

Electroencephalogram asymmetry and spectral power during sleep in the northern fur seal

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SUMMARY The fur seal (*Callorhinus ursinus*), a member of the Pinniped family, displays a highly expressed electroencephalogram (EEG) asymmetry during slow wave sleep (SWS), which is comparable with the unihemispheric sleep in cetaceans. In this study, we investigated the EEG asymmetry in the fur seal using spectral analysis. Four young (2–3 years old) seals were implanted with EEG electrodes for polygraphic sleep recording. In each animal, EEG spectral power in the frequency range of 1.2–16 Hz was computed in symmetrical cortical recordings over two consecutive nights. The degree of EEG asymmetry was measured by using the asymmetry index [$AI = (L - R)/(L + R)$, where L and R are the spectral powers in the left and right hemispheres, respectively]. In fur seals, EEG asymmetry, as measured by the percent of 20-s epochs with absolute $AI > 0.3$ and > 0.6 , was expressed in the entire frequency range (1.2–16 Hz). The asymmetry was significantly greater during SWS (25.6–44.2% of all SWS epochs had an absolute $AI > 0.3$ and 2.1–12.2% of all epochs had $AI > 0.6$) than during quiet waking (11.0–20.3% and 0–1.9% of all waking epochs, respectively) and REM sleep (4.2–8.9% of all REM sleep epochs and no epochs, respectively). EEG asymmetry was recorded during both low- and high-voltage SWS, and was maximal in the range of 1.2–4 and 12–16 Hz. As shown in this study, the degree of EEG asymmetry and the frequency range in which it is expressed during SWS in fur seals are profoundly different from those of terrestrial mammals and birds.

KEYWORDS asymmetry index, eeg asymmetry, northern fur seal, pinnipedia, spectral analysis, unihemispheric sleep

INTRODUCTION

Cetaceans display an unusual form of sleep called unihemispheric slow wave sleep (USWS; Lyamin *et al.*, 2002b, 2004; Mukhametov, 1984, 1987; Mukhametov *et al.*, 1977; Ridgway, 2002). Pinnipeds are a group of semi-aquatic mammals, belonging to three families: Otariidae, Phocidae and Odobenidae. All pinnipeds can sleep both on land and in water. Fur seals and sea lions (members of the family Otariidae) display both bilateral slow wave sleep (SWS), and SWS with interhemispheric electroencephalogram (EEG) asymmetry.

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When fur seals are on land, their SWS is primarily bihemispheric, as seen in terrestrial mammals. However, when seals sleep in water EEG asymmetry significantly increases, and resembles USWS of cetaceans (Lyamin and Chetyrbok, 1992; Lyamin and Mukhametov, 1998; Lyamin *et al.*, 2002a; Mukhametov *et al.*, 1985). Evident interhemispheric EEG asymmetry has not been recorded during SWS on land or in water in seals belonging to the family Phocidae (Castellini *et al.*, 1994; Lyamin *et al.*, 1993; Mukhametov *et al.*, 1984).

There are some apparent similarities between the phenomenology of sleep in cetaceans and fur seals. USWS in dolphins can occur during swimming (Mukhametov, 1984; Mukhametov *et al.*, 1977). When fur seals sleep in water they usually float on their sides and constantly paddle with one foreflipper. During these times, the hemisphere contralateral to

the paddling flipper is more desynchronized (awake) than the ipsilateral hemisphere (Lyamin and Mukhametov, 1998). This suggests an association between motion and USWS both in cetaceans and otariids. Fur seals can sleep briefly, opening one eye while the other eye remains closed (Lyamin *et al.*, 2004). These episodes are usually correlated with interhemispheric EEG asymmetry; the hemisphere contralateral to the open eye is awake or in a state of lower voltage SWS and the hemisphere contralateral to the closed eye is in a state of higher voltage SWS. A similar association between USWS and eye state has been described in the bottlenose dolphin and the beluga (Lyamin *et al.*, 2002b, 2004). Therefore, maintenance of visual contact with conspecifics and detection of predators may be an adaptive advantage of USWS in fur seals and cetaceans. Rapid eye movement (REM) sleep has not been convincingly shown to be present in cetaceans (Mukhametov, 1984). Interestingly, long episodes of REM sleep (up to 15 min) have been recorded in fur seals while sleeping on land, whereas only brief (< 5 s long) episodes of REM sleep have been usually observed when fur seals were kept in water over a course of 2–3 weeks (Lyamin and Mukhametov, 1998). Fur seals display USWS, bilateral SWS and REM sleep which allows for comparisons of these behavioral states within a single animal, making them an ideal species to study the mechanisms of sleep control.

Prior to this study, sleep stage scoring and estimates of EEG asymmetry in fur seals were assessed visually. Sleep in fur seals has not yet been investigated using continuous long-term EEG spectral analysis as it has been for several terrestrial mammalian (mainly rodents; e.g. Borbely *et al.*, 1984; Huber *et al.*, 2000; Tobler and Deboer, 2001; Tobler *et al.*, 1993) and avian species (e.g. Amlaner and Ball, 1994; Rattenborg *et al.*, 1999, 2000, 2001). Therefore, our primary objectives were to quantify the degree of EEG asymmetry in different frequency ranges in the fur seal and to compare the expression of this asymmetry with that of terrestrial mammals and birds.

METHODS

Animals

Data were collected from four northern fur seals (*Callorhinus ursinus*; one male and three females; 23–25 kg, 2–3 years old). The seals were captured on the Commander Islands one year before the study and were well adapted to captivity. All studies were conducted at the Utrish Marine Station of the Severtsov Institute of Ecology and Evolution (Black Sea, Russia) and were approved by the VA-GLAHS Sepulveda and UCLA Animal Research Committees.

Three days before surgery, the seal to be studied was moved to a 1.5 × 1.5-m² enclosure located in a sound-attenuated room. Seals were fed fish twice per day (08:00–09:00 and 18:00–19:00 hours) and sprayed with water for 15–20 min after each feeding. During the daytime (08:00–18:00 hours), the enclosure was illuminated by using bright electric lamps (400–500 lux at floor level). At night, the level of illumination

was reduced (≤ 50 lux at floor level). Room temperature during recording varied between 20 and 25 °C.

Surgery

Aseptic surgery was performed on seals anesthetized with isoflurane (1–3%). Rectal temperature, heart rate, respiration rate and oxygen saturation were monitored continuously during the surgery. Three pairs of stainless steel screws (1 mm in diameter) were implanted epidurally over bilaterally symmetrical occipital (15 mm posterior to bregma and 10 mm lateral to the midline), parietal (at the level of bregma and 20 mm lateral to the midline) and frontal (10 mm anterior to bregma and 10 mm lateral to the midline) cortical areas and served as EEG electrodes. One additional screw served as the indifferent electrode and was implanted along the midline above the nasal cavity. Four teflon-coated multistranded stainless steel wires (0.3 mm in diameter) were implanted into the neck musculature to record electromyogram (EMG). Two pairs of nichrome-insulated wires (0.5 mm in diameter) were placed into an orbit along the nasal wall for electrooculogram (EOG) recordings. All electrodes were soldered to a plug and cemented to the skull with acrylic cement. All seals were allowed 4–6 days to recover before recording began. During this time, the seals were given antibiotics and analgesics twice per day with fish. Seals resumed eating fish within 2–5 days of the surgery. By the end of the second day after surgery, all animals appeared in good condition, showing well-coordinated movements and paying attention to the activity around the enclosure.

Experimental protocol and data acquisition

After surgery, each seal was returned to the experimental enclosure, in which it was housed alone during the entire period of recording. Each animal was connected to a polygraph by using low-noise coaxial cables. EEG from two symmetrical pairs of cortical electrodes (fronto-occipital or fronto-parietal), EMG and EOG were continuously recorded for several days. Each seal was continuously videotaped and observed by an experimenter in an adjoining room. To attenuate any noise made in the room and thereby decrease the possibility of disturbing the animal, we played sounds of ocean waves (50–60 dB) throughout the experiment.

Bipolar EEG recordings from each hemisphere were band pass filtered (0.3–30.0 Hz), amplified, digitally sampled at 200 Hz and stored using CED1401 plus and Spike 2 Software (Cambridge Electronic Design, Cambridge, UK). In three seals, EEG spectral power was computed in symmetrical frontal–occipital bipolar recordings in 5-s epochs by using fast Fourier transform (FFT) in the frequency ranges of 1.2–4, 4–8, 8–12 and 12–16 Hz using Spike 2 software. In one seal, the EEG from the left fronto-occipital derivation was contaminated with occasional artifacts. Therefore, we computed the EEG spectral power in symmetrical fronto-parietal bipolar recordings. To characterize EEG asymmetry during sleep, we

used two periods of continuous 12-h recording obtained between 20:00 and 08:00 hours across two consecutive nights. During the daytime, seals were occasionally disturbed by noise from outside of the laboratory and as such these data were excluded from the analysis. To characterize spectral composition of EEG during different behavioral states, power spectra measures in each seal were computed during one night in 0.8 Hz bins in the range of 1.2–16 Hz.

