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Investigation of Non-Painful Tactile Stimuli in Sleep: Amplitude and Frequency Analysis

Gonca Inanc[1], Murat Ozgoren[1], Adile Oniz[2]

[1]Department of Biophysics, Near East University Faculty of Medicine, Nicosia, North Cyprus
[2]Department of Health Management, Near East University Faculty of Health Sciences, Nicosia, North Cyprus

Abstract

BACKGROUND/AIMS: The aim of this study was to investigate evoked potentials elicited in the brain by non-painful tactile stimuli during sleep in amplitude-time and frequency-time domains.

MATERIALS AND METHODS: Ten volunteers attended this study (mean age: 22.30±1.49 years). Non-painful, single type tactile stimuli were applied to the index and middle fingers of the volunteers' right hand. During the night, the electroencephalography (EEG) of the subject was recorded via 40 channel EEG amplifier. The stages of the sleep were determined according to the standards of the American Academy of Sleep Medicine. Continuous wavelet transform was used for frequency analysis. The amplitude-time and the frequency-time findings relating to the periods of prior to sleep (PS), light sleep (LS), deep sleep, and REM were examined.

RESULTS: While P50, N100, P200, N300, P900 and N_late components were observed both during the PS and the LS periods, the P350 and N450 were observed only in the PS, and the P450 and N550 components were observed only during the all-night sleep periods.

CONCLUSION: In this study, it was also demonstrated by frequency-time analysis that there is a different information processing process during the PS and all-night sleep stages. In addition, with this study, we opened the way to show the dynamics of the non-painful somatosensory area associated with sleep stages.

Keywords: Amplitude, frequency, tactile awareness in sleep, wavelet transform, evoked frequency responses in sleep

INTRODUCTION

The examination of the brain's responses to external stimuli during sleep can be useful in investigating the structure and functions of sleep. Even further, the processing of external stimuli varies between sleep and wakefulness. Hence, sleep can be regarded as a different level of consciousness.[1-3]

Basically, a polysomnography (PSG) system is used to record sleep. PSG refers to the recording (and analysis) of many different physiological data at the same time during sleep. Some main recording components are required for the determination of sleep stages. These are electroencephalography (EEG), electrooculography (EOG) and electromyography (EMG). In addition to these components, additional ones are used to monitor changes in respiratory and cardiac parameters, continuous blood pressure, snoring, body position etc. in order to determine sleep physiology and disorders. The sleep recorded with the PSG system is divided into stages with the standard sleep scoring methods.

While the guidelines of Rechtschaffen and Kales (R&K) had been used in the determination of sleep stages until 2007, the rules of the American Academy of Sleep Medicine are used today in determining sleep stages.[4] Sleep is not a steady state, rather it consists of constantly changing stages. One of these stages is the REM stage with rapid eye movements,

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ORCID IDs of the authors: G.I. 0000-0003-2317-7653; M.O. 0000-0002-7984-2571; A.O. 0000-0002-6619-4106.

Address for Correspondence: Gonca Inanc
E-mail: gonca.inanc@gmail.com
ORCID ID: orcid.org/0000-0003-2317-7653

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and the other is NREM (without rapid eye movements). Typical NREM sleep consists of three sub-stages. These stages are stage 1 (N1), stage 2 (N2), and stage 3 (N3). In the literature, the N1 and N2 stages are accordingly named as light sleep (LS), while N3 is named as deep sleep (DS) or delta sleep.

The first stage seen in the transition from wakefulness to sleep is N1. In this stage, EEG signals are low amplitude and mixed frequency activity is seen, although the theta band (4-7 Hz) is more prominent. Slow eye movements are observed in EOG, and tonic muscle activity is observed in EMG. In the N2 stage, sleep spindles and K-complexes with a frequency of 11-16 Hz are seen. K-complexes are sharp waves consisting of a negative and a subsequent positive component. In the N3 stage, high amplitude (>75 μV), 0.5-2 Hz frequency delta activity is observed. During this stage, muscle tone decreases. REM shows signal characteristics very similar to N1. However, while rapid eye movements are seen in EOG, muscle tone decreases in EMG.[4]

There are a limited number of studies in the literature examining brain responses to non-painful tactile stimuli during sleep in healthy adults.[1,5,6] Frequency analysis was not found to have been used for evoked potentials in sleep studies. In the literature, frequency analyzes were generally applied in determining sleep stages.[7,8]

In this study, it was aimed to investigate brain responses to non-painful tactile stimuli in sleep healthy individuals with amplitude-time and frequency-time space.

