, P = 0.63). The statistical interaction between CPAP and sex trended to be significant (adjusted P for interaction = 0.10).

CONCLUSION: In patients with OSAS and CAD, the initiation of CPAP is associated with a significant reduction in MACCE compared with patients left untreated.