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Effect of lateral hypothalamic lesion on sleep-waking pattern and EEG power spectra in the rat

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Abstract. Bilateral, electrolytic lesion of the lateral hypothalamus (LH) in rats produces hyposomnia and qualitative EEG changes which are difficult to assess by conventional visual inspections of electroencephalograms. In the present study the spectral analysis of EEG was applied in LH-lesioned rats and confronted with a standard visual scoring method. One-hour samples of hippocampal and cortical EEG were taken from the light part of the circadian cycle before and after electrolytic or sham LH damage. In half of the LH-lesioned rats a power spectral analysis was performed using a Fast Fourier Transform routine at 1 Hz bands from 0.5 to 25 Hz; in the other half, as well as in the sham-lesioned group, EEG records were visually scored for the amount of waking, slow wave sleep and paradoxical sleep. Significant hyposomnia effects were found in LH-lesioned rats. Power spectral analysis of hippocampal EEG revealed a significant increase in power density at 4-6 Hz and a reduction at 7-10, 14-17, 19-22 and 23-24 Hz. In neocortical EEG there was a significant increase in power density at 5-6 Hz band and a reduction at 7-8 Hz. The results are discussed in the context of the effects of selective destruction of the specific neurotransmitter systems occupying the LH area.

Short communication

Key words: EEG, LH lesion, hyposomnia, power spectral analysis

Bilateral, electrolytic lesion of the lateral hypothalamus (LH) produces disruption of the sleep--waking pattern consisting of an increase in waking time and a decrease in sleep, both slow wave (SWS) and paradoxical (PS) (Danguir and Nicolaidis 1980, Trojniar et al. 1987, 1990, Jurkowlaniec et al. 1994). Hyposomnia may be accompanied by an abnormal cortical hypersynchronization (Trojniar et al. 1990) and by a reduction in the frequency of hippocampal theta rhythm both during waking and PS (Jurkowlaniec et al. 1989). These findings were based on visual scoring of the rats EEG. In this report we present the power spectral analysis of EEG in LH-lesioned rats and confront it with the effects of LH damage as revealed by a conventional visual analysis. As has been found in numerous studies, spectral analysis of EEG may disclose effects that could not be recognized by a conventional sleep--waking scoring procedure. For example, it may give a more precise quantitative expression of abnormal cortical and hippocampal synchronization found in LH hyposomniac rats.

The experiment was done on 22 male Wistar (Lod) rats implanted with bilateral, chronic electrodes for EEG recording over the occipital cortex and in the dorsal hippocampus, and with lesion electrodes bilaterally in the tuberal part of LH. Stereotaxic coordinates were as follows: cortex - 10.0 mm posterior to bregma, 3.0 mm lateral to the midline and 1.0 mm below the skull surface; hippocampus 2.5-2.8 mm posterior to bregma, 2.5 mm lateral to the midline and 2.5-4.0 mm below the skull surface; LH - 1.5-1.7 mm posterior to bregma, 1.7-2.0 mm lateral to the midline and 8.4 -9.0 below the surface of the skull. A silver wire EMG electrode in the neck muscles, the earth screw electrode and the reference electrode were also implanted.

After the rats recovered from surgery and were properly adapted to the experimental conditions, cortical and hippocampal EEG was recorded using a 16-channel Medicor electroencephalograph (bandpass 0.4-70 Hz). The recordings were done in 260 x 260 x 400 mm glass cages placed in a sound attenuating chamber for one hour daily (morning hours) for 3 days (baseline conditions). Then, the animals were divided into 3 groups. Under short--lasting anaesthesia (50 mg/kg of Ketamine i.m.) 16 animals (2 experimental groups, $n = 8$ each) were subjected to bilateral electrolytic lesions of LH (anodal current, 2 mA/15 s), and 6 rats were sham-lesioned (control group). EEG was recorded in all rats on the second postlesion day when the LH hyposomnia is usually most intense. Half of the LH-lesioned rats were subjected to the automatic analysis of the EEG. Their prelesion and postlesion EEG signals were amplified, filtered at 0.4-70 Hz, passed through the AD converter (sampling rate 102.4 Hz) of an IBM PC computer and collected at the magneto-optic disk. Power spectral analysis was performed using a Fast Fourier Transform routine (SOMNOSCAN package). At the end of the experiment, percentage values of power density were computed for the consecutive 5-s epochs in the frequency range of 0.4 to 25 Hz at 1 Hz bands.

