

Sleep Patterns in a Carbon Monoxide (CO) Poisoning Patient

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Abstract

Importance: The functional anatomy of the brain, especially of the subcortical structures, is one of the least understood areas in neurophysiology. A great deal of the understanding of the functional neuroanatomy is derived from the study of patients whose brain has been damaged under different circumstances. Carbon monoxide (CO) poisoning affects particularly the basal ganglia and subcortical white matter, providing insight into the functional neuroanatomy of this complex region of the central nervous system. Since the regulating mechanisms of the sleep-wake cycle depend on multiple brain regions, damage of any of these regions may result in states of vigilance disturbances.

Methods: Sleep was recorded and scored using 30-s epochs according to standard methods, including central and occipital EEG (C3-A1, C4-A2, O1-A1 and O2-A2), submental EMG and periorbital EOG. Oronasal airflow and thoracic and abdominal respiratory effort were also monitored throughout the night.

Results: In addition to disruption of continuity and alterations in the sleep architecture, total sleep time was significantly reduced in the patient under study; consequently, sleep efficiency was severely affected. Reduction in total time spent in REM sleep was related to the mean duration but not to the number of REM sleep episodes displayed across the recording of sleep. Cardiac and respiratory activities exhibited a tendency across the sleep-wake cycle different to that observed in healthy subjects.

Conclusions: This report suggests that cortical and subcortical brain damage caused by CO poisoning induces sleep disturbances and functional modification of the autonomic nervous system. Therapies to improve the sleep quality of patients exposed to CO poisoning should be implemented.

Keywords: CO poisoning; Insomnia; Fragmented sleep; Sleep efficiency

Introduction

The functional anatomy of the brain, especially of the subcortical structures, is one of the least understood areas in neurophysiology. A great deal of the understanding of the functional neuroanatomy is derived from the study of patients whose brains have been damaged under different circumstances.

Carbon monoxide (CO) poisoning affects particularly the basal ganglia and subcortical white matter, providing insight into the functional neuroanatomy of this complex region of the central nervous system [1].

Initial symptoms displayed by individuals under CO poisoning usually include severe headache, nausea, weakness, confusion, heart arrhythmias, myocardial infarction, coma, or death [2,3]. If the patient survives, he or she will develop diverse neuropsychological sequelae [4-7].

Recent studies using detailed neuropsychological evaluations show that significant decrements in cognitive performance may be common, even years after recovery from the main symptoms [6,8,9].

Some reports integrate several cases to assess different kinds of brain damage during the first week after CO poisoning [10,11]. In these reports, it was described that about two-thirds of the patients under study had abnormal imaging studies, the globus pallidus was the most frequently injured area (39-63%), followed by the deep subcortical white matter (28-32%). Cortical, mesial temporal lobe and other subcortical lesions were occasionally detected.

It has been suggested that there may be a significant correlation between the regions that are hypoperfused during the acute stage and the neuropsychiatric disorders that develop later [12]. Some studies have described more lesions in the white matter than in the globus pallidus, whereas others have observed a similar incidence [13]. The precise identification of brain lesions and neuropsychological deficits that may benefit from therapy is important for patient recovery.

On the other hand, the sleep wake cycle may be affected by different factors. Since the regulating mechanisms of this cycle depend on multiple brain regions, any damage of some of these regions may result in states of vigilance disturbances.

Sleep is a reversible behavioral state [14], which consists of rapid eye movement (REM) sleep and non-REM (NREM) sleep. NREM sleep is further divided into stages N1, N2, and N3 based on electroencephalographic (EEG) patterns. N3 is also termed slow-wave

sleep (SWS) or delta sleep and comprises stages 3 and 4 of older nomenclature [15]. In adult humans, sleep consists of about 5% wake, 5% N1, 50% N2, 15% N3, and 25% of REM sleep.

There are multiple hypotheses about the primary function of sleep. Among these hypotheses, restorative and cognitive effects are the most accepted. There is increasing evidence that sleep is necessary for neural plasticity and memory consolidation [16]. NREM sleep is important for declarative memory consolidation, whereas REM sleep helps non declarative and emotional memory. NREM spindle density is positively linked to verbal memory and slow-wave density is positively linked to retention of same day memory.