Scoring behavioral states and EEG spectral analysis

For each seal, active waking (AW), quiet waking (QW), SWS and REM sleep were scored visually in 20-s epochs, according to the conventional criteria used in our previous studies (Lyamin *et al.*, 2002a; Mukhametov *et al.*, 1985). AW was scored when seals were moving around within the enclosure, grooming or feeding. The epochs during which the animals were laying or sitting on the floor occasionally looking around or changing positions were considered QW. SWS was scored when a low- or high-voltage-synchronized EEG appeared in at least one of the two symmetrical recordings. SWS was subdivided into low-voltage (slow waves and spindles exceeded waking EEG amplitude by at least 1.5 times, but waves of maximal amplitude occupied less than 50% of the epoch time) and high-voltage (slow waves of maximal amplitude occupied more than 50% of the epoch time). REM sleep was scored when low-voltage EEG, typical of waking, was present with a lower (compared with SWS) and occasionally atonic neck EMG. Muscle jerks, body twitches and REMs accompanied REM sleep, as indicated by visual observations and polygrams. Duration of SWS and REM sleep episodes was calculated for the second recording night as the number of consecutive 20-s epochs scored as SWS and REM sleep, respectively. Additionally, to allow comparisons with our prior published data in other pinniped species (Lyamin and Chet-yrbok, 1992; Lyamin and Mukhametov, 1998; Lyamin *et al.*, 1993, 2002a), the duration of SWS episodes was also calculated allowing 100 s or less interruption by QW.

Five-second epochs were visually inspected and epochs with artifacts in the EEG were excluded from further analysis. The majority of excluded epochs represented AW and a portion of QW (35–50% of all QW epochs across seals) during which movements occurred. Whenever three or four of four consecutive 5-s epochs were artifact free, the spectral power was averaged for the artifact-free epochs and correlated with the visual scoring data in corresponding 20-s epochs. In preliminary experiments, we found differences in the EEG power across seals and between both hemispheres within each seal, presumably resulting from small variations in electrode impedance and distance from the cortex. Therefore, we standardized EEG power in each of the four frequency bands (1.2–4, 4–8, 8–12 and 12–16 Hz) to the average power in the same band, in the same hemisphere, during REM sleep. We chose to standardize to REM sleep instead of to QW because the majority of REM sleep epochs were artifact free. We chose not to standardize to the average power in the same

hemisphere during SWS (Rattenborg *et al.*, 1999, 2001) because the total amount of sleep in two hemispheres and the spectral power in the range of 1.2–4 Hz in the same seal could vary between days and nights (Lyamin and Mukhametov, 1998).

At the beginning of each night, polygraphic recordings, approximately 2-h in length, which included at least one episode of high-voltage SWS, were scored visually in each seal as described above. Upon correlating the visual scoring data with the spectral analysis data for each seal, we found that the standardized power in the range of 1.2–4 Hz was < 2 for 92–96% of the waking epochs in the right and left hemisphere, respectively, and > 2 in more than 88% of all SWS epochs. A standardized power > 10 corresponded to high-voltage SWS in 80% or more of the cases scored visually. Ratios of > 2 and < 10 allowed for the detection of, on average, 75% of the low-voltage SWS that was scored visually. Therefore, the 1.2–4 Hz power threshold of 2 and 10 were applied to score ‘no SWS’, SWS1 and SWS2 in each seal. All ‘no SWS’ epochs were then inspected visually and subdivided into QW or REM sleep.

To estimate the expression of interhemispheric EEG asymmetry, we used the asymmetry index (AI). It was calculated for 20-s QW, SWS1, SWS2, SWS (SWS1 + SWS2) and REM sleep epochs in four frequency ranges (1.2–4, 4–8, 8–12 and 12–16 Hz) as follows: $AI = (L - R)/(L + R)$, where L and R are standardized spectral powers in the left and right hemispheres, respectively (spectral power in each hemisphere was divided by the average power in the same hemisphere in the same frequency range during REM sleep). To evaluate the laterality of the EEG between the left and right hemispheres in different frequency bands, we calculated the proportion of 20-s epochs with $AI > +0.3$ and $AI < -0.3$ during each recording night. To measure the degree of EEG asymmetry, we compared the percentage of epochs with absolute $AI > 0.3$ and $AI > 0.6$. In our preliminary study (Pokidchenko *et al.*, 2005), we found that in the rat most 20-s epochs, irrespective of behavioral state, had an absolute $AI < 0.3$ in the range of 1.2–4 Hz (88–99% of all W, SWS and REM) and no epochs had an absolute $AI > 0.6$. By contrast, in dolphins, 80% and 60% of SWS had absolute $AI > 0.3$ and $AI > 0.6$ respectively. Sleep in rats is traditionally considered bilaterally symmetrical when compared with the USWS of dolphins. Visual inspection of polygrams in fur seals confirmed that SWS epochs with an absolute $AI > 0.3$ were usually characterized by noticeable differences in the EEG of the two hemispheres and epochs with an $AI > 0.6$ corresponded to profound EEG asymmetry (Fig. 1). Therefore, we considered that the number of sleep epochs with an absolute $AI < 0.3$ would be an estimate of the bilaterally symmetrical EEG pattern and that the number of epochs with absolute $AI > 0.3$ and $AI > 0.6$ would represent an estimate of the asymmetrical and highly asymmetrical (or rather unihemispheric) EEG pattern, respectively. The duration of SWS episodes with interhemispheric EEG asymmetry (or asymmetrical SWS, ASWS) was calculated as the number of consecutive 20-s epochs with an absolute $AI > 0.3$.

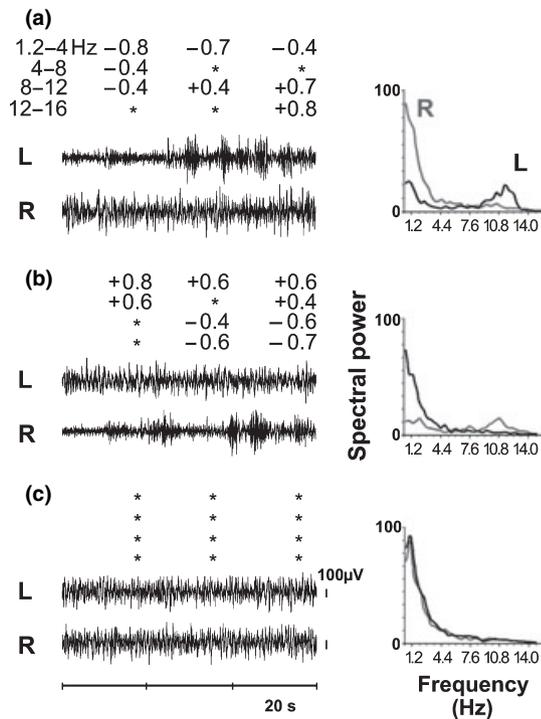


Figure 1. Representative examples of interhemispheric EEG asymmetry and spectral power distribution during slow wave sleep (SWS) in a fur seal (1-03). EEG polygrams (60 s) are displayed on the left-hand side and represent an episode of (a) asymmetrical SWS with higher voltage slow waves in the right (R) hemisphere, (b) asymmetrical SWS with higher voltage slow waves in the left (L) hemisphere and (c) bilaterally symmetrical high-voltage SWS. The polygrams were recorded during one night. The numbers above each polygram correspond to the asymmetry index (AI) of the spectral power in two hemispheres calculated for each of the four frequency ranges (1.2–4, 4–8, 8–12 and 12–16 Hz) in 20-s epochs as described in the Methods and Results sections. An asterisk denotes those epochs in which the AI was > -0.3 or $< +0.3$ indicating no or only subtle EEG asymmetry. Note that the absolute AI was < 0.3 for all frequency ranges during bilateral SWS, whereas the absolute AI was > 0.3 for the majority (17/24) of the asymmetrical SWS epochs. The graphs to the right of the polygrams display the distribution of absolute spectral power ($\mu\text{V}^2/0.8 \text{ Hz}$) in the range of 1.2–16 Hz in the R and L hemispheres for the corresponding 60-s polygrams.

