

The Influence of the Respiratory Cycle on the EEG

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Summary

In order to evaluate the influence of the respiratory cycle on the EEG, we compared the power spectral analysis of the EEG performed by fast Fourier transformation during inspirium and expirium in 10 healthy subjects. The measurement was performed during spontaneous breathing and then during eupnoe (0.25 Hz), bradypnoe (0.1 Hz) and tachypnoe (0.5 Hz) paced by a metronome. In the course of spontaneous breathing and bradypnoe, there was an increase in the delta power and in the total power in the anterior temporal region during inspirium in comparison with expirium. The eupnoe was characterized by an inspiratory decrease in the delta power in the parietal region and in the total power in the frontal region. The tachypnoe resulted in a decrease of the beta power in the central region and a decrease of the theta power in the posterior temporal and in the occipital region during inspirium. In comparison of the EEG in eupnoe, bradypnoe and tachypnoe, a decrease of spectral power of all spectral bands was found except for delta during faster breathing frequencies and *vice versa* with a significant difference which was found mostly between bradypnoe and tachypnoe, less frequently between eupnoe and tachypnoe.

Key words

Electroencephalogram • *Locus coeruleus* • Nucleus of the solitary tract • Respiration • Thalamocortical circuit

Introduction

Relationship between respiration and the EEG activity was first mentioned by Hobson (1967) in frogs which during excitement breath rhythmically and synchronously with the EEG. The oscillation of the amplitude of the EEG in man during the respiratory cycle was described by Faber *et al.* (1970) who found an increase of amplitude of the EEG curve during inspiration and an inverse response during expiration. The changes of respiration accompanying the onset of the EEG cyclic alternating pattern in sleep can be observed (Evans 1992). Nevertheless it is not clear whether the changes of brainstem autonomic centers cause simultaneous changes in the respiratory pattern and the arousal of the neocortex,

or if the changes of respiration, heart rate and blood pressure are an epiphenomenon of the neocortical arousal reaction (Maling 1986, Okada *et al.* 1991, Somers *et al.* 1993). The influence of forced alternate nostril breathing consisting of left nostril inspiration and right nostril expiration and then *vice versa* was studied in 18 subjects with the result of an increase of mean power in the beta and partially in the alpha band (Stančák and Kuna 1994). Another study showed that paced breathing at frequencies of 0.25 and 0.20 Hz enhanced mean power in the beta band and low-frequency beta power variability (0.12-0.04 Hz) and that total variability of alpha power was reduced in the right parietal and occipital electrodes during paced breathing at 0.1 Hz (Stančák *et al.* 1993).

In sporadic cases examined in our EEG

laboratory, prominent oscillation of the background EEG activity reflecting the respiratory cycle was accidentally observed (Bušek 2003). The clinical significance of this rare phenomenon remains uncertain. To elucidate whether or not there is some measurable oscillation of the EEG activity during the respiratory cycle in healthy subjects we compared the spectral power of the EEG in inspirium and expirium during spontaneous breathing and then during paced respiration at frequencies of 0.1, 0.25 and 0.5 Hz.

Methods

Ten young healthy volunteers (7 males and 3 females), age range from 20 to 39 years, mean age 28.3 ± 5.0 years were included in our study. The EEG was registered from 14 electrodes: F3, F4, F7, F8, T3, T4, T5, T6, C3, C4, P3, P4, O1, O2, according to international Jasper's 10-20 system. The parameters of computerized EEG registration were $100 \mu\text{V}/10 \text{ mm}$, high frequency filter 70 Hz, time constant 0.3 s, sampling rate 250 Hz. The respiratory cycle was recorded by a thermistor. The spectral power in inspirium and expirium at different breathing rates was evaluated. Firstly, the inspirium and expirium was compared when the subjects were breathing spontaneously and after that when the respiration was paced by a metronome – during eupnoe (0.25 Hz), bradypnoe (0.1 Hz) and tachypnoe (0.5 Hz). In order to maximally eliminate other influences on the EEG signal, only the neighbouring and artifacts-free EEG sequences of inspirium and expirium were included in the analysis. In each subject, 10 inspirations and 10 expirations were assessed, thus in all 100 inspirations and 100 expirations were analyzed.

