Event-Related Potentials in Sleep-Related Breathing Disorders and Insomnia

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Abstract

Background: Since sleep may affect information processing and therefore event related potentials (ERPs) an increased P300 latency and reduced amplitude are expected to be present when sleep is disrupted and shortened**.**

Objective: This study aims at 1) Comparing evening to morning ERPs in controls, insomnia and sleep related breathing disorders (SRBDs) to explore the impact of good or bad sleep on ERPs. 2) Shedding the light on ERPs affection in patients with SRBDs and insomnia. 3) Assessing the association between the severity of subjective and objective sleep alterations and the changes in amplitude and latency of ERPs.

Methods: 30 patients suffering from SRBDs and insomnia were subjected to polysomnography, as well as visual and auditory ERPs administered twice, pre-sleep and post-sleep. 15 age and sex matched healthy subjects were considered control group.

Results: We found significant decrease in ERPs latencies, and increase in their amplitudes in the morning in control group, but neither decrease in morning ERPs latencies nor increase in their amplitudes were observed in patients. Evening ERPs were not significantly different among the three groups. Morning ERPs in SRBDs had longer latencies and smaller amplitudes with respect to controls. Evening to morning difference comparison revealed the subtle ERPs abnormalities in insomnia.

No significant correlation was found between the changes of ERPs in patients and their Epworth sleepiness scales scores and polysomnographic data.

Conclusion: Normal uninterrupted sleep greatly enhances ERPs. Multiple P300 measurements especially in the morning provide more sensitive marker for assessment of sleep effects on attention processes. The difference between evening and morning ERPs is very sensitive parameter and can detect subtle abnormalities especially in insomnia patients. Neither subjective nor objective estimates of sleep continuity can strongly explain the changes in the magnitude of ERPs.

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Key words: Event-related potentials, insomnia, P300, sleep, sleep related breathing disorders. .

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List of Abbreviations

5HT2a	*Serotonin 2a*
ADHD	*Attention-deficit/hyperactivity disorder*
AHI	*Apnea-Hypopnea Index*
APAP	*Auto-adjusting positive airway pressure*
BIPAP	*Bilevel positive airway pressure*
BMI	*Body mass index*
BzRAs	*Benzodiazepine receptor agonists*
CNS	*Central nervous system*
COPD	*Chronic obstructive pulmonary disease*
CPAP	*Continuous positive airway pressure*
CSAHS	*Central Sleep Apnea-Hypopnea Syndrome*
CSAS	*Central sleep apnea syndrome*
CSB	*Cheyne-Stokes breathing*
CSBS	*Cheyne-Stokes breathing syndrome*
ERPs	*Event-related potentials*
ESS	*Epworth sleepiness scale*
GABAa	*g-aminobutyric acida*
MSLT	*Multiple sleep latency test*
MVC	*Motor vehicle crashes*
ODI	*Oxygen desaturation index*
OSAHS	*Obstructive sleep apnea/hypopnea syndrome*
OSAS	*Obstructive sleep apnea syndrome*
PNI	*People not complaining of insomnia*
PSG	*Polysomnography*
PWI	*People with insomnia*
REM	*Rapid eye movement*
RERA	*Respiratory effort-related arousal*
SAS	*Sleep apnea syndrome*
SD	*Sleep deprivation*
SHVS	*Sleep hypoventilation syndrome*
SRBDs	*Sleep related breathing disorders*

SRPs	*Stimulus related potentials*
SSS	*Stanford Sleepiness Scale*
TIB	*Time in bed*
TSP	*Total sleep period*
TST	*Total sleep time*
UARS	*Upper air way resistance syndrome*
VarPAP	*Variable positive airway pressure*

Introduction

The hypothesis that sleep may play a role in the process of memory formation and cognition dates back to the report of Jenkins and Dallenbach in 1924, claiming that recall performance improves following an intervening period of sleep **(Mograss, Godbout, and Guillem, 2006).**

Event-related potentials (ERPs) have been used as a neurophysiologic marker of information processing, discrimination, and working memory. Some recent data have shown that ERPs and P300 amplitude and latency may be affected by the sleep-onset period, sleep deprivation, and experimental sleep fragmentation. These data suggest that sleepiness, sleep loss, and sleep fragmentation may affect attention-dependent and attention-independent processing and, therefore, cognitive functioning **(Sforza and Rubio, 2006).**

Few studies have investigated the use of ERPs in sleep related breathing disorders (SRBDs). Mixed results were reported with some evidence for an increased P300 latency to visual **(Kottebra et al., 1998)** and auditory stimuli **(Walsleben et al., 1989)** although no effect on auditory P300 latency has also been reported **(Afifi et al., 2003)**. Some studies have **(Rumbach et al., 1991)** and some have not found SRBDs patients to have reduced auditory P300 amplitude **(Kottebra et al., 1998).**

As for insomnia, the role of ERPs in assessing daytime function is much more controversial. Some studies supported hypoarousal theory and found evidence of an increased P300 latency and decreased amplitude in insomnia **(Anderer et al., 2004; Bruder et al., 1991).** Other studies supported hyperarousal theory and presented evidence of increased P300 amplitude at sleep onset **(Devoto et al., 2003; Regestein et al., 1993).**

Aim of work

This study aims at 1) Comparing evening to morning ERPs in controls, insomnia and sleep related breathing disorders (SRBDs) to explore the impact of good or bad sleep on ERPs. 2) Shedding the light on ERPs affection in patients with SRBDs and insomnia. 3) Assessing the association between the severity of subjective and objective sleep alterations and the changes in amplitude and latency of ERPs.