Statistical analysis

All statistical comparisons were performed in four seals. The difference between the amount of SWS and REM sleep during the two recording nights was measured using paired *t*-test. Differences between behavioral states and the frequency ranges for the EEG spectral power and for the percent of epochs with an absolute AI > 0.3 or AI > 0.6 were tested using one- and two-way ANOVAS (factors ‘behavioral state’ and ‘frequency range’). The contrast between paired values was tested by using the *post hoc* Tukey test or paired *t*-test. Differences between proportions of epochs with AI $> +0.3$ and AI < -0.3 was evaluated with Z-test. A value of $P < 0.05$ was required to reach statistical significance. To avoid inflating the sample size and to allow comparison of parameters with similar sample size, in each animal we used 60 randomly chosen epochs of

waking and sleep stages during each recording night or 30 epochs from each of the two recording nights (explained in the results), except for in seal 2-02. This animal displayed the smallest amount of REM sleep and only 16 REM sleep epochs were artifact free on the first recording night. In the other three seals, the total number of epochs varied between 62 (REM sleep epochs during night 2 in seal 2-02) and 750 (SWS epochs in seal 3-03 during night 1) depending on the behavioral state and the night of recording.

RESULTS

Sleep variables and phenomenology

Fur seals prefer sleeping while lying on their sides on the floor or sitting and leaning against the enclosure. SWS occurred while in both of these sleeping positions. REM sleep was recorded only when animals were lying and usually followed SWS. Fur seals studied here slept between 34% and 74% of the night-time. The average amount of SWS and REM sleep in each seal during the two recording nights were not significantly different (paired *t*-test, $P > 0.05$ both for SWS and REM sleep), with the average amount accounting for $47.4 \pm 5.4\%$ and $5.4 \pm 0.5\%$ of the recording time, respectively (Table 1). During the second night, eight to 11 REM sleep episodes were recorded in each of the different seals. These episodes lasted between 1 and 11.3 min (three and thirty-four 20-s epochs respectively) and the average REM sleep episode was approximately 4 min in length (Table 2). Most SWS episodes (when applying the 100-s maximal interruption criteria) were shorter than 40 min and the average duration for all seals was 25 min. However, in two fur seals, the longest SWS episodes lasted more than 80 min.

The transition from wakefulness to SWS was accompanied by a significant increase of the standardized power of the EEG in the range of 1.2–4 and 8–16 Hz (Fig. 2). The power in these frequency ranges increased up to 60-fold in some 20-s epochs compared with that of REM sleep. Spindles in fur seals had a typical bursting pattern and usually lasted 1–3 s. The peaks of the spectral power in epochs containing spindles occurred at 10–13 Hz (Fig. 1a and b). The spectral power in the range of 8–16 Hz usually increased at the beginning and end of SWS as well as during brief arousals (Fig. 2). The EEG spectral power in the range of 4–8 Hz showed a smaller increase (up to 20-fold) compared with the 1.2–4 and 8–16 Hz range (Fig. 2). The time course of activity in the range of 1.2–4 and 4–8 Hz in each hemisphere was clearly synchronized over most sleep–wake cycles (Fig. 2).

As shown in Figs 1 and 2, some episodes of SWS were characterized by a distinct EEG asymmetry recognized visually in the raw signal and by the difference in spectral power in the left and right hemispheres over the entire range (1.2–16 Hz). Finer time resolution examples of EEG asymmetry in fur seals have been provided in our previous publications (e.g. Lyamin and Chetyrbok, 1992). Even though some episodes of EEG asymmetry in fur seals lasted longer than 6 min (Fig. 2, episode a), the majority of these episodes were less than 1 min

Table 1 Total duration of vigilance states and maximal values of the asymmetry index (AI) during asymmetrical slow wave sleep in fur seals

Seal	Night	Duration of vigilance states (percent of night-time)						Maximal values of AI	
		SWS	REM	BSWS	LASWS	RASWS	LASWS – RASWS	LASWS	RASWS
2-02	1	36.9	4.9	29.2	1.8	5.9	-4.1	0.66	-0.71
	2	28.4	5.5	23.7	3.1	1.6	1.5	0.60	-0.65
1-03	1	65.8	8.0	37.3	10.6	17.9	-7.3	0.92	-0.88
	2	64.5	6.7	35.5	14.7	14.3	0.4	0.92	-0.94
2-03	1	58.4	3.9	37.6	9.8	11.0	-1.2	0.77	-0.73
	2	49.7	4.5	31.8	8.4	9.5	-1.1	0.73	-0.73
3-03	1	41.4	3.9	19.8	18.4	3.2	15.2	0.91	-0.77
	2	34.1	5.6	15.9	14.2	4.0	10.2	0.96	-0.86
Mean (<i>n</i> = 4)	1	50.6 ± 6.8	5.2 ± 1.0	31.0 ± 4.2	10.2 ± 3.4	9.5 ± 3.2			
Mean (<i>n</i> = 4)	2	44.2 ± 8.1	5.6 ± 0.5	26.7 ± 4.4	10.1 ± 2.7	7.4 ± 2.8			
Mean (<i>n</i> = 8)	1–2	47.4 ± 5.4	5.4 ± 0.5	28.9 ± 2.9	10.1 ± 2.0	8.4 ± 2.0			

The average values are given as mean ± SE. SWS, slow wave sleep; REM, rapid eye movement sleep; BSWS, bilateral SWS; RASWS and LASWS, right and left hemisphere asymmetrical SWS. LASWS – RASWS is the difference between the amount of LASWS and RASWS.

(Table 2). The average duration of ASWS episodes were as much as one-fourth of the duration of SWS episodes when calculated for all sleep episodes and approximately one-half when only episodes longer than 1 min were considered (Table 2). During bilaterally symmetrical SWS (BSWS; Figs 1c and 2, episodes *c* and *e*), there was no significant difference in the spectral power between the two hemispheres. REM sleep (Fig. 2, episodes *b* and *f*) occurred after both BSWS (episode *e*) and ASWS (episode *a*). EEG spectral power in the range of 1.2–4 Hz during BSWS was often higher than that achieved in the 'dominant' hemisphere during episodes of ASWS (Fig 2, compare BSWS episodes *c* and ASWS episode *a*). However, during some of ASWS episodes, the slow wave power in the 'deeper' sleeping hemispheres was similar to that during high-voltage BSWS (Fig 2, compare ASWS episode *d* and BSWS episodes *c* and *e*).

The total duration of BSWS (all epochs with an absolute AI < 0.3), ASWS in the left hemisphere (all epochs with AI > +0.3 in the range of 1.2–4.0 Hz) and ASWS in the right hemisphere (all epochs with AI < -0.3) in each seal during two recording nights is presented in Table 1. One seal (2-03) spent approximately the same amount of time displaying left and right hemispheric ASWS (the difference during both nights was ~1% or 10 min per night). In two seals (2-02 and 1-03), the difference in the amount of sleep in two hemispheres was substantial during the first night (more than 4% of the recording time in seal 2-02 and 7% in seal 1-03 or ~30 and 50 min per night, respectively). In both cases, the seals showed more SWS in the left hemisphere than in the right hemisphere. During the second night, the difference between the amount of left and right ASWS in these two seals was minimal (less than 1.5% of the recording time) as in seal 2-03. In the remaining seal (3-03), the total amount of sleep in the right hemisphere was considerably greater than that in the left hemisphere during both recording nights (15% and 10% of the recording time, respectively, or > 80 min per night). Despite the significant difference in the amount of SWS in two hemispheres in three seals, the magnitude of left and right hemispheric dominance

(as shown by using the maximal values of AI in the range of 1.2–4.0 Hz) was substantial in only one of these seals (seal 3-03; Table 1).

Spectral composition of EEG during sleep and waking

There was no difference in the spectral composition of the EEG during QW, SWS and REM sleep between the left and right hemispheres for each seal (one-way ANOVA for repeated measures with the factor 'hemisphere'; $P > 0.05$ for each state and for each recording night). Spectral power of the EEG in the left hemisphere is shown in Fig. 3. Power in all frequency bins during SWS was significantly greater than that of QW and REM sleep, regardless of the location of the EEG electrodes (symmetrical fronto-occipital or fronto-parietal). The difference in power between SWS and QW, and between SWS and REM sleep was statistically significant ($P < 0.05$) for most of the frequency bins (1.2–16 Hz) in both the left (Fig. 3) and right hemispheres (not shown). EEG spectral power between QW and REM sleep in the range of 1.2–16 Hz was not significantly different (Fig. 3).