We also compared the spectral power of the EEG between different breathing frequencies (paced eupnoe 0.25 Hz, bradypnoe 0.1 Hz and tachypnoe 0.5 Hz) irrespective of phase of the respiratory cycle. The values for this comparison were obtained by averaging the spectral power of all inspirations and expirations during individual breathing frequencies in each subject.

The spectral power was calculated by fast Fourier transformation which was decomposed into the following spectral components: delta (0.5-3.5 Hz), theta (4.0-7.5 Hz), alpha (8.0-12.0 Hz) and beta (12.5-30.3 Hz). The spectral power was assessed separately in different regions. The frontal region included mean activity from F3, F4, F7 and F8 electrodes, the central region from C3 and C4, the anterior temporal region from

T3, T4, the posterior temporal region from T5 and T6, the parietal region from P3 and P4 and the occipital region from O1 and O2 electrodes. The total spectral power including all spectral bands in the aforementioned regions, the total spectral power over the whole surface of the skull and mean values of spectral power of the individual above mentioned spectral bands over the whole surface of the skull were also evaluated.

Data are expressed as means \pm SD. The statistical analysis included analysis of variance (ANOVA), the Tukey honest significant difference test for the *post hoc* comparison, the t-test for dependent samples and the Shapiro-Wilks test. Some data had to be transformed by a logarithm to obtain a normal distribution.

Results

We found several significant changes of the spectral power of EEG activity in the course of the respiratory cycle, which were different during the tested breathing frequencies. The spontaneous breathing was considerably irregular and had a mean frequency of 0.2 ± 0.06 Hz, ranging from 0.1-0.29 Hz. Significant differences of the spectral power of the EEG between inspiration and expiration during spontaneous breathing were found in the anterior temporal region with an increase in the delta spectral band of 9.3 ± 11.9 % ($P < 0.05$) and in the total power of 4.4 ± 6.2 % ($P < 0.05$) during inspirium in comparison with expirium. In eupnoe, a decrease in the total power of 2.6 ± 3.2 % ($P < 0.05$) in the frontal region and a decrease in the delta band of 7.7 ± 7.6 % ($P < 0.05$) were found in the parietal region during inspirium. In bradypnoe, there was an inspiratory increase in the delta band of 17.0 ± 14.5 % ($P < 0.01$) and in the total power of 5.8 ± 6.0 % ($P < 0.05$) in the anterior temporal region. Compared to expirium, we found a reduction of 3.8 ± 4.0 % ($P < 0.05$) in the beta power in the central region during inspirium in tachypnoe; the power of the theta band was decreased by 6.4 ± 6.9 % ($P < 0.05$) in the posterior temporal region and by 6.8 ± 10.3 % ($P = 0.05$) in the occipital region. The tachypnoe further resulted in an inspiratory decrease of 4.5 ± 7.3 % ($P < 0.05$) in the mean theta power over the whole skull, but due to the fact that 95 % confidence interval of the I/E ratio (= the ratio of the value of spectral power in inspirium to the value in expirium) is too large including the value of 1.0, the statistical significance of the difference of this parameter between

inspiration and expiration is only borderline. The mean values of the spectral power in the regions where significant differences between inspiration and expiration were found are shown in the Table 1. The EEG changes in the Table 1 were also expressed as a mean of ratios of the spectral power in inspiration and expiration (the I/E ratio) and its 95 % confidence interval.

The EEG during eupnoe, bradypnoe and

tachypnoe significantly differed in the total power ($F=3.90$; $P<0.05$) over the whole skull, the total power in bradypnoe being significantly higher than in tachypnoe ($P<0.05$). The differences in the total power were found in the frontal region ($F=4.27$; $P<0.05$) and in the occipital region ($F=4.27$; $P<0.05$). In both cases the total power was higher in bradypnoe in comparison with tachypnoe ($P<0.05$).

Table 1. The mean values (\pm S.E.M.) of power in μV^2 of the spectral bands in the regions where significant differences between inspiration and expiration were found and the ratio of the value of spectral power in inspiration to the value in expiration (I/E ratio) and its 95 % confidence interval ($P=0.05$, $*P<0.05$; $**P<0.01$; t-test for dependent samples).

