topes of Li are initially transported in the hydrated form. Based upon lattice constant measurements the ionic volume of (Li-6)⁺ is greater than (Li-7)^{+8,22}. However, it is the hydrated form (Li-7)⁺(H₂O) that has a greater ionic volume than (Li-6)⁺(H₂O). Because of its smaller ionic volume, the passage of (Li-6)⁺(H₂O) by passive diffusion through a membrane channel would be more rapid than the passage of (Li-7)⁺(H₂O). An energy dependent mechanism of transport would of necessity make an explanation more complex.

Because of the differential treatment of the two Li isotopes by membrane systems in vitro and in vivo, the possibility was raised that harmful sideeffects of Li during prolonged clinical use in manic-depressive patients might be reduced by administering only Li-7, the less toxic of the two stable isotopic forms. There is ample justification for clinical trials of this hypothesis because of the data indicating both the greater in vivo toxicity and the more rapid penetration in vitro of Li-6 than Li-7. Whether Li-7 alone would have therapeutic efficacy equivalent to Li-N remains to be established.

The finding that biological systems can discriminate between isotopes of a given element is in itself provocative. Relative rates at which isotopes cross biological membranes might be used to provide further information regarding the mechanisms of ion transfer. They could also provide further information pertinent to explaining the mechanisms of the differential effects of these isotopes on neuronal activity and behavior. Finally, these observations may have clinical relevance for ameliorating toxicity in clinical disorders for which Li treatment is indicated.

- 1 Alexander, G., Lieberman, K. W., and Stokes, P., Differential lethality of Li isotopes in mice. Biol. Psychiat. 15 (1980) 469–471.
- 2 Alexander, G., Lieberman, K. W., Okamoto, M., and Stokes, P., Stable isotopes of Li: effects on behavior in rodents. Fedn Proc. 41 (1983) 1583.
- 3 American Psychiatric Association Taskforce, The current status of Li therapy. Am. J. Psychiat. 132 (1975) 997-1007.
- 4 Birch, N.J., Robinson, D., Ince, R. A., and Hullin, R. P., Li-6 stable isotope determination by atomic absorption spectrophotometry and its application to pharmacokinetic studies in man. J. Pharm. Pharmac. 30 (1978) 683-685.

- 5 Birch, N.J., in: Lithium in Medical Practice, pp. 87-144. Eds F. N. Johnson and S. Johnson. University Park Press, Baltimore 1978.
- 6 Brost, D. F., Brackett, J. M., and Bunch, R. W., Determination of Li by optically monitored stable isotope dilution. Analyt. Chem. 51 (1979) 1512–1516.
- 7 Cotton, F.A., and Wilkinson, G., Advanced Inorganic Chemistry, 3rd Edn. Interscience, New York 1975.
- 8 Covington, E.J., and Montgomery, D.J., Lattice constants of separated Li isotopes. J. Chem. Phys. 27 (1957) 1030–1032.
- 9 Greenspan, K., Aronoff, M., and Bogdanski, D., Effects of lithium carbonate on turnover and metabolism of norepinephrine in rat brain. Pharmacology 3 (1970) 129–136.
- 10 Johnson, F. N., and Wormington, S., Effect of Li on rearing activity in rats. Nature, New Biol. 235 (1972) 159–160.
- 11 Lieberman, K. W., Alexander, G., and Stokes, P., Dissimilar effects of Li isotopes on motility in rats. Pharmac. Biochem. Behav. 10 (1979) 933–935.
- 12 Lieberman, K. W., Stokes, P., and Kocsis, J., Characteristics of the uptake of Li isotopes into erythrocytes. Biol. Psychiat. 14 (1979) 845-849
- 13 Lieberman, K. W., Meltzer, H. L., and Stokes, P., Transport studies of Li isotopes. Fedn Proc. 39 (1980) 405.
- 14 Lieberman, K. W., Chen, C., Mann, J., and Rubino, R., Erythrocyte differentition of naturally occurring isotopic Li abundances. Pharmac. Biochem. Behav. 23 (1985) 145–146.
- 15 Perez-Cruet, J., Tagliamonte, A., Tagliamonte, P., and Gessa, G. L., Li and motility studies in rats. J. Pharmac. expl Ther. 178 (1971) 325–330.
- 16 Schou, M., What happened to Li babies: a followup study of children without malformations. Acta psychiat. scand. 54 (1976) 193–197.
- 17 Sechzer, J., Lieberman, K. W., Stokes, P., and Falasco, J., Effects of isotopically Li on maternal behavior, development and learning. Pharmacologist 24 (1982) 196.
- 18 Sherman, W.R., Munsell, L.Y., and Wong, Y., Differential uptake of Li isotopes by rat cerebral cortex and its effect on inositol phosphate metabolism. J. Neurochem. 42 (1984) 880–882.
- 19 Smith, D.F., and Smith, H., Effect of prolonged Li administration on activity, reactivity and endurance in the rat. Psychopharm. 30 (1973) 83–88.
- 20 Stokes, P., Lieberman, K. W., Okamoto, M., and Alexander, G., Stable isotopes of Li: in vivo differential distribution between plasma and CSF. Biol. Psychiat. 17 (1982) 413–421.
- 21 Thellier, M., Stelz, T., and Wissocq, J., Detection of stable isotopes of lithium or boron with help of a (n, alpha) nuclear reaction. Biochim. biophys. Acta 437 (1974) 604–627.
- 22 Thewlis, J., Unit-cell dimensions of LiF made from Li-6 and Li-7. Acta crystallog. 8 (1955) 36–38.
- 23 Weinstein, M. R., The international register of Li babies. Drug Inf. J. 10 (1976) 94–100.