During SWS, a wide distinct peak in the range of 9–15 Hz (sigma rhythm) was observed in the spectral power of both hemispheres in three of four seals (Fig. 3a). The maximum peak values were between 10.8 and 13.2 Hz for the different animals. This activity was distinct in both occipital (seals 2-03 and 3-03) and parietal derivations (seal 1-03). Small peaks within the range of 6–8 Hz (theta rhythm) were present in spectrograms of some REM sleep episodes in two seals. However, there were no evident peaks within this range for the averaged spectra composition of QW and REM sleep in any of the seals studied (Fig. 3).

Quantitative estimate of the extent of EEG asymmetry in different frequency ranges

Representative distributions of the percentage of 20-s epochs with different AI during QW, SWS and REM sleep for two

Table 2 SWS and REM sleep episode parameters in fur seals

Seal	SWS			ASWS		
	Duration (min) of			Duration (min) of		
	REM sleep episode duration (min)	Episodes (100-s interruption criteria)	All episodes	REM sleep episode duration (min)	Episodes (100-s interruption criteria)	All episodes
2-02	3.3 ± 0.9 (9.0, 9)	13.9 ± 2.2 (30.7, 11)	3.2 ± 0.2 (13.3, 115)	4.4 ± 2.4 (13.3, 21)	18	4.4 ± 0.03 (1.3, 51)
1-03	6.0 ± 1.1 (11.3, 8)	35.8 ± 6.0 (88.7, 15)	2.6 ± 0.3 (34.3, 185)	5.3 ± 0.7 (34.3, 79)	43	0.6 ± 0.03 (4.3, 357)
2-03	3.2 ± 0.7 (8.0, 11)	32.0 ± 4.9 (82.7, 15)	2.5 ± 0.3 (22.0, 181)	6.2 ± 0.7 (22.0, 62)	34	0.6 ± 0.04 (4.7, 238)
3-03	2.4 ± 0.5 (6.0, 9)	17.0 ± 3.3 (39.7, 14)	1.4 ± 0.2 (9.7, 167)	3.8 ± 0.4 (9.7, 47)	28	0.8 ± 0.1 (6.7, 156)
Mean (n = 4)	3.7 ± 0.8	24.7 ± 5.5	2.4 ± 0.4	4.9 ± 0.5	31 ± 5	2.3 ± 0.3 [†]

The data are presented as mean ± SE or percent of all episodes. Maximal values and number of measurements are given in parentheses. REM, rapid eye movement sleep; SWS, slow wave sleep; ASWS, SWS with interhemispheric EEG asymmetry or asymmetrical SWS. The duration of all SWS, ASWS and REM sleep episodes was calculated as the number of consecutive 20-s epochs of a given state. The duration of SWS episodes was also calculated allowing 100 s or less interruption by quiet waking.

*Only one episode was recorded during this night.

[†]The mean is calculated for n = 3.

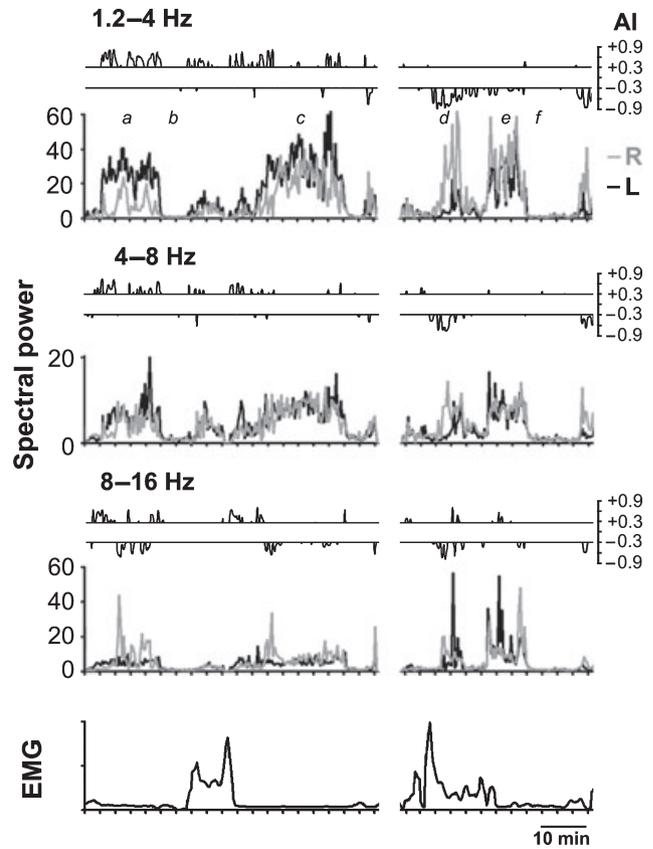


Figure 2. EEG spectral power in the right (R) and left (L) symmetrical fronto-occipital derivations and the asymmetry index (AI) of spectral power in three frequency ranges (1.2–4, 4–8 and 8–16 Hz) in a fur seal (1-03). The power of each 20-s epoch was standardized to the average power in rapid eye movement (REM) sleep for the corresponding frequency band in the same hemisphere. AI is shown for the epochs in which the value was > +0.3 or < -0.3. Note the letter *a* marks a period of asymmetrical slow wave sleep (SWS) with higher voltage slow waves in the L hemisphere, *d* – asymmetrical SWS with higher voltage slow waves in the R hemisphere, *c* and *e* – bilaterally symmetrical SWS. The letters *b* and *f* mark two episodes of REM sleep. EMG is shown in relative units. High EMG levels at the beginning of episode *c* were because the seal was sleeping while sitting. The two episodes displayed here were recorded during a single night with an interval of 94 min.

seals are shown in Fig. 4. During REM sleep, the distribution range of AI in all frequency bands was narrow and approximately symmetrical around zero for all seals. The mean AI for all frequency bands ranged between -0.01 and +0.01 for all seals. These data indicate minimal asymmetry between the power spectra of the two hemispheres during REM sleep. The distribution range of AI was much wider during SWS, varying between -0.7 and +0.9 in the ‘most asymmetrical’ seals 1-03 and 3-03. In three seals, the distributions remained approximately symmetrical around the central area for all frequency ranges (the histogram for one of these animals, seal 1-03 is shown in Fig. 4). In the one remaining animal (seal 3-03), the distribution was shifted to the right-hand side for all frequency bands (Fig. 4) indicating greater spectral power in the left

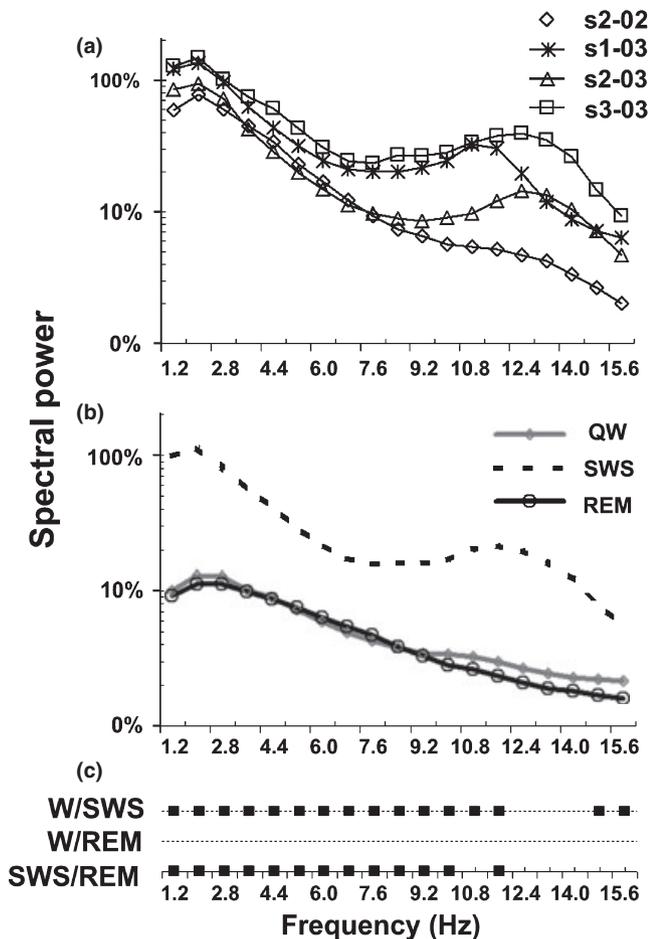


Figure 3. Electroencephalogram spectral power during quiet waking (QW), slow wave sleep (SWS) and rapid eye movement (REM) sleep in fur seals for fronto-occipital (seals 2-02, 2-03 and 3-03) and fronto-parietal (seal 1-03) derivations of the left hemisphere. In each seal, the calculations were conducted for 0.8 Hz bins in the range of 1.2–16 Hz on 60 randomly selected 20-s epochs during the second recording night. (a) Spectral power during SWS (low- and high-voltage SWS combined) for each seal is plotted on a logarithmic scale as percent of the total power in the range of 1.2–16 Hz during REM sleep. (b) Average power during QW, SWS and REM sleep calculated for all seals during the second recording night. (c) Squares indicate the frequency bins in which the difference in power reached significance between two states ($P < 0.05$, two-tailed paired t -test; $P < 0.05$ significance in a one-way ANOVA for repeated measures with the factor 'behavioral state').

hemisphere. During QW, the distribution of epochs with different AI was intermediate compared with that of REM sleep and SWS values.