	Inspirium (I)	Exspirium (E)	I/E ratio 95 % conf. interval
SPONTANEOUS VENTILATION			
<i>Anterior temporal region</i>			
<i>delta</i>	179.8 \pm 8.1*	165.9 \pm 7.7	1.093 (1.022; 1.164)
<i>Total power</i>	375.6 \pm 10.1*	359.3 \pm 9.5	1.045 (1.009; 1.081)
EUPNOE (0.25 Hz)			
<i>Frontal region</i>			
<i>Total power</i>	320.6 \pm 4.8*	329.0 \pm 4.7	0.976 (0.957; 0.996)
<i>Parietal region</i>			
<i>delta</i>	93.2 \pm 2.0*	100.6 \pm 1.7	0.922 (0.846; 0.998)
BRADYPNOE (0.1 Hz)			
<i>Anterior temporal region</i>			
<i>delta</i>	150.7 \pm 3.2**	130.1 \pm 2.8	1.169 (1.080; 1.258)
<i>Total power</i>	353.8 \pm 7.7*	334.7 \pm 7.3	1.058 (1.022; 1.094)
TACHYPNOE (0.5 Hz)			
<i>Central region</i>			
<i>beta</i>	73.3 \pm 2.6*	76.3 \pm 2.8	0.963 (0.938; 0.988)
<i>Posterior temporal region</i>			
<i>theta</i>	36.1 \pm 1.0*	38.0 \pm 1.2	0.935 (0.893; 0.977)
<i>Occipital region</i>			
<i>theta</i>	41.6 \pm 1.4	45.4 \pm 1.7	0.932 (0.869; 0.995)
<i>Over the whole skull</i>			
<i>theta</i>	31.3 \pm 0.6*	33.1 \pm 0.8	0.955 (0.910; 1.000)

The spectral power of the alpha band changed significantly during different breathing frequencies over the whole skull ($F=7.46$; $P<0.01$), the value of the spectral power being significantly higher during bradypnoe than during tachypnoe ($P<0.01$) and in eupnoe in comparison with tachypnoe ($P<0.05$). When individual regions were assessed, significant differences were found in the frontal region ($F=9.34$; $P<0.01$), where the spectral power was higher in eupnoe ($P<0.01$) and bradypnoe

($P<0.01$) compared to tachypnoe, in the central region ($F=6.04$; $P<0.01$) with the spectral power being higher in eupnoe ($P<0.05$) and bradypnoe ($P<0.05$) than in tachypnoe, in the anterior temporal region ($F=5.62$; $P<0.05$) with higher spectral power in bradypnoe ($P<0.05$) compared to tachypnoe. In the parietal region ($F=6.22$; $P<0.01$) a higher spectral power was found in eupnoe ($P<0.05$) and bradypnoe ($P<0.05$) than in tachypnoe. Finally, a higher spectral power was observed

in eupnoe ($P<0.01$) and bradypnoe ($P<0.01$) in the occipital region ($F=10.05$; $P<0.01$) as compared with tachypnoe.

In the theta band, significant differences between individual breathing frequencies were found in the frontal region ($F=6.07$; $P<0.01$), the spectral power being significantly higher in bradypnoe than in tachypnoe ($P<0.01$) and in the central region ($F=4.63$; $P<0.05$), where the spectral power was higher in eupnoe compared to tachypnoe ($P<0.05$). In the posterior temporal region

($F=5.50$; $P<0.05$), the spectral power was higher in bradypnoe than in tachypnoe ($P<0.05$). Finally, higher spectral power was found in bradypnoe than in tachypnoe ($P<0.05$) in the occipital region ($F=5.22$; $P<0.05$).

We did not manage to find any statistically significant differences in the delta band between eupnoe, bradypnoe and tachypnoe. The values of the spectral power in the regions, where significant differences between individual breathing frequencies were found are shown in the Table 2.