The lower brain stem is an essential area to generate waking, NREM, and REM sleep states; however when other several brain regions are injured, such as the medulla, mesencephalon, preoptic area of the hypothalamus, thalamus, and neocortex, the amount of NREM and REM sleep is reduced. Similarly, waking state is regulated by several neuronal groups localized in the midbrain, the posterior and lateral hypothalamus, and the basal forebrain. These arousal systems are characterized by long axons and extensive projections to widespread brain regions, involving the diencephalon, the limbic system, and neocortex. Arousal systems also control the thalamocortical neurons, which in turn, regulate the oscillatory mechanisms intrinsic to thalamocortical networks that underlie NREM or synchronized EEG patterns.

On the other hand, sleep is characterized by rapid fluctuations in autonomic activity controlling systemic blood pressure, and heart rate. In normal subjects non-REM sleep is related to a very high vagal activity while REM sleep is associated with a significant withdrawal of vagal activity and an increased influence of sympathetic control of heart rate [17].

Therefore sleep represents a physiological state for a better understanding of the variability of heart rate since autonomic activity can be studied in the absence of factors such as physical activity and cortical functions which modulate heart rate variability

As previously described, brain damage induced by CO poisoning involves different areas related to regulating mechanisms of states of vigilance. Consequently, patients suffering from this damage have a high risk of presenting sleep-wake disturbances.

The aim of this study is to analyze the sleep characteristics of a patient that was exposed to CO inhalation and as consequence, suffers extensive brain damage.

Material and Methods

The study was approved by the institutional Research Ethics Committee. It was carried out in a 30-year-old female found unconscious after 36 hours of CO inhalation and brought to the hospital for medical attention. After intubation, she was transferred to the intensive care unit, where she remained for two weeks after which; she was transferred to the Department of Neurology Services. Her vital signs at admission were as follows: blood pressure: 110/70; pulse rate: 82 beats/min; respiratory rate: 20/min; temperature: 36.6°C. After assessing her clinical history, the diagnosis of CO poisoning was suggested and oxygen therapy via face mask (15 lit/min) was immediately started. Hyperbaric O₂ therapy was not available.

Personal history showed that prior CO poisoning, the patient was healthy without antecedents of tabaquism or alcoholism. Additionally, she has not had any sleep or depressive problems before the accident.

Her brain computed tomography scan demonstrated generalized mild cerebral cortex damage. Differentiation between grey and white matter on the left frontal and parietal regions became confuse.

MRI showed multiple cerebral lesions affecting the cortical grey matter and the subcortical white matter from the frontal, parietal, and temporal lobes, as well as on the left occipital lobes, left hippocampal gyrus, both cerebellar hemispheres and both globus pallidus.

Central nervous system damage coincided with cognitive and neurologic disturbances [9]. These observations lead to the diagnosis of syndrome of upper motoneurone, secondary right hemiparesis, ischemic encephalopathy, sensory aphasia, anomies, confabulations, amnesic syndrome, and left hemineglect. The patient's intellectual coefficient was severely deteriorated.

Brain stem evoked potentials

Auditory evoked potentials were normal; in contrast, visual evoked potentials showed bilateral long lasting latencies for P100 components suggesting a slowing conduction of bilateral optic nerves.

Sleep studies

Previous to polysomnographic recording, the patient's sleep habits were integrated by means of a sleep questionnaire. Then, a Grass Comet Model 25 Acquisition System was used to obtain a polysomnographic recording throughout the night from 23:00 to 8:00 hr.

Sleep was recorded and scored using 30-s epochs according to standard methods, including central and occipital EEG (C3-A1, C4-A2, O1-A1 and O2-A2), submental EMG and periorbital EOG with a high-pass filter at 0.5 Hz and a low-pass filter at 45 Hz [18].

Oronasal airflow and thoracic-abdominal respiratory effort were also monitored throughout the night.

Total sleep time was obtained and the sleep efficiency was calculated. The total time spent in each sleep stage during the recording period was assessed and the percentage within the period was calculated. Mean duration of each sleep state as well as of the sleep cycles were obtained. Sleep and REM sleep latencies were also obtained. Scoring reliability was 91%, when comparing the independent judgment of two scorers.

Results

EEG

EEG recordings across the sleep-wake cycle were similar to those of normal subjects.

At the beginning of the recording, the patient was awake. During this period, brain activity consisted of a low voltage mixed frequency wave pattern and alpha rhythm (Figure 1).



Figure 1: Polysomnographic recording during Wakefulness. EEG is characterized by low voltage mixed frequency waves and alpha rhythm recorded particularly on occipital leads.

After a variable period of relaxed wakefulness, the patient entered stage N1 of sleep, a transitional phase between full wakefulness and light sleep. During this stage, the EEG patterns were similar to those in normal individuals (Figure 2).