MATERIALS AND METHODS

This study is a descriptive study for the examination of brain responses in the PS and all-night sleep stages in terms of amplitude-time and frequency-time space.

Subject

The study was conducted with 10 volunteers (5 females and 5 males; age range 22.30±1.49 years). None of the participants reported any psychiatric, neurologic, chronic illnesses or sleep disorders. In addition, their sleep behavior, coffee intake and or other sleep altering conditions were reported.

Scales

Following the introductory remarks of the study design and procedures, the participants filled in a number of reports and scales. These included the Edinburgh Handedness test, the STAI Form TX-1, SCL-90R tests, the sleep quality and daytime sleepiness Pittsburgh SQI and the Epworth Sleep scale.

The Sleep Laboratory

The volunteers went through a first night of sleep in an isolated room. The room was designed with a Faraday cage to minimize electric and electromagnetic noise and spikes. Furthermore, acoustic isolation provided a conveniently quiet room. The room was dimly lit. An interactive audio system enabled communication when necessary. The entire session was video recorded with real time stamps.

Recording System

The PSG recording was managed by the NuAmps 40 channel (EEG, EOG, EMG) system together with the Embedded Microcontroller Stimulation Unit,[9] pneumatic stimulation unit (Somatosensory Stimulus Generator 4-D Neuroimaging) and recording PC unit.

During the EEG recording, the participants wore an appropriate size Quick Cap (Neuromedical Supplies). The cap enabled a long-term comfortable whole-head recording and conductance was assured with the electro gel (Electro-Gel, Electro-Cap International, Inc. US). EEG referencing was managed by interlinked ear lobe electrodes [(A1+A2)/2].

The eye movements of the participants were monitored by electrodes placed at the outer canthus of the right eye and left supraorbital areas. EMG activity was monitored by electrodes placed over the supra and inferior chin areas. The overall electrode impedance was targeted to be kept lower than 5 KOhm and continuous EEG recording sampling was maintained at 1 KHz sampling frequency.

Experimental Design and Stimuli

The non-painful tactile stimulation was enabled by a pneumatic stimulation unit (4-D Neuroimaging Somatosensory Stimulus Generator).

Tactile stimulations were administered using a modified finger clip mechanism over the index and mid fingers of the right hand during the entire sleep period. The modified finger clip mechanism incorporated a moving membrane with a contact area radius of 8-9 mm. This membrane was positioned to apply a soft pressure over the finger tips. The pneumatic stimulation unit administered a certain amount of air upon being triggered via an in-house MATLAB stimulation system. This pressurized dry air puff action would move the membrane, thus resulting in a soft touch sensation on the participants' finger tips.

The current study was composed of a single type of tactile pressure stimulation. The experimental design had blocks of 60 stimulations that would repeat about 10 times throughout the night. Each block duration was 7 to 8 minutes and the interval between the blocks were about 40 minutes. The inter stimulus interval was around 3 to 3.5 seconds and the order of the stimulations was randomized.

Ethics Statement

This study was approved by the Institutional Ethics Evaluation Board [Dokuz Eylül University Non-Invasive Research Ethical Committee (approval number: 2011/16-16)]. Consent of individuals was obtained before starting the recordings. The participants were given detailed information about the research and the methods to be applied to them in the study. Individuals who agreed to participate in the study filled in the informed volunteer information and consent form and signed that they participated in the study voluntarily.

Statistical Analysis

EEG evaluation was carried out post session after recording. The stages of sleep records were determined according to the AASM scoring system. The 30-second-long recordings were examined one-by-one and the N1, N2, N3 and REM stages were evaluated.

The stimuli and consequent responses (EEG traces) were evaluated separately for all sleep stages.

The epochs were arranged as 1000 ms pre-stimulus and 2000 ms post-stimulus sweeps. Out of these sweeps, the corresponding EOG channel was monitored and any amplitude exceeding ±100 μV was eliminated. Furthermore, baseline correction and 0.5-30 Hz band pass filter (digital

band filter with 12 dB/oct and zero phase shift, Neuroscan 4.5) were applied. Following these procedures, average files were formed for each sleep phase and each participant. Out of the 40 channel EEG recordings, for the sake of simplicity (which is already among the region of interest for non-painful tactile stimulations), only central (Cz) electrode potentials were reported in this manuscript.