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Full Papers

Long-term motor activity recording of dogs and the effect of sleep deprivation

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Summary. Motor activity of laboratory dogs was recorded for several weeks with an ambulatory monitoring device. The effect of 24 h sleep deprivation (SD) on motor activity during recovery was investigated. A clear rest-activity rhythm was established. The dogs exhibited a similar mean daily rest-activity pattern: 1) rest occurred mainly in the dark; 2) the amimals were most active after light onset; activity increased during the last two dark hours; 3) a rest period was found at noon and reduced activity during afternoon hours. There was a marked difference in total activity

between individual dogs. Activity patterns varied as a function of the day of the week; this may have been a reflection of variations in the level of human activities in the laboratory. There was a significant reduction of motor activity during the 24-h period following SD. This was particularly evident in the first 6 h of the light period immediately following the deprivation.

In addition, there was a significant increase in the number of episodes with activity ≤ 5 counts during recovery. The study confirms the possibility of measuring motor activity to assess compensatory mechanisms during recovery after SD. Sleep regulation, therefore, does not necessarily need to be exclusively examined by the invasive technique of EEG registration.

Key words. Rest-activity rhythm; motor activity; dog; sleep deprivation.

Introduction

Continuous long-term activity data from freely moving animals other than small laboratory species are scarce. A recently developed wristworn activity monitor has been repeatedly applied in man to assess the effect of drugs², to investigate activity patterns in elderly subjects (Loepfe et al., unpublished), and to assess sleep disturbances in psychiatric patients¹³. Due to the lack of data on rest-activity rhythms in dogs it seemed pertinent to test the feasibility of obtaining continuous long-term activity recordings of laboratory dogs. Scott and Causey¹⁴ measured the activity of feral dogs by radiotracking at 2-h intervals for 11 days. Only the frequency of activity found during the day as related to season was reported. Dogs were found to be more active at night during all seasons.

Several authors have recorded the EEG and behavior of dogs for 24-h periods^{5, 6, 8, 10-12, 16, 17, 21, 22}. With the exception of Takahashi¹⁷ who contrary to his former findings¹⁶ found only a slight difference in sleep length between the light and dark period, all authors reported a clear predominance of sleep during the dark phase of the LD cycle. Under a 12 h light – 12 h dark cycle circa 30% sleep took place during the light period⁸. Wanquier^{21, 22} recorded under LL conditions.

Sleep deprivation (SD) has often been used in man and animals to investigate sleep homeostasis^{1,19}. The loss of sleep is followed by a relative small enhancement of sleep time and a prominent rebound in slow-wave activity¹. Takahashi^{16,17} investigated the effect of several periods of SD differing in duration on sleep stages in dogs. The results were comparable to those obtained in other mammals; 24 h SD were followed by enhanced 'deep sleep'. It has been shown for several species that motor activity was reduced after SD when recovery was allowed during the habitual active phase of the LD cycle^{19,20}. On the basis of these results it was suggested that the compensatory response after SD may serve as a tool to investigate sleep in animals in which it is either not appropriate or not feasible to measure EEG.

Material and methods

Mongrel dogs (n = 15) of 17–35 kg, aged 1–7 years, well adapted for at least 4 weeks to laboratory conditions were used. They were kept for 7 consecutive days in each of three enclosures which differed in size, structure, and degree of isolation from the laboratory environment: 1) 'cage' (80/120/80 cm), 10 cages per room separated by solid walls; 2) 'run' (160/220/200 cm), three enclosures per room; neither cages nor run were separated from laboratory activities; and 3) 'kennel' (215/170/230 cm), a sound shielded, isolated room which was subdivided into

two compartments separated by wire mesh. Three dogs were kept in one compartment. The sleep deprivation experiments were carried out with 10 dogs in the kennel. The dogs were kept under a 12 h light-12 h dark schedule. Light was