Table 2. The mean values (\pm S.D.) of power in μV^2 of the spectral bands in the regions where significant differences between eupnoe (0.25 Hz), bradypnoe (0.1 Hz) and tachypnoe (0.5 Hz) were found (the difference from tachypnoe * $P<0.05$; ** $P<0.01$; t-test for dependent samples).

	Tachypnoe	Eupnoe	Bradypnoe
Total power			
<i>over the whole skull</i>	4813 \pm 1013	4893 \pm 824	5170 \pm 916*
<i>frontal region</i>	318 \pm 61	325 \pm 47	348 \pm 61*
<i>occipital region</i>	499 \pm 121	504 \pm 120	540 \pm 116*
The beta band			
<i>frontal region</i>	90.2 \pm 29.1	94.4 \pm 27.3	101.4 \pm 32.1**
<i>central region</i>	74.8 \pm 26.9	77.6 \pm 23.4	82.6 \pm 29.1*
<i>parietal region</i>	94.7 \pm 30.3	101.2 \pm 30.5	105.4 \pm 31.4*
<i>occipital region</i>	155.0 \pm 58.6	165.8 \pm 56.5	167.8 \pm 56.6*
The alpha band			
<i>over the whole skull</i>	83.3 \pm 29.1	93.4 \pm 27.7*	94.1 \pm 26.4**
<i>frontal region</i>	63.5 \pm 22.1	72.7 \pm 23.2**	73.1 \pm 22.7**
<i>central region</i>	51.8 \pm 17.6	56.9 \pm 17.3*	57.3 \pm 17.1*
<i>anterior temporal region</i>	52.1 \pm 14.4	56.8 \pm 11.7	59.3 \pm 13.8*
<i>parietal region</i>	71.9 \pm 25.7	83.3 \pm 24.4*	85.0 \pm 23.2*
<i>occipital region</i>	157.6 \pm 65.9	176.6 \pm 67.6**	174.7 \pm 62.9**
The theta band			
<i>frontal region</i>	30.7 \pm 4.8	31.6 \pm 5.2	33.7 \pm 7.3**
<i>central region</i>	24.0 \pm 3.4	27.1 \pm 5.5*	25.9 \pm 4.6
<i>posterior temporal region</i>	37.6 \pm 10.8	39.7 \pm 10.2	41.9 \pm 12.9*
<i>occipital region</i>	43.5 \pm 15.3	45.3 \pm 15.5	47.2 \pm 17.1*

Discussion

The impact of the respiratory cycle on the spectral power of the EEG differed between the tested breathing frequencies. The inspirium increased the power in the delta band in the anterior temporal region together with an increase in the total power in this area during bradypnoe and spontaneous breathing. The eupnoe and tachypnoe compared to spontaneous breathing and

bradypnoe caused to a certain extent an opposite effect on the EEG. During eupnoe the inspirium brought about a reduction of the delta power in the parietal region and of the total power in the frontal region. The inspirium in the course of tachypnoe resulted in the reduction of beta power in the central region and in a decrease in the theta band in the posterior temporal and in the occipital region. Thus the respiratory cycle was reflected mainly by changes of the spectral power of slower EEG frequencies;

the faster respiratory cycle (eupnoe and tachypnoe) results in its decrease, and the slower respiratory frequency (bradypnoe) leads to its increase during inspirium compared to the expirium. Based on this finding it may be hypothesized that the inspirium during the slower respiratory cycle enhances the synchronization in the thalamocortical circuit, while the inspirium during faster respiratory frequencies has an opposite effect.

The observation that the inspiratory and expiratory changes during spontaneous breathing and paced eupnoe are to some extent contradictory in spite of similar mean breathing frequencies can be, according to our opinion, explained by the fact that the spontaneous breathing was extremely irregular in the studied subjects, ranging from 0.1-0.29 Hz (= 6-17.4 breaths per minute). This fact makes the results obtained during spontaneous ventilation less comparable with paced breathing.

Apart from the EEG changes during the respiratory cycle we also observed differences in the spectral power between paced eupnoe, bradypnoe and tachypnoe. These differences were found in all spectral bands except for the delta band. In general, with decreasing respiratory frequency the value of spectral power in different regions increased and *vice versa*. Statistically significant differences were mostly found between bradypnoe and tachypnoe and less frequently between eupnoe and tachypnoe. The differences between bradypnoe and eupnoe were small and not significant.