Chapter 1

Sleep–Related Breathing Disorders

Syndrome Definitions and Classification

Over the past thirty years many types of abnormal breathing during sleep have been described that are related to, but not accurately described as apneas. Partial airway obstruction can lead to a reduction in tidal volume, referred to as a hypopnea, with the same consequences as an apnea **(Gould et al., 1988)**. More subtle abnormalities have been described such as progressive increases in respiratory effort, due to increasing upper airway resistance, that terminate after an arousal, which is called upper air way resistance syndrome (UARS) **(Guilleminault et al., 1993)**. Some patients have periods of hypoventilation during sleep and not always associated with apneic events. These patients are often obese, usually have awake hypercapnia, and signs of corpulmonale in a syndrome usually named Pickwickian syndrome or sleep hypoventilation syndrome (SHVS) **(Olson and Zwillich, 2005)**.

Still another type of breathing abnormality consists of those apneic events that are not associated with inspiratory effort, indicating reduced central respiratory drive, referred to as central apneas. Central apneas can occur in otherwise healthy individuals but they are also a feature of Cheyne-Stokes breathing syndrome (CSBS), which is commonly seen in patients with congestive heart failure. Mixed apneas refer to periods of absent airflow that are initially associated with an absence of respiratory effort and that persist upon resumption of respiratory effort indicating upper airway obstruction **(White, 1985)**.

The lack of uniform definitions as well as the clinical overlap between the Pickwickian syndrome, obstructive sleep apnea/hypopnea syndrome (OSAHS), and central sleep apnea syndrome (CSAS) has created confusion in clinical settings and has hindered comparisons of results from research studies. In this chapter we will focus on different syndrome definitions and classification.

I. Obstructive Sleep Apnea-Hypopnea Syndrome (OSAHS)

OSAHS is characterized by recurrent episodes of partial or complete upper airway obstruction during sleep. This manifests as a reduction in (hypopnea) or complete cessation (apnea) of airflow despite ongoing inspiratory efforts. The lack of adequate alveolar ventilation usually results in oxygen desaturation and in cases of prolonged events, a gradual increase in $PaCO_2$. The events are often terminated by arousals. Patients may demonstrate a lack of respiratory effort during the initial apnea period followed by gradually increasing effort against an occluded upper airway; such events are referred to as mixed apneas. These events are felt to be pathophysiologically related to obstructive apneas and are considered to be part of the OSAHS **(Tarsa et al., 2009)**.

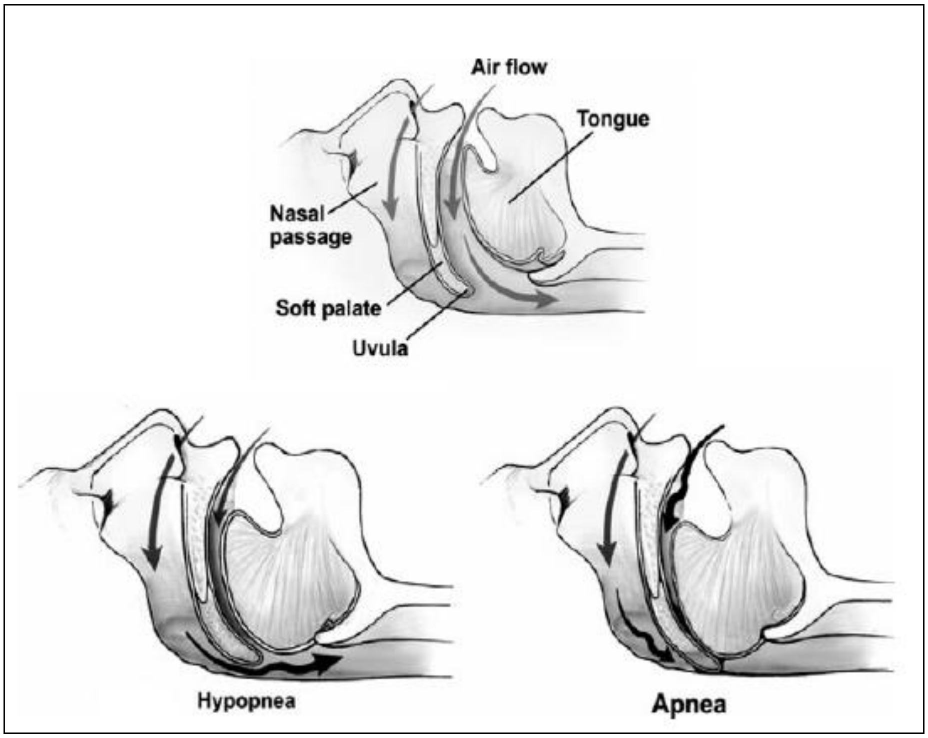

Fig. 1: Partial and complete airway obstruction resulting in hypopnea and apnea, respectively ***(Hahn and Somers, 2007)***.

I.a. Prevalence

OSAHS is a common disorder affecting more than 4% of the general population and 25% of the elderly. Snoring is reported by 40-60% of adults. The combination of snoring and "breathing apnea" have been reported in 2.5% of adults. OSAHS should be