To compare the laterality of EEG asymmetry between behavioral states and frequency ranges, we calculated the average number of epochs with an AI $> +0.3$ and AI < -0.3 . For all frequency ranges, the difference between the percentage of epochs with AI $> +0.3$ and AI < -0.3 during REM sleep was not statistically significant (Z -test, $P > > 0.05$ in all seals). During SWS, an evident laterality in the spectral power of the EEG was found in two animals (seals

2-03 and 3-03; Table 3). In seal 3-03, the proportion of epochs with AI $> +0.3$ was greater than that with AI < -0.3 for all frequency ranges ($P < 0.05$ for both nights) except for the range of 4–8 Hz on the second night, indicating a greater power in the left hemisphere compared with the right hemisphere (see also Fig. 4). In seal 2-03, during SWS consistent laterality was detected only in the range of 12–16 Hz. In this animal, the proportion of epochs with AI $> +0.3$ was also greater than that with AI < -0.3 ($P < 0.05$ for both nights), as in seal 3-03. During QW, a laterality in the spectral power of the EEG was found in seal 2-03. The percentage of epochs with AI < -0.3 was significantly greater than that with AI $> +0.3$ in the range of 4–8 and 8–12 Hz during both recording nights, indicating a greater power in the right hemisphere compared with the left hemisphere. In one additional seal (1-03), a significant difference between the two hemispheres in the EEG spectral power was found during both QW and SWS. However, the laterality was present in different frequency ranges and only during one of the two recording nights (Table 3). To summarize, the data available show that consistent inter-hemispheric asymmetry in the EEG spectral power of the two hemispheres can be present in some seals during both SWS and the transition from waking to SWS at least during two consecutive nights.

We used the average number of epochs with an absolute AI > 0.3 calculated for two recording nights to estimate the degree of EEG asymmetry across behavioral states (QW, SWS1, SWS2 and REM) and within each frequency range (1.2–4, 4–8, 8–12 and 12–16 Hz) (Fig. 5). During SWS, the average percent of epochs with an absolute AI > 0.3 varied between 26% and 44% of all SWS epochs in individual animals and was maximal during SWS2 in the range of 12–16 Hz. In QW, the range of the AI was considerably smaller (11–21%). During REM sleep the average percentage of epochs with an absolute AI > 0.3 was $< 9\%$. Comparison of percentage of epochs with an absolute AI > 0.3 showed a highly significant effect for the factor 'behavioral state' (two-way ANOVA, $F_{3,48} = 21.84$, $P < < 0.001$) but not for the factor 'frequency range' ($F_{3,48} = 1.51$, $P = 0.22$). A one-way ANOVA performed separately within each frequency band followed by a *post hoc* Turkey test revealed that the difference in the percentage of epochs between behavioral states was the greatest in the range of 1.2–4 Hz. For this frequency range, the difference in the degree of EEG asymmetry was statistically significant for all comparisons ($P < 0.01$) except between QW and REM sleep ($P > 0.05$) and between SWS1 and SWS2 ($P > 0.05$). The difference between REM sleep and SWS2 was highly significant in all four frequency ranges ($P < 0.05$ for the range 12–16 Hz and $P < 0.01$ for the ranges of 1.2–4, 4–8 and 8–12 Hz) and between REM sleep and SWS1 in the range of 1.2–12 Hz ($P < 0.01$). Therefore, interhemispheric EEG asymmetry in the fur seal, as measured by using the AI, is maximally expressed during SWS in all four frequency bands examined. In addition, the extent of EEG asymmetry is not only a feature of low-voltage but also high-voltage SWS.

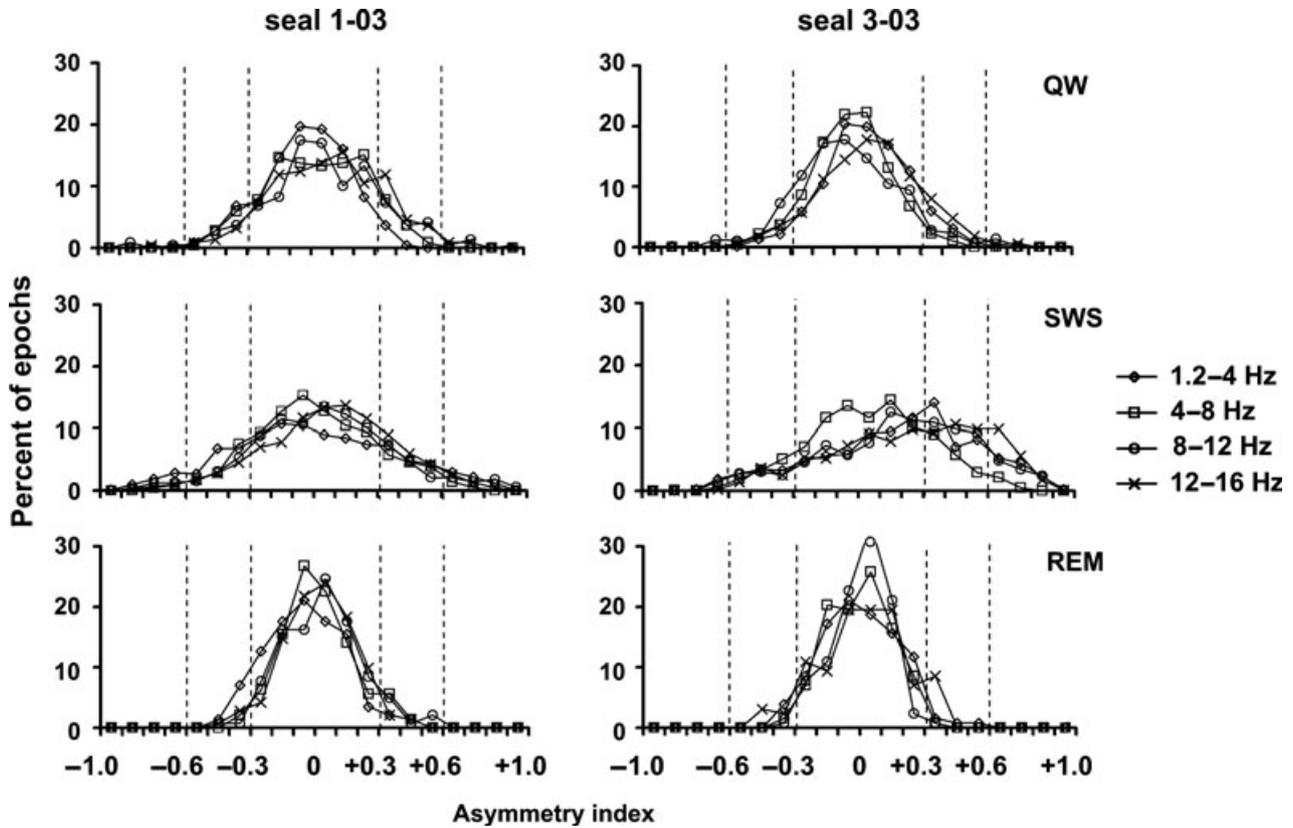


Figure 4. Distribution of the number of epochs with different asymmetry index (AI) of the EEG spectral power in the left and right hemispheres in two fur seals (1-03 and 3-03). The data are presented for each of the four frequency ranges (1.2–4, 4–8, 8–12 and 12–16 Hz). The ordinate is percentage of 20-s epochs of quiet waking (QW), slow wave sleep (SWS; low and high voltages combined) and rapid eye movement (REM) sleep recorded during the second night. The vertical dotted lines are drawn at the –0.6, –0.3, +0.3 and +0.6 AI values.

Table 3 Comparison of the standardized EEG spectral power between two brain hemispheres in four fur seals during two recording nights

Seal	Night	Frequency range (Hz)							
		QW				SWS			
		1.2–4	4–8	8–12	12–16	1.2–4	4–8	8–12	12–16
2-02	1								
	2								
1-03	1								
	2				+				
2-03	1	–	–	–					+
	2		–	–	–				+
3-03	1					+	+	+	+
	2					+		+	+

The table shows statistical significance of the difference in the number of epochs with AI > +0.3 and AI < –0.3 for each state (QW, quiet waking; SWS, slow wave sleep) and frequency range (Z-test, $P < 0.05$). ‘+’ indicates that the percentage of epochs with AI > +0.3 was greater than that with AI < –0.3 and ‘–’ that the percentage of epochs with AI < –0.3 was greater than that with AI > +0.3.