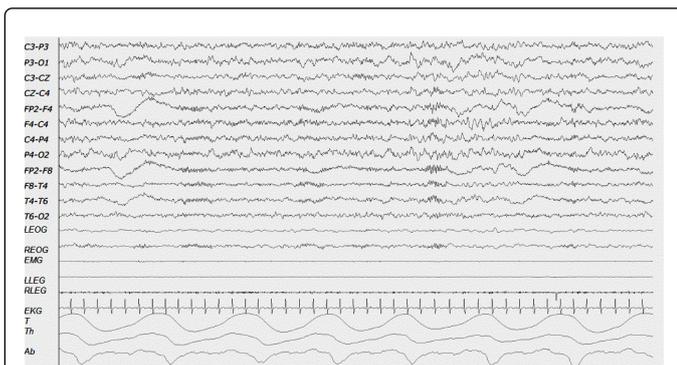


Figure 2: Stage N1 of sleep. Mixed frequency and theta waves are observed. Some vertex waves are observed on central recordings.

Stage N1 of sleep was usually followed by stage N2, where sleep spindles sometimes presented interhemispheric asynchrony (Figure 3).

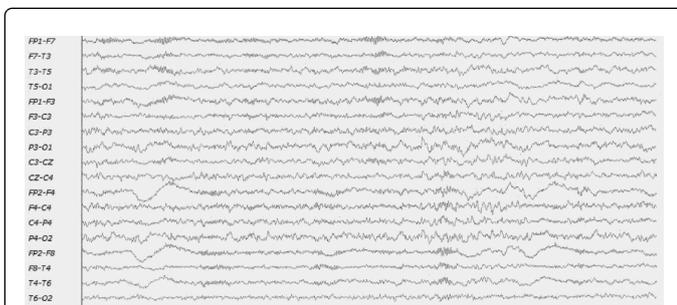


Figure 3: Stage N2 of sleep. Interhemispheric asymmetry of sleep spindles distribution is observed.

As stage N2 of sleep developed, sporadic high voltage slow waves appeared gradually, until meet the criteria for stage N3 of sleep (Figure

4). After a variable period of sleeping time, the patient went into REM sleep displaying the characteristic EEG patterns (Figure 5).



Figure 4: Stage N3 of sleep. Delta waves on EEG recordings are observed.



Figure 5: REM sleep. An EEG pattern of mixed frequency and theta waves is observed. Rapid eye movements are also present on EOG recordings.

When present, saw tooth waves sometimes preceded or coincided with eye movements.

Quantitative data

Sleep recordings revealed that in comparison with normative data¹⁴ this patient show lower sleep efficiency, more nocturnal wake time, and more awakenings lasting longer than 3 minutes. These disturbances were related to an important sleep fragmentation. The patient also showed altered sleep architecture, with higher percentage of nonrapid eye movement (NREM) stage 1 and lower percentage of rapid eye movement (REM) sleep compared to those in normative data. Quantitative sleep data are integrated in Table 1.

Latency to stage N2	25 min
Wake after sleep onset	128 min
Sleep efficiency	58%
Total sleep time	280 min
Total recording time	483 min

Time awake (%)	42
Stage N1 (%)	17
Stage N2 (%)	59
Stage N3 (%)	13
REM sleep (%)	11
Latency of REM sleep	91 min
Number of REM periods	4
Total number of stage changes	114
Stage changes index	24.4

Table 1: Quantitative data.

EMG

In contrast to waking state, low amplitude EMG activity was present throughout all NREM sleep stages. A discrete change in EMG amplitude in the waking to sleeping transition was generally observed. The EMG during stage 2 sleep was usually present at low amplitude. When passing to delta sleep, it was still present although its tracing occasionally fell to very low levels, similar to those of REM sleep. At this stage, muscle tone was extremely low or absent, though some twitches were present.

Heart rate

Patient showed across the sleep-waking cycle a mean heart rate of 90.10 ± 10.20 (Mean \pm SD). The extremes between minimal (32 bpm) and maximal (145 bpm) values were greater during wakefulness followed by those in SWS (68 against 111 bpm), whereas during REM sleep the shortest extremes were displayed (81 against 106 bpm). Heart variability expressed as bradycardia and tachycardia were present during wakefulness, but not during both SWS and REM sleep.