The amplitude measurements were taken as 0-2000 ms maximum responses (μV). Following this, continuous wavelet transform was applied to the epochs to provide visual scalogram for frequency-time space. This study consisted of NREM sleep with two subcategories of N1 and N2 assessed as LS while N3 was assessed as DS (LS and DS respectively). The rapid eye movements stage results were also assessed as REM.

RESULTS

In the current study, PS records and all-night sleep (LS, DS, REM stages) sessions were evaluated for all of the participants. None of the participants reported or showed any signs of anxiety, chronic, psychiatric or neurological disorder, nor any sleep disorder. All of the volunteers were right-handed (handedness score: 91.00±9.94).

The non-painful tactile stimulations were successfully obtained from all of the above-mentioned stages. The waveforms resulted in average deflections of certain time windows. Thus, these were labelled as P50, P50, N100, P200, N300, P900 and N_late. To clarify, the P and N denote positive and negative deflections, whereas the numbers refer to the time window of the waveform (latency after stimulation in ms). Out of these waveforms, P350 and N450 were observed only in wakefulness, while P450 and N550 were sleep waveforms.

Prior to Sleep

In the period before sleep, the latency of the response components against painless tactile stimuli (applied to the right-hand index and middle fingers) were examined. Here, the P50 component appeared 94 to 148 ms after the stimulus. Among the prominent peaks, N100 fell into 132-204 ms, P200 appeared from 210 to 290 ms, N300 response was observed between 274 to 360 ms, P350 was at 316 to 424 ms, N450 from 398 to 550 ms, P900 ranged from 646 to 926 and N_late was observed from 1164 to 1352 ms (Table 1).

The brain responses to non-painful tactile stimulation during the wakeful period resulted in the following amplitudes of wave deflections.

Table 1. Prior to sleep wakefulness period for non-painful tactile responses

	Latency (ms) Mean ± SD	Amplitude (μV) Mean ± SD
P50	125.00±19.58	1.74±1.43
N100	178.40±22.09	-1.92±2.58
P200	237.20±25.69	2.74±2.48
N300	309.20±23.16	-0.56±2.22
P350	356.00±31.82	1.37±1.97
N450	465.40±53.22	-3.22±2.24
P900	829.00±81.09	2.02±1.16
N_late	1,256.40±58.20	-1.52±0.94

The latency periods (ms) and peak to peak maximal amplitudes (μV) are presented in columns. Each measurement is accompanied by the standard deviation values. SD: standard deviation.

P50 ranged from 0.04 to 5.16 μV, N100 from 0.41 to -7.04 μV, P200 from 0.44 to 8.08 μV, N300 from -4.86 to -3.22 μV, P350 varied from -0.98 to 5.68 μV, N550 waveform was observed between -0.75 to -8.70 μV, P900 as 0.25 to 4.06 μV and finally N_late from -0.40 to -3.13 μV. These values are shown in table form with their standard deviation as well (Table 1).

The prior to sleep (PS) stimulus waveforms are shown as both amplitude-time and frequency time domains in Figure 1. The time values are represented in the range of 0.5-1.5 s and their frequency range from 0 to 5 Hz.

Light Sleep

During the whole night recording, N1 and N2 stage EEG segments (denoted as light sleep, LS) were evaluated for right-hand index and mid-finger tactile responses. This led to sleep tactile waveforms with positive and negative deflections. The latencies for P50 waveforms were between 64-170 ms, N100 from 90 to 242 ms, P200 ranged from 166 to 290 ms, N300 varied from 258 to 388 ms, P450 appeared from 440 to 560 ms, N550 were observed from 484 to 774 ms, P900 from 668 to 900 ms and N_late from 954 to 1,292 ms. The brain responses to non-painful tactile stimulation during the LS period resulted in the following amplitudes of wave deflections. P50 ranged from -0.73 to 1.93 μV, N100 from 1.14 to -2.17 μV, P200 from -0.11 to 3.02 μV, N300 from -0.96 to -9.31 μV, P450 varied from 0.17 to 6.74 μV, N550 waveform was observed between 1.57 and -1.03 μV, P900 was -0.16 to 4.18 μV and finally N_late was from -0.74 to -3.51 μV. These values are given in table form with their standard deviation in Table 2.