The influence of respiration on EEG activity may be mediated by a modulation of the thalamocortical circuit by different pathways originating in brainstem structures. The neurons in the medullary lateral tegmental field, among them the ventral respiratory group being the most important, have a pivotal role in respiratory control. The ventral respiratory group is in the close anatomical vicinity of neurons of other functional systems, e.g. cardiovascular neurons, the nucleus of the solitary tract, the neurons of the so-called common brainstem system of the reticular formation and of the C1 adrenergic cell group that has projections to the nucleus of the solitary tract, the locus coeruleus, and the hypothalamus (Hopkins and Ellenberger 1994, Spyer 1999). The locus coeruleus plays probably the most important role in influencing the cortical EEG activity. Electrical stimulation of the noradrenergic locus coeruleus leads to desynchronization of the EEG (Berridge and Foote 1991), induces the neocortical low voltage fast activity, and suppresses the large irregular slow activity (Dringenberg and Vanderwolf 1997). This effect is abolished after

administration of the antimuscarinic agent scopolamine and of the beta-antagonist timolol. This means that the noradrenergic and muscarinic receptors are involved in the EEG-activating effect of the projections from the locus coeruleus, which exerts its desynchronizing effect on cortex *via* the cholinergic medial septum (Berridge and Foote 1994, 1996, Berridge *et al.* 1996, Liljenström and Hasselmo 1995). It is important to note that the activity of locus coeruleus is modulated synchronously with the respiratory cycle with transient increase in discharge frequency accompanying the initial phase of inspirium followed by a transient expiratory inhibition of the discharge (Guyenet *et al.* 1993, Oyamada *et al.* 1998). The length of inhibitory phase is progressively shortened as the respiratory frequency increases. This fact could explain the observed decrease of EEG spectral power with increased breathing frequency in our study – the desinhibited locus coeruleus would exert more pronounced desynchronizing effect on the cortex. The inhibitory effect of expirium is probably mediated by an $\alpha 2$ -adrenergic pathway from C1 neurons, which are excited during expirium and the excitation of locus coeruleus in the course of inspirium originates from glutamate-mediated input from the nucleus paragigantocellularis within the medulla (Oyamada *et al.* 1998).

Another link between the respiratory neurons and the neocortex represents the nucleus of the solitary tract (NTS). As mentioned earlier, the NTS receives direct innervation from the bulbar respiratory nuclei. In rats, the electrical stimulation of the NTS synchronizes the EEG by increasing the power of 4-6 Hz activity (Golanov and Reis 2001). The activity of the NTS may also be influenced by the Hering-Breuer reflex, which is mediated by receptors in the large airways attached to myelinated nerves, which are stimulated by physiological stretch during lung inflation. The afferent pathway of this reflex terminates in the NTS, which influences the heart rate and might perhaps mediate the EEG changes during the respiratory cycle (Hainsworth 1996).

Some studies have shown that the communication between neuronal populations of different functional systems in the brainstem is reflected by modifications of their spontaneous oscillatory activity and that the synchronization of the oscillatory rhythm in several neuronal populations increases their influence on a common effector system (Lambertz and Langhorst 1998). It has also been shown that there is a correspondence between oscillatory rhythm of some brainstem neurons and the EEG. The complexity of all

aforementioned mechanisms probably results in the fact that different respiratory frequencies can exert an opposite effect on the EEG spectra during individual phases of the respiratory rhythm.

We do not suppose that the observed EEG findings in our study result from changes of pCO₂ or pO₂ as in the case of apnoe or hyperventilation used as an activating method in the clinical practice (van der Worp *et al.* 1991, Kraaier *et al.* 1992, Achenbach *et al.* 1994, Yamatani *et al.* 1994, Schellart and Reits 1999). We analyzed a short initial part of each sequence with a

tested respiratory pattern, where no biochemical changes should occur. When we evaluated the differences between inspirium and expirium always the neighboring inspirium and expirium was analyzed, so that any potential long-lasting change of the EEG would influence both phases of the respiratory cycle in the same manner.

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