The difference in AI between behavioral states and between seals became even more evident when EEG asymmetry was measured as the percentage of epochs with an absolute

AI > 0.6 (Fig. 5). There were no episodes of REM sleep with an absolute AI > 0.6 for any of the four frequency ranges examined for any of the four seals. In one seal (2-03), only several of such epochs were recorded over two nights (0.1–0.8% of all epochs depending on the stage and the frequency range). In three of four remaining seals, only a small proportion of QW epochs (less than 4%) had an absolute AI > 0.6 in the range of 8–12 and 12–16 Hz. During SWS, epochs with AI > +0.6 or AI < –0.6 were recorded mainly in two seals (1-03 and 2-03). In the range of 1.2–4 Hz, the percent of such epochs was the highest during high-voltage SWS (20% and 21% of all SWS2 in seals 1-03 and 2-03, respectively, compared with 12% and 6% during SWS1). In the range of 12–16 Hz, this type of profound EEG asymmetry was even more expressed in seal 1-03 (32% of all SWS2) but substantially less in seal 2-03 (<7%) compared with the range of 1.2–4 Hz. In seal 3-03, the EEG asymmetry with an absolute AI > 0.6 was maximal in the range of 12–16 Hz (9% of all SWS) and lower in all other frequency ranges (<4%). A two-way ANOVA revealed a significant difference for the factor ‘behavioral state’ ($F_{3,32} = 11.10, P < 0.001$) but not for the factor ‘frequency range’ ($F_{3,32} = 2.01, P = 0.13$) when calculated for the three seals, which exhibited this type of profound EEG asymmetry.

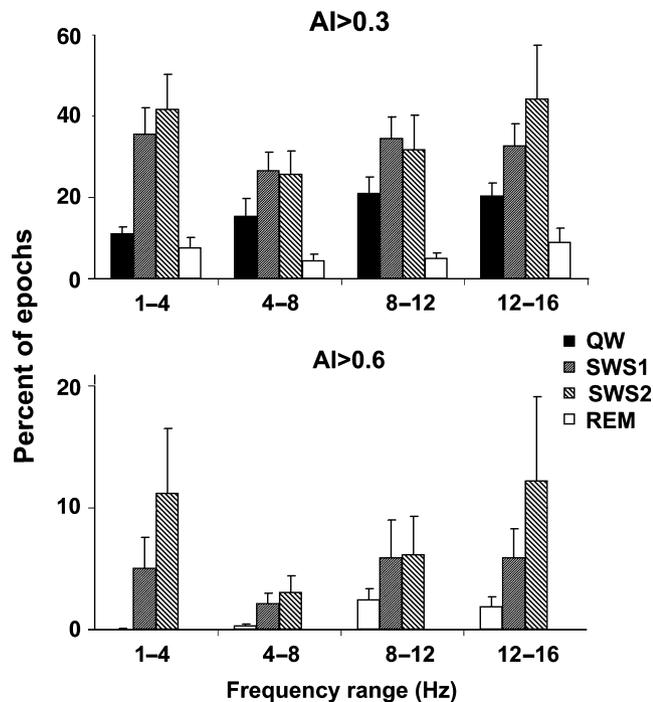


Figure 5. Mean percentage (\pm SE) of 20-s epochs with an absolute AI > 0.3 (top diagram) and an absolute AI > 0.6 (bottom diagram) in the range of 1.2–16 Hz during quiet waking (QW), slow wave sleep (SWS1 and SWS2, low- and high-voltage SWS, respectively) and rapid eye movement (REM) sleep in fur seals. For each of the four seals, the AI was calculated for each of the four frequency bands (1.2–4, 4–8, 8–12 and 12–16 Hz) on 60 randomly selected epochs (30 for each of the two recording nights).

DISCUSSION

This is the first study designed to investigate EEG by using spectral analysis in the fur seal, a semi-aquatic mammalian species, which displays a pronounced interhemispheric EEG asymmetry during SWS. The comparison of the EEG spectra of the three main behavioral states in the fur seal shows a large similarity to the spectra of the cat (e.g. Bronzino *et al.*, 1973) and the dog (e.g. John *et al.*, 2004). On the other hand, there was an apparent difference between the spectra in fur seals and that of most rodents (e.g. Borbely *et al.*, 1984; Huber *et al.*, 2000; Tobler and DeBoer, 2001; Tobler *et al.*, 1993) because of the absence of the pronounced theta rhythm during REM sleep in the fur seal. Theta activity is clearly expressed during REM sleep in the hippocampus in dogs (Dobermans) but not in the cortex (John *et al.*, 2004). As in Dobermans, the absence of a distinct peak in the theta activity range in cortical recordings in fur seals is probably attributed to the large distance between the hippocampus and the cortex. Rhythmic activity in the range of 8–16 Hz was expressed in three of four seals both in fronto-occipital and fronto-parietal derivations, as reported in most mammalian species. We also noted some evidence of a functional difference between lower (8–11 Hz) and upper (11–15 Hz) bands of this activity in the fur seal, which most likely represents alpha-like and sigma activity

respectively. Alpha activity was recorded during relaxation with both eyes closed as in carnivores, primates and humans (Hughes and Crunelli, 2005). Sigma activity with an evident bursting pattern has been so far recorded in most terrestrial mammals (e.g. Sobieszek, 1968; Tobler and Borbely, 1986; Vyazovskiy *et al.*, 2004), in two species of Phocidae seals (Lyamin *et al.*, 1993; Mukhametov *et al.*, 1984) and in bottlenose dolphins (Mukhametov *et al.*, 1977).

All seals studied here showed clear episodes of EEG asymmetry during SWS, which lasted longer than 6 min. In this study, we used the AI to estimate the degree of interhemispheric EEG asymmetry. This parameter has been used to evaluate the EEG asymmetry in several human studies (e.g. Baehr *et al.*, 1998; Clemens and Menes, 2000). To evaluate the degree of EEG asymmetry, we set the absolute AI value equal to 0.3 based on our preliminary results obtained from rats (Pokidchenko *et al.*, 2005). We determined that 88–100% of epochs in the rat had an AI > –0.3 and < +0.3 regardless of the functional state (QW, SWS or REM sleep) and the EEG frequency range examined. Therefore, the degree of EEG asymmetry as measured by using the AI across the sleep–wake cycle in the rat is not state specific. The EEG asymmetry as measured by using an absolute AI = 0.3 indicates a 1.8-fold difference between spectral power in two hemispheres. In the four fur seals studied here, on average, $92 \pm 3\%$ of REM sleep epochs had AI < 0.3. This proportion of epochs is within the AI range in the rat. As estimated in our previous study, asymmetrical SWS in the fur seal comprised, on average, 35% of the total SWS time when scored manually (Lyamin and Mukhametov, 1998). In this study, the percentage of epochs with AI > +0.3 or AI < –0.3 in the range of 1.2–4 Hz was 35–40% of SWS, which is similar to the visual inspection estimate of asymmetrical SWS.

Considerable differences between seals were found in the amount of sleep in the two hemispheres and laterality of the EEG spectral power, as shown by the proportion of the epochs with AI > +0.3 (indicating greater power in the left hemisphere) and AI < –0.3 (greater power in the right hemisphere). The bias in the amount of left and right ASWS was consistent in one of the four seals during each of the two consecutive nights and the laterality in the expression of the EEG in one of two hemispheres was apparent in two of four seals. However, these data are not sufficient to suggest an individual-based asymmetry in the fur seal in the expression of the EEG asymmetry between the two hemispheres, especially considering that the magnitude of the EEG asymmetry during left and right ASWS was very similar. In our previous studies on fur seals, we noted that the average amount of SWS in one hemisphere may differ over any given 24-h or night-time period (Lyamin and Mukhametov, 1998). In the bottlenose dolphin, this difference could be as much as fourfold during a single day (Mukhametov, 1984). However, when the SWS time in each hemisphere was averaged over several days, the difference between the two hemispheres in the amount of time asleep in dolphins was negligible. Additional studies with a

longer period of recording in each seal need to be carried out to examine whether hemispheric dominance in the expression of EEG rhythms and SWS is present or not in fur seals.