The wavelet transformed waveforms are shown in Figure 2. Here, the frequency and amplitude domains in time provide us with the specific frequency shifting patterns of sleep induced brain activities.

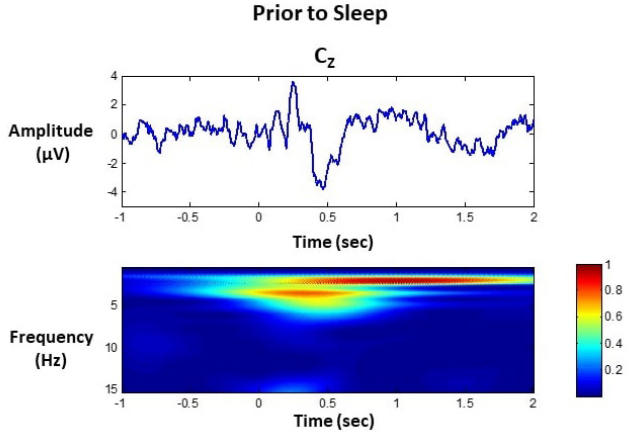

Figure 1. The average prior to sleep wakefulness responses from 10 volunteers to non-painful tactile stimulations (applied to right-index and mid-finger tips) are presented from central electrode (Cz). The upper panel represents the electrophysiological waveform. Here, the vertical axis denotes amplitude in μV and the horizontal axis shows time values (in seconds from -1 to 2 seconds). The "0" in the time axis represents the time of tactile stimulation. The lower panel shows the scalogram in frequency and amplitude domains. The scalogram provides the frequency-time in the horizontal axis while the vertical axis is denoted by frequency time (in Hz). The amplitude information is provided by a color bar next to the figure.

Furthermore, the responses are given as frequency-amplitude-time space. Accordingly, the first 500 milliseconds following the tactile stimulations were prominent in 0 to 5 Hz whereas the late responses from 500 milliseconds onwards resulted in a diminished activity.

Deep Sleep

In the course of the whole night sleep, N3 stage EEG segments (denoted as deep sleep, DS) were evaluated for right-hand index and mid-finger tactile responses. This led to typical sleep tactile waveforms with positive and negative deflections. The latencies for P50 waveforms were between 86-122 ms, N100 from 132 to 246 ms, P200 ranged from 180 to 306 ms, N300 varied from 310 to 386 ms, P450 appeared from 446 to 574 ms, N550 were observed from 490 to 658 ms, P900 from 658 to 808 and N_late from 964 to 1,136 ms.

Table 2. The light sleep (N1 and N2 non-REM stages) period non-painful tactile responses (recorded from Cz)

	Latency (ms) Mean ± SD	Amplitude (μV) Mean ± SD
P50	114.20±25.84	0.90±0.73
N100	162.00±40.47	-0.41±0.91
P200	222.00±33.74	1.40±1.03
N300	333.00±34.17	-3.69±2.51
P450	485.40±34.65	1.67±1.96
N550	589.60±90.26	0.00±0.75
P900	741.40±68.10	1.41±1.27
N_late	1,100.20±123.41	-1.66±0.89

The latency periods (ms) and peak to peak maximal amplitudes (μV) are presented in columns. Each measurement is accompanied by the standard deviation values. SD: standard deviation.