Respiratory activity

During steady NREM sleep, breathing was remarkably regular in both amplitude and frequency showing the lowest index of variability of all vigilance states. During quiet wakefulness and throughout N1, N2, and N3 sleep phases breathing frequency averaged 16.0 breaths/min, it slightly decreased to 14.0 breaths/min when passing to the first episode of REM sleep and it oscillated from 15 to 21 breaths/min during the second REM sleep episode. Breathing irregularity during REM sleep consisted of sudden changes involving both amplitude and frequency of respiratory movements, which were at times interrupted by central apneas lasting 10 to 30 sec. The breathing irregularities did not occur at random but were linked to bursts of REMs.

Oximetry

Oximetry values were periodically checked throughout sleep. The patient displayed high oxygen saturation levels reaching a total average of 95.53% distributed as follows: wakefulness, 96.01%; NREM sleep, 94.86; and REM sleep, 94.98%. Any event of oxygen desaturation was not observed.

Discussion

People suffering brain damage usually develop sleep disturbances [19-22], as confirmed in this study. These disturbances can lead to mood disorders, anxiety, irritability, and a general feeling of physical and mental fatigue. It can also originate poor work performance and occupational accidents.

Sleep disturbances have been observed in people having different levels of brain damage from mild to severe. Since sleep is a complex process involving several parts of the brain, a variety of sleep disturbances can develop after brain injury.

Some studies show that sleep abnormalities may persist months and even years following brain damage [23,24].

In addition to disruption of sleep continuity, alterations in its architecture were observed in the patient under study. Total sleep time was significantly reduced; consequently, sleep efficiency was severely affected. These findings are similar to those of other authors who observed sleep fragmentation after traumatic brain injury (TBI) [23-25]. Light sleep (stages N1 and N2) showed percentage proportions higher than those in normative data, while time percentage spent in REM sleep showed an important reduction. This reduction was related to the mean duration but not to the number of REM sleep episodes displayed across the recording of sleep.

Longer time spent awake after sleep onset and more frequent awakenings observed in this patient affected total sleep time and sleep efficiency. These results are in line with previous studies which have found mainly an increment of wakefulness and number of awakenings into the sleeping period after TBI [23-26].

Apart from the increasing in sleep stages N1 and N2, no other differences were noted in the distribution of sleep stages in TBI patients. Poor sleep exhibited by our patient may be a result of brain lesions affecting sleep-regulating mechanisms, as well as psychological factors such as anxiety and depression.

The complex interactions between depression, anxiety or post-traumatic stress disorder symptoms and sleep disturbances deserve further attention since these psychiatric conditions affect sleep architecture. Prospective studies should, therefore, include thorough evaluations for such conditions.

Autonomic variables

It has been reported that there is a fall in heart rate and respiratory activity when passing from relaxed wakefulness to light sleep. These physiological variations are a reflex of parasympathetic activation. The increase in parasympathetic activity remains across NREM sleep [27-32]. During REM sleep, HR returns to waking levels or it remains below waking, but above NREM sleep levels [33-35], while respiratory activity becomes irregular.

These sleep related changes in heart and respiratory rates appear to be mediated mainly by changes in autonomic circulatory control [36].

Studies that have investigated the effect of sleep and sleep stages on autonomic control have made the assumption that stage effects are independent of time during the sleep period. A number of studies have described that cardiac activity shows systematic changes over the sleep period [27,34,37,38]. The present results indicate that HR does not change significantly over time within both NREM and REM sleep. It

appears that regulation of the autonomous nervous systems on the cardiac activity was absent across the sleep period.

In contrast, an important increase of heart rate was observed in the early morning coinciding with patient's arousal. This HR acceleration may reflect an activation of the sympathetic tone.

The present results contrast with normative findings related to autonomic control of cardiac activity during sleep [39]. The data indicate that parasympathetic nervous system activity remains at a low level throughout both NREM sleep and REM sleep. In contrast, sympathetic nervous system activity, as indicated by the high heart rate average, remains elevated throughout the sleep period showing an additional increase during the early morning that coincides with the awaking period. These findings may reflect a damage of cerebral regions that regulate the heart rate variability induced by carbon monoxide poisoning.

Usually, respiratory activity undergoes important modifications becoming deeper and more regular with NREM sleep, while it turns shallower, irregular, and more frequent during REM sleep.

However, average respiratory rate of the studied patient shows regular levels across the vigilance states from waking state to NREM sleep and a slight non-significant decrement in the first REM sleep episode. This activity became faster and irregular during the second REM sleep episode. Our findings about sleep stage-dependent variations in the heart rate Variability signal and respiratory rate contrast with previous reports.

Conflict of Interest

The authors declare that there is no conflict of interest in this study.

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