The absolute AI during SWS in fur seals reached 0.8 for different frequency ranges indicating a 10-fold difference between the spectral powers in the two hemispheres. Majority of epochs with $AI > +0.6$ or $AI < -0.6$ (a fourfold difference in spectral power) were recorded from two seals. In the beluga, the average difference between the two hemispheres in the slow wave spectral power (1.2–4.0 Hz) was 10-fold (Lyamin *et al.*, 2002b), which would indicate an absolute $AI > 0.8$. In two bottlenose dolphins, on average, 88% of SWS epochs had an absolute $AI > 0.3$ in the range of 1.2–4 Hz and 62% had an absolute AI between 0.6 and 1.0 (Pokidchenko *et al.*, 2005). Therefore, dolphins have a greater degree of EEG asymmetry during SWS than do fur seals as estimated both visually and by using the AI. The absolute AI in fur seals during QW varied between 0 and 0.5. This was largely because only 5-s epochs, which did not contain movement-related artifacts, were selected for spectral analysis. Therefore, most of the selected QW epochs represented a transitional state between waking and low-voltage SWS.

The EEG asymmetry of SWS extends over a wide range, such that the bilaterally symmetrical SWS of terrestrial mammals lies at one extreme, whereas the USWS of cetaceans represents the other. The data available from other studies allow us to make some comparisons on the extent of the EEG asymmetry between marine mammals, humans, terrestrial mammals and birds. In normal human subjects, the average AI in the range of alpha activity (8–13 Hz) was between -0.09 and $+0.08$ (Baehr *et al.*, 1998). In another study, AI was used to assess sleep spindle asymmetry in patients with different symptoms of epilepsy (Clemens and Menes, 2000). This study showed that the epileptogenic cortex facilitates spindle generation. Even in patients with a clearly lateralized epileptic process in one hemisphere, the AI ranged between -0.23 and $+0.29$.

Rats, which were subjected to unilateral sensory stimulation during waking or sleep deprivation, showed on average, $< 10\%$ difference (absolute $AI < 0.1$) in the EEG power (range of 1–6 Hz) between the two hemispheres (Vyazovskiy *et al.*, 2000, 2002). In these studies, the data were scored in 4-s epochs, while in our study we used 20-s epochs for calculations. It is likely that in rats, the difference in EEG power between the two hemispheres would have been even less had a 20-s epoch duration been used.

Interhemispheric EEG asymmetry has been recorded in several bird species (Amlaner and Ball, 1994; Rattenborg *et al.*, 1999, 2001). As shown in mallard ducks, a statistically significant difference in the EEG spectra power between the two hemispheres during SWS with both eyes or only one eye closed was present in the range of 2–4 Hz, but did not exceed 70% (Rattenborg *et al.*, 1999), which represents an absolute $AI < 0.3$. As in the rat (Vyazovskiy *et al.*, 2000, 2002), the EEG in mallards was scored in 4-s epochs. In another bird

species, the pigeon, the difference between the power spectra in the two hemispheres during SWS with both eyes or only one eye closed was also detected in the range of 2–4 Hz. It was even less expressed than that of the mallards (Rattenborg *et al.*, 1999).

In this study, we found considerable differences in the expression of EEG asymmetry and EEG rhythms between fur seals. It is possible that some of these differences (e.g. the expression of sigma activity) are due to some variability in the localization of EEG electrodes in relation to gyri. On the other hand, the available data clearly indicate that unihemispheric sleep in dolphins and ASWS in seals (primarily scored based on the presence of EEG slow wave activity) are whole cortex phenomena (Lyamin and Mukhametov, 1998; Mukhametov *et al.*, 1977). Another factor to consider is sex-related differences, as the asymmetry was less expressed in the only studied male. However, this suggestion does not appear to be as likely because in a different study performed on a large group of animals we did not see significant differences in the pattern of SWS in male and female fur seals (Lyamin and Mukhametov, 1998). It is known that the EEG asymmetry correlates with asymmetrical eye state in cetaceans (Lyamin *et al.*, 2004) as well as in some birds (Rattenborg *et al.*, 1999, 2000). For instance, in one studied beluga and one dolphin during USWS, the eye contralateral to the more deeply sleeping hemisphere was usually closed (40% and 52% of the total sleep time in the contralateral hemisphere in the beluga, respectively, for the left and right eyes; 55% and 60% in the dolphin) or in an intermediate state (46% and 31% in the beluga; 37% and 35% in the dolphin: Lyamin *et al.*, 2002b, 2004). A similar association was observed in fur seals (Lyamin and Mukhametov, 1998; Lyamin *et al.*, 2004). As we showed, during SWS with interhemispheric EEG asymmetry, the fur seal eye contralateral to the hemisphere with lower voltage EEG briefly opened about 60% of the time while the eye which was opposite to the more deeply sleeping hemisphere was closed more than 95% of the time (Lyamin *et al.*, 2004). These data suggest that individual differences in the level of anxiety and hence vigilance, and the extent of bilateral eye closure in different seals, could affect the composition of SWS. This explanation is consistent with the hypothesis that one of the functions of unihemispheric sleep is more efficient sensory monitoring of the environment during sleep (Lyamin *et al.*, 2002b, 2004).

More than 40% of the epochs in fur seals scored as high-voltage SWS had an absolute $AI > 0.3$ in the frequency band of 12–16 Hz. It is known that spindles are generated within the thalamus, due to thalamic reticular neurons that impose rhythmic inhibitory sequences onto thalamo-cortical neurons (Steriade and Timofeev, 2003). We recently showed that acetylcholine release in the cortex is lateralized during ASWS with maximal release in the hemisphere displaying lower voltage activity (Lapierre *et al.*, 2007). Across mammals, the nucleus basalis of the basal forebrain is considered the primary source of ACh released in the cortex and this projection is ipsilateral (Semba, 2004). Therefore, the EEG

asymmetry we recorded in fur seals and dolphins at the cortical level may reflect a functional asymmetry between thalamic (primarily, glutamatergic) and basal forebrain (cholinergic) areas, which promote wakefulness and sleep and send ascending projections to the cortex. Therefore, we hypothesize that 'unihemispheric sleep' in cetaceans and pinnipeds of the Otariidae family is not solely a cortical phenomenon. The suggestion that EEG asymmetry is recorded during ASWS between symmetrical thalamus and hypothalamic regions does not exclude the possibility that other neuronal subcortical groups are activated unilaterally during ASWS in fur seals. For instance, recent publications by Krueger and colleagues showed that the EEG spectral power can be enhanced in rats by an unilateral application of TNF and IL1 to the cortex (Churchill *et al.*, 2005; Yasuda *et al.*, 2007). These data suggest that cytokines may be involved in the induction of EEG asymmetry in the rat and possibly in marine mammals.

The two major findings of this study are that EEG asymmetry was: (1) expressed during SWS across the entire range of 1.2–16 Hz; and (2) present during both low- and high-voltage SWS and during the transition from QW to SWS. The AI is one parameter that allows us to quantitatively estimate the degree of EEG asymmetry between different species. It shows that a large difference in the degree of the EEG asymmetry exists between 'bilaterally' sleeping rats, 'bilaterally' and 'asymmetrically' sleeping fur seals and 'unihemispherically' sleeping dolphins. It appears that there is also a considerable difference between fur seals and avian species in both the degree of the asymmetry and the frequency range in which it is expressed.

It has been proposed that the subtle EEG asymmetry recorded in rats and in humans, may reflect: (1) a difference in the metabolic restorative processes of the two brain hemispheres ('global' and 'local sleep'; Krueger and Obal, 1993); (2) a difference in the prior activation of the symmetrical cortical regions during wakefulness (e.g. Kattler *et al.*, 1994; Vyazovskiy *et al.*, 2000); and (3) hemispheric dominance in the expression of different behaviors (Vallortigara *et al.*, 1999) and the major EEG rhythms (Vyazovskiy *et al.*, 2002). We hypothesized that the EEG asymmetry during SWS in the fur seal allows motion (while in water), sensory processing and continuous vigilance (while in water or on land) when asleep (Lyamin *et al.*, 2004). Therefore, the EEG asymmetry in the fur seal reflects involvement of the awake hemisphere (or the hemisphere which is in a state of lower voltage SWS) in real-time processing of sensory information and motor coordination during SWS.