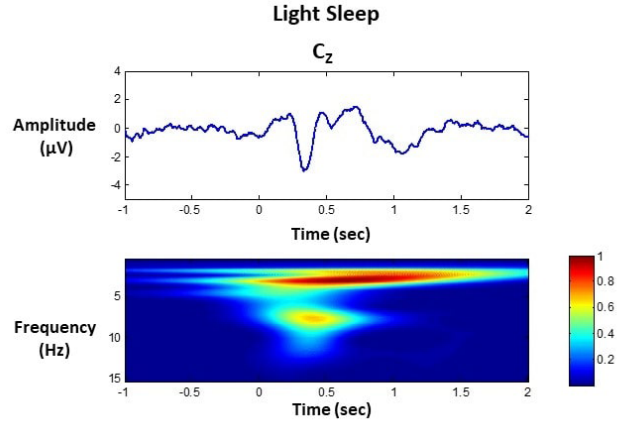

Figure 2. The average light sleep stage responses from 10 volunteers to non-painful tactile stimulations (applied to right-index and mid-finger tips) are presented from central electrode (Cz). The upper panel represents the electrophysiological waveform. Here, the vertical axis denotes amplitude in μV and the horizontal axis shows time values (in seconds from -1 to 2 seconds). The "0" in time axis represents the time of tactile stimulation. The lower panel shows the scalogram in frequency and amplitude domains. The scalogram provides the frequency-time in horizontal axis while the vertical axis is denoted by frequency time (in Hz). The amplitude information is provided by the color bar next to the figure.

The brain responses to non-painful tactile stimulation during the DS period resulted in the following amplitudes of wave deflections. P50 ranged from -0.05 to 2.39 μV, N100 from 1.73 to -2.87 μV, P200 from -0.65 to 3.51 μV, N300 from -1.26 to -11.22 μV, P450 varied from -0.28 to 8.53 μV, N550 waveform was observed between 4.60 and -1.00 μV, P900 was from -0.23 to 6.21 μV and finally N_late from -1.30 to -6.04 μV. These values are given in table form with their standard deviations (Table 3).

The brain responses are presented in a scalogram of frequency-amplitude space. This allows us to evaluate the changes specific to this stage. The activity as a response to tactile stimulations are also present in the DS stages (Figure 3).

Table 3. The deep sleep (N3 non-REM stage) period non-painful tactile responses (recorded from Cz)

	Latency (ms) Mean ± SD	Amplitude (μV) Mean ± SD
P50	105.60±12.10	1.06±0.80
N100	159.80±33.22	-0.21±1.25
P200	215.60±35.19	1.37±1.34
N300	345.00±22.16	-4.85±3.26
P450	511.20±40.12	2.41±2.60
N550	577.50±59.40	0.53±1.80
P900	719.00±40.61	2.51±2.19
N_late	1,028.40±52.96	-3.43±1.88

The latency periods (ms) and peak to peak maximal amplitudes (μV) are presented in columns. Each measurement is accompanied by the standard deviation values. SD: standard deviation.

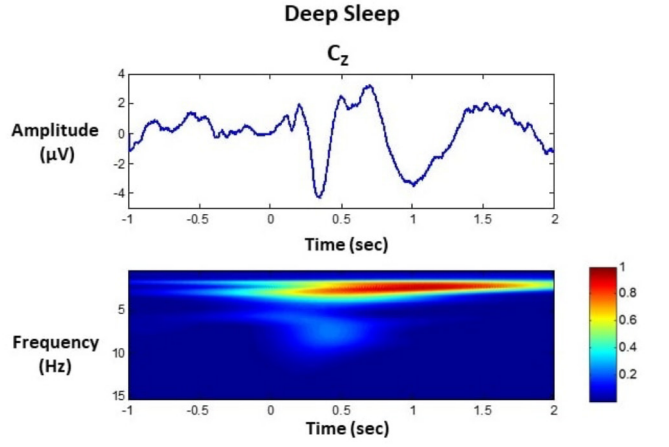

Figure 3. The average deep sleep stage responses from 10 volunteers to non-painful tactile stimulations (applied to right-index and mid-finger tips) are presented from central electrode (Cz). The upper panel represents the electrophysiological waveform. Here, the vertical axis denotes amplitude in μV and horizontal axis shows time values (in seconds from -1 to 2 seconds). The "0" in time axis represents the time of tactile stimulation. The lower panel shows the scalogram in frequency and amplitude domains. The scalogram provides the frequency-time in horizontal axis while the vertical axis is denoted by frequency time (in Hz). The amplitude information is provided by the color bar next to the figure.