In the other half of the experimental rats, as well as in the sham-lesioned group, EEG records were scored visually and counted for the amount of waking, SWS and PS according to the procedure described in detail in our previous paper (Trojniar et al. 1987). The amount of the particular type of EEG activity was expressed as a percentage of the total recording time.

After completion of the experiment, localization of the lesions was verified using standard histological procedures.

Visual scoring of EEG records of LH-lesioned rats revealed an increase in waking from the baseline, 46.3±4.7% of the total recording time, to 83.9±6.5% ($P \leq 0.001$) after LH damage, which was accompanied by a decrease in SWS (from 44.6±3.4% to 13.6±4.9% , $P \leq 0.001$), and PS (from 9.1±1.7% to 2.4±1.7% , $P \leq 0.001$). No significant effect on the sleep-waking pattern was found in the sham-lesioned rats, and the respective values in this group before and after the lesion were: waking - 46.9±6.1% and 43.5±7.2% , SWS - 44.5±4.8% and 46.7±5.3%; and PS - 8.5±1.5 and 9.8±2.6%. These results, based on 1 h samples of the day-time EEG, are comparable with those of our previous studies (Trojniar et al. 1987, 1990), as well as with the

sleep-waking distribution in 12 h (Jurkowlaniec et al. 1994) and in 24 h (Danguir and Nicolaidis 1980) EEG samples of LH damaged rats. As we argued in our previous paper (Jurkowlaniec et al. 1994) 1 h EEG samples taken from the light part of the circadian cycle are sufficient to diagnose the presence of the LH-hyposomnia.

Power spectral analysis was performed in another group of rats bearing similar (histologically verified) LH-lesions, separately for hippocampal and neocortical EEG at 1 Hz bands from 0.4 to 25 Hz (the whole registered spectrum). The results (frequency distribution calculated as a percent of the total power) are shown in Table I. In the hippo-

TABLE I

Power density distribution (% of total power) in the 1 Hz frequency bands of the hippocampal and neocortical EEG. Asterisks indicate significant differences between the prelesion and postlesion data ($P \leq 0.05$, Wilcoxon matched pairs ranks test)

	EEG power density (% of total power)			
	hippocampus		neocortex	
frequency (Hz)	prelesion (n=8) mean±SE	postlesion (n=8) mean±SE	prelesion (n=8) mean±SE	postlesion (n=8) mean±SE
0.4-1.0	14.46±1.03	12.95±1.11	12.27±1.15	11.77±1.54
1.1-2.0	17.89±1.04	16.09±0.94	18.71±1.44	20.51±2.08
2.1-3.0	12.99±0.65	12.19±0.71	14.96±0.68	15.00±0.89
3.1-4.0	9.48±0.49	9.15±0.41	10.74±0.63	10.46±0.75
4.1-5.0	7.94±0.43	9.73±0.55*	8.53±0.61	8.66±0.56
5.1-6.0	7.94±0.44	14.82±2.46*	7.79±0.64	10.16±1.37*
6.1-7.0	9.42±0.86	8.96±0.63	8.53±0.94	6.84±0.65
7.1-8.0	6.96±0.63	4.76±0.32*	5.95±0.56	3.97±0.37*
8.1-9.0	3.80±0.23	3.05±0.20*	3.25±0.17	2.77±0.35
9.1-10.0	2.52±0.16	2.22±0.16*	2.23±0.11	2.11±0.31
10.1-11.0	1.84±0.12	1.82±0.14	1.70±0.10	1.70±0.25
11.1-12.0	1.45±0.11	1.42±0.11	1.41±0.09	1.51±0.28
12.1-13.0	1.17±0.10	1.08±0.09	1.16±0.09	1.30±0.30
13.1-14.0	0.93±0.08	0.85±0.08	0.94±0.08	1.01±0.23
14.1-15.0	0.75±0.06	0.65±0.06*	0.72±0.06	0.78±0.17
15.1-16.0	0.61±0.05	0.52±0.04*	0.56±0.04	0.59±0.09
16.1-17.0	0.49±0.05	0.41±0.03*	0.44±0.03	0.47±0.06
17.1-18.0	0.40±0.04	0.34±0.03	0.37±0.03	0.42±0.06
18.1-19.0	0.33±0.04	0.27±0.02	0.31±0.03	0.38±0.06
19.1-20.0	0.28±0.03	0.23±0.02*	0.28±0.03	0.30±0.05
20.1-21.0	0.23±0.03	0.19±0.01*	0.24±0.03	0.27±0.05
21.1-22.0	0.19±0.02	0.16±0.01*	0.21±0.03	0.22±0.04
22.1-23.0	0.16±0.02	0.13±0.01	0.17±0.02	0.19±0.04
23.1-24.0	0.14±0.02	0.11±0.01*	0.13±0.01	0.16±0.03
24.1-25.0	0.12±0.01	0.09±0.01	0.11±0.01	0.14±0.04