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REFERENCES

- Amlaner, C. J. and Ball, N. J. Avian sleep. In: M. H. Kryger, T. Roth and W. C. Dement (Eds) *Principles and Practice of Sleep Medicine*, 2nd edn. Saunders, Philadelphia, PA, 1994: 81–94.
- Baehr, E., Rosenfeld, J. P., Baehr, R. and Earnest, C. Comparison of two EEG asymmetry indices in depressed patients vs. normal controls. *Int. J. Psychophysiol.*, 1998, 31: 89–92.
- Borbely, A. A., Tobler, I. and Hanagasioglu, M. Effect of sleep deprivation on sleep and EEG power spectra in the rat. *Behav. Brain Res.*, 1984, 14: 171–182.
- Bronzino, J. D., Brusseau, J. N., Stern, W. C. and Morgane, P. J. Power density spectra of cortical EEG of the cat in sleep and waking. *Electroencephalogr. Clin. Neurophysiol.*, 1973, 35: 187–191.
- Castellini, M. A., Milsom, W. K., Berger, R. J., Costa, D. P., Jones, D. R., Castellini, J. M., Rea, L. D., Bharna, S. and Harris, M. Patterns of respiration and heart rate during wakefulness and sleep in elephant seal pups. *Am. J. Physiol.*, 1994, 266: R863–R869.
- Churchill, L., Yasuda, K., Yasuda, T., Blindheim, K. A., Falter, M., Garcia-Garcia, F. and Krueger, J. M. Unilateral cortical application of tumor necrosis factor alpha induces asymmetry in Fos- and interleukin-1beta-immunoreactive cells within the corticothalamic projection. *Brain Res.*, 2005, 1055: 15–24.
- Clemens, B. and Menes, A. Sleep spindle asymmetry in epileptic patients. *Clin. Neurophysiol.*, 2000, 111: 2155–2159.
- Huber, R., Deboer, T. and Tobler, I. Effects of sleep deprivation on sleep and sleep EEG in three mouse strains: empirical data and simulations. *Brain Res.*, 2000, 857: 8–19.
- Hughes, S. W. and Crunelli, V. Thalamic mechanisms of EEG alpha rhythms and their pathological implications. *Neuroscientist*, 2005, 11: 357–372.
- John, J., Wu, M. F., Boehmer, L. N. and Siegel, J. M. Cataplexy-active neurons in the hypothalamus: implications for the role of histamine in sleep and waking behavior. *Neuron*, 2004, 42: 619–634.
- Kattler, H., Dijk, D. J. and Borbely, A. A. Effect of unilateral somatosensory stimulation prior to sleep on the sleep EEG in humans. *J. Sleep Res.*, 1994, 3: 159–164.
- Krueger, J. M. and Obal, F. A neuronal group theory of sleep function. *J. Sleep Res.*, 1993, 2: 63–69.
- Lapierre, J. L., Kosenko, P. O., Lyamin, O. I., Kodama, T., Mukhametov, L. M. and Siegel, J. M. Cortical acetylcholine release is lateralized during asymmetrical slow-wave sleep in northern fur seals. *J. Neurosci.*, 2007, 27: 11999–12006.
- Lyamin, O. I. and Chetyrbok, I. S. Unilateral EEG activation during sleep in the Cape fur seal, *Arctocephalus pusillus*. *Neurosci. Lett.*, 1992, 143: 263–266.
- Lyamin, O. I. and Mukhametov, L. M. Organization of sleep in the northern fur seal. In: V. E. Sokolov, A. A. Aristov and T. U. Lisitzina (Eds) *The Northern Fur Seal. Systematic, Morphology, Ecology, Behavior*. Nauka, Moscow, 1998: 280–302 (in Russian).
- Lyamin, O. I., Oleksenko, A. I. and Polyakova, I. G. Sleep in the harp seal (*Pagophilus groenlandica*) Peculiarities of sleep in pups during the first month of their lives. *J. Sleep Res.*, 1993, 2: 163–169.
- Lyamin, O. I., Mukhametov, L. M., Chetyrbok, I. S. and Vassiliev, A. V. Sleep and wakefulness in the southern sea lion. *Behav. Brain Res.*, 2002a, 128: 129–138.
- Lyamin, O. I., Mukhametov, L. M., Siegel, J. M., Nazarenko, E. A., Polyakova, I. G. and Shpak, O. V. Unihemispheric slow wave sleep and the state of the eyes in a white whale. *Behav. Brain Res.*, 2002b, 129: 125–129.
- Lyamin, O. I., Mukhametov, L. M. and Siegel, J. M. Relationship between sleep and eye state in Cetaceans and Pinnipeds. *Arch. Ital. Biol.*, 2004, 142: 557–568.
- Mukhametov, L. M. Sleep in marine mammals. *Exp. Brain Res.*, 1984, 8(Suppl.): 227–238.
- Mukhametov, L. M. Unihemispheric slow-wave sleep in the Amazonian dolphin, *Inia geoffrensis*. *Neurosci. Lett.*, 1987, 79: 128–132.

- Mukhametov, L. M., Supin, A. Y. and Polyakova, I. G. Interhemispheric asymmetry of the electroencephalographic sleep patterns in dolphins. *Brain Res.*, 1977, 134: 581–584.
- Mukhametov, L. M., Supin, A. Y. and Poliakova, I. G. Sleep of Caspian seals. *Zh. Vyssh. Nerv. Deiat. Im. I. P. Pavlova*, 1984, 34: 259–264 (in Russian).
- Mukhametov, L. M., Lyamin, O. I. and Polyakova, I. G. Interhemispheric asynchrony of the sleep EEG in northern fur seals. *Experientia*, 1985, 41: 1034–1035.
- Pokidchenko, T. M., Lyamin, O. I., Mukhametov, L. M. and Siegel, J. M. Comparative study of EEG asymmetry in dolphins, fur seals and rats. *Abstract of the Second Interim Congress of the WFSRSMS*, 22–26 September, 2005, New Delhi, India: 189.
- Rattenborg, N. C., Lima, S. L. and Amlaner, C. J. Facultative control of avian unihemispheric sleep under the risk of predation. *Behav. Brain Res.*, 1999, 105: 163–172.
- Rattenborg, N. C., Lima, S. L. and Amlaner, C. J. Behavioral, neurophysiological and evolutionary perspectives on unihemispheric sleep. *Neurosci. Biobehav. Rev.*, 2000, 24: 817–842.
- Rattenborg, N. C., Amlaner, C. J. and Lima, S. L. Unilateral eye closure and interhemispheric EEG asymmetry during sleep in the pigeon (*Columba livia*). *Brain Behav. Evol.*, 2001, 58: 323–332.
- Ridgway, S. H. Asymmetry and symmetry in brain waves from dolphin left and right hemispheres: some observations after anesthesia, during quiescent hanging behavior, and during visual obstruction. *Brain Behav. Evol.*, 2002, 60: 265–274.
- Semba, K. Phylogenetic and ontogenetic aspects of the basal forebrain cholinergic neurons and their innervation of the cerebral cortex. *Prog. Brain Res.*, 2004, 45: 3–43.
- Sobieszek, A. Spontaneous sleep and barbiturate spindles in dog EEG. *J. Physiol.*, 1968, 197: 29P–30P.
- Steriade, M. and Timofeev, I. Neuronal plasticity in thalamocortical networks during sleep and waking oscillations. *Neuron*, 2003, 37: 563–576.
- Tobler, I. and Borbely, A. A. Sleep EEG in the rat as a function of prior waking. *Electroencephalogr. Clin. Neurophysiol.*, 1986, 64: 74–76.
- Tobler, I. and Deboer, T. Sleep in the blind mole rat *Spalax ehrenbergi*. *Sleep*, 2001, 24: 147–154.
- Tobler, I., Franken, P. and Jaggi, K. Vigilance states, EEG spectra, and cortical temperature in the guinea pig. *Am. J. Physiol.*, 1993, 264: R1125–R1132.
- Vallortigara, G., Rogers, L. J. and Bisazza, A. Possible evolutionary origins of cognitive brain lateralization. *Brain Res. Rev.*, 1999, 30: 164–175.
- Vyazovskiy, V., Borbely, A. A. and Tobler, I. Unilateral vibrissae stimulation during waking induces interhemispheric EEG asymmetry during subsequent sleep in the rat. *J. Sleep Res.*, 2000, 9: 367–371.
- Vyazovskiy, V. V., Borbely, A. A. and Tobler, I. Interhemispheric sleep EEG asymmetry in the rat is enhanced by sleep deprivation. *J. Neurophysiol.*, 2002, 88: 2280–2286.
- Vyazovskiy, V. V., Achermann, P., Borbely, A. A. and Tobler, I. The dynamics of spindles and EEG slow-wave activity in NREM sleep in mice. *Arch. Ital. Biol.*, 2004, 142: 511–523.
- Yasuda, K., Churchill, L., Yasuda, T., Blindheim, K., Falter, M. and Krueger, J. M. Unilateral cortical application of interleukin-1beta (IL1beta) induces asymmetry in fos, IL1beta and nerve growth factor immunoreactivity: implications for sleep regulation. *Brain Res.*, 2007, 1131: 44–59.