REM

Via the throughout-the-night recording, the REM segments were evaluated for right-hand index and mid-finger tactile responses. This led to a number of waveforms in positive and negative deflections. The latencies for P50 waveforms were between 70-150 ms, N100 from 122 to 172 ms, P200 ranged from 202 to 272 ms, N300 varied from 296 to 372 ms, P450 appeared from 396 to 494 ms, N550 were observed from 452 to 668, P900 from 668 to 900 ms and N_late from 820 to 1,098 ms. The brain responses to non-painful tactile stimulation during the REM period resulted in the following amplitudes of wave deflections. P50 ranged from -0.07 to 1.69 μV, N100 from 0.43 to -1.75 μV, P200 from 0.22 to 2.20 μV, N300 from -0.58 to -3.23 μV, P450 varied from 0.37 to 1.84 μV, N550 waveform was observed between 0.40 to -2.16 μV, P900 as 0.10 to 1.55 μV and finally N_late from -0.09 to -1.18 μV. The values are shown in table form with their standard deviations (Table 4).

Observing the related scalogram in the frequency-amplitude space, the peak Z dimension (bright red colors, see attached color bar) values are confined to the early stage of the post-stimulus time domain (Figure 4).

The REM specific activity of the brain as a response function to external stimulations are represented in Figure 4. Here, also the frequency-amplitude scalogram is provided.

DISCUSSION

Our project and its results are the first study examining external tactile stimulation assessed in the frequency specific domain in healthy individuals. A review of studies even with a broader scope reveals a limited number of studies within the somatosensory domain.[1,5,6]

Wakefulness recordings are reported as 8-13 Hz sinusoidal or 0.5-2 Hz conjugated eye movements in the literature. The sleep stage N1 presents 4-7 Hz oscillations, N2 as 11-16 Hz, whereas N3 shows 0.5 to 2 Hz oscillations.[4]

Our study incorporated the PS period rather than daytime wakefulness. This also enabled the extension of this recording into regular PSG. Accordingly, the evoked frequency response revealed higher activity of 0-5 Hz in 0.5 s to 1 s, and lower activity of 0-5 Hz within -1 to 2 s time range. As N1 and N2 sleep stages were regarded as LS, the cortical responses to tactile stimulations resulted in high activity in the 0-5 Hz frequency band in the 0.5 s to 1 s window, and a low activity in the 5-10 Hz band at 500 ms.

The DS (N3) results revealed lower activity in the lower frequency band during the early phase (0.5 s) and 0-5 Hz band high activity at the 1 s time mark. During the REM recordings, the 0 to 0.5 s period revealed high activity in the 5 to 15 Hz band.

The current study reveals external tactile processing in the form of frequency responses as well as sleep stage related oscillatory shifts.

The sleep literature contains a number of studies on amplitude and latency differences in the auditory modality used to assess the brain processing during sleep.[2,3,10] Similar to the current study, the brain responsiveness continued throughout the sleep stages including DS. Thus, the auditory and tactile processes can be effectively used as cognitive tools for sleep research. The current study expands the scope to PS, and also into frequency-amplitude space.

We propose that the current method proposed in this manuscript may pave the way to become a standard domain for enlightening the cortical processing during sleep as well as providing insight to automated sleep assessment research.

Sleep studies have long benefitted from electrophysiological signals, namely PSG. However, this heavily relies on sleep experts to evaluate hours long data. This data analysis is more on the appearance of waveforms in certain time frames etc. Thus, in a number of cases, inter-rater reliability or reproducibility can be questionable.

The time stamps of complex stimulations are also not available in these classical systems. Hence a new approach is necessary to provide further understanding of this domain. The tactile signals are of an interesting

Table 4. The REM sleep stage period non-painful tactile responses (recorded from Cz)

	Latency (ms) Mean ± SD	Amplitude (μV) Mean ± SD
P50	107.20±25.69	0.56±0.65
N100	154.00±16.68	-0.69±0.69
P200	231.80±20.14	1.14±0.64
N300	329.00±20.25	-1.94±0.83
P450	439.20±34.18	1.16±0.57
N550	558.00±75.05	-0.66±0.72
P900	769.80±59.94	0.50±0.43
N_late	959.60±95.53	-0.69±0.31

The latency periods (ms) and peak to peak maximal amplitudes (μV) are presented in columns. Each measurement is accompanied by the standard deviation values. SD: standard deviation.