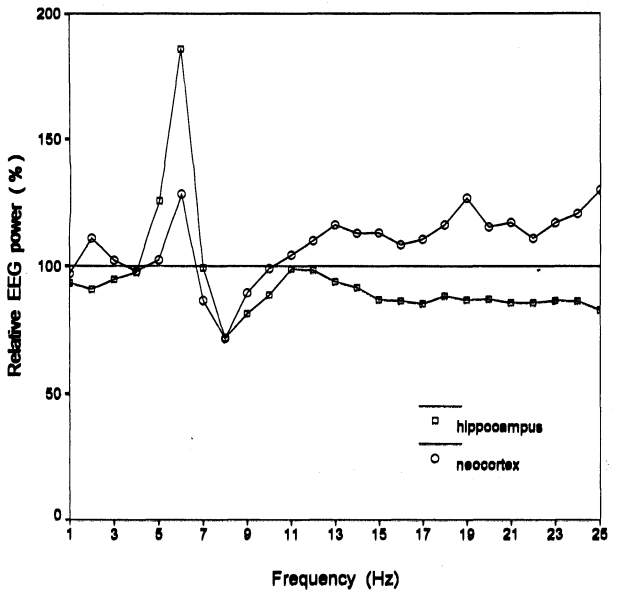

Fig. 1. Relative EEG power densities for the neocortical and hippocampal spectrum power. All values are expressed relative to the EEG power densities in the control (prelesion) conditions (= 100%).

campal EEG there was a significant increase in power density at 4-6 Hz with a simultaneous reduction of density at 7-10, 14-17, 19-22 and 23-24 Hz. These results are compatible with findings from a visual analysis that in the LH-lesioned rats the low frequency theta rhythm predominated in the hippocampus (Kolb and Whishaw 1977, De Ryck and Teitelbaum 1978, Jurkowlaniec et al. 1989). In the neocortical EEG the only significant change was an increase in power density at 5-6 Hz band and a reduction at 7-8 Hz. Figure 1 illustrates the mean values of the relative EEG power density (for each animal power densities were calculated relative to the mean values in the prelesion period taken as 100%). Clear enhancement of the neocortical EEG power spectra at the higher frequencies is visible, although these changes do not reach statistical significance.

Histological verification of the brains showed rather large destruction of the LH area at the level of the tuberal and anterior hypothalamus with partial involvement of the neighbouring tissue of the zona incerta, internal capsula and the ventral thalamus. No marked difference in the localization of the lesions was found between the two experimental groups (visually and automatically analysed).

We are not aware of any other study employing EEG spectral analysis in LH-lesioned rats. However, there are data on the selective disruption of neuronal systems passing through LH, which undoubtedly must have been damaged by our electrolytic lesions. The most interesting in the context of the present results are studies concerning the serotonergic and cholinergic systems. Serotonin depletion reduces sleep, both SWS and PS, and increases the amount of waking (Jouvet 1972, Ursin et al. 1989, Bjorvatn and Ursin 1994). The cortical power spectra calculated for the distinguishable stages of the vigilance state showed reduction of the power densities especially pronounced at the higher frequencies both during waking and SWS (Bjorvatn and Ursin 1994). Cholinergic insufficiency also results in increased waking and reduced SWS and PS (Szymusiak et al. 1993). In this case the resemblance to the effect of LH lesion is even greater as both manipulations affect the sleep-waking relationship selectively during the light part of the circadian cycle (Szymusiak et al. 1993, Jurkowlaniec et al. 1994). However, no change in the EEG power densities was found in acetylocholine deficient rats (Szymusiak et al. 1993). Thus, although serotonergic, cholinergic and lesion-induced lateral hypothalamic inactivations give similar hyposomnia effects the EEG power spectra changes after these manipulations do not follow the same pattern. The difference may be indicative of a different mechanism for each type of hyposomnia. However, to obtain more direct comparisons, in future studies the power spectral analysis in LH rats should be repeated for sleep and waking separately.

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