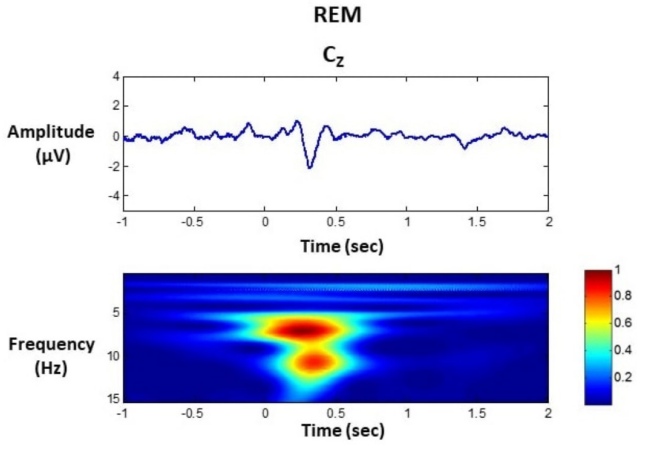

Figure 4. The average REM (rapid eye movements) sleep stage responses from 10 volunteers to non-painful tactile stimulations (applied to right-index and mid-finger tips) are presented from central electrode (Cz). The upper panel represents the electrophysiological waveform. Here, the vertical axis denotes amplitude in μV, and the horizontal axis shows time values (in seconds from -1 to 2 seconds). The "0" in time axis represents the time of tactile stimulation. The lower panel shows the scalogram in frequency and amplitude domains. The scalogram provides the frequency-time in horizontal axis while the vertical axis is denoted by frequency time (in Hz). The amplitude information is provided by the color bar next to the figure.

nature as they not only have an influx of information from the outside world, but also they have been widely used in BCI methods.[11]

The brain reveals to us not only the spontaneous activity of the background and even state changes (i.e. the shifts of sleep stages), but also the responsiveness of the brain to the external world. This relies on both sensory processing as well as cognitive capacity. The so-called sleep-tactile-relationship is a fresh step to address these issues.

The bottom-up to top-down processing of the brain paves the way for us to reveal brain connectivity and dynamic processing. The further tools that might be used may include the coherence, frequency domain approach as well as entropy.

Sleep is not a state of an unconscious brain. We have (similar to a number of other studies) hereby shown that even in DS, the brain is "open" to outside stimulation. Therefore, the brain continuously responds to the outside world even in a limited or altered capacity. It is no wonder that tactile stimulation is also a common practice to wake someone up in addition to the auditory stimulation. Here, we have paved the way to show the dynamics of the non-painful somatosensory domain in relationship to sleep stages.

An interesting phenomenon should also be addressed at this stage. The brain while being monitored with external stimulations, in fact, could alter its state due to the stimulus itself. Therefore, we may liken this to Schrodinger's cat, where observing a scientific phenomenon may itself be including alterations to the original state. However, the brain is the ultimate organ which serves as an external stimulation processor throughout our life cycle. No wonder one is regarded as dead only with the death of the brain.[12] The brain computer interface era is fast approaching so any objective data set with the same set of parameters across a healthy population by itself is a useful measure.

CONCLUSION

The responsiveness of the brain during sleep therefore can be regarded as a useful tool to shed light on the human brain. Finally, the current speculative approach to the brain for longer hibernation states etc. require objective screening of the brain in various states of brain functioning. Accordingly, our method could provide insight to somatosensory processing, disorders of the tactile nature, the brain in altered states etc.

MAIN POINTS

- Sleep studies constitute an increasingly important area in the field of human health.
- The current study is a pioneering one into how tactile stimuli are processed at every stage of sleep by frequency and amplitude analysis and also in comparison to immediately before sleep.
- This study may interest a wide audience of health-related scientists, sleep based neuroscientists, clinical and basic scientists, etc.
- In addition, the responses to tactile stimuli have been examined from an engineering point of view.
- Accordingly, we believe this manuscript will open a window to further sleep research methodology.

ETHICS

Ethics Committee Approval: This study was approved by the Institutional Ethics Evaluation Board [Dokuz Eylül University Non-Invasive Research Ethical Committee (approval number: 2011/16-16)].

Informed Consent: Consent of individuals was obtained before starting the recordings.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: G.I., M.O., A.O., Design: G.I., M.O., A.O., Supervision: M.O., A.O., Fundings: M.O., A.O., Materials: G.I., M.O., Data Collection and/or Processing: G.I., Analysis and/or Interpretation: G.I., Literature Search: G.I., M.O., A.O., Writing: G.I., M.O., A.O., Critical Review: G.I., M.O., A.O.

DISCLOSURES

Conflict of Interest: No conflict of interest was declared by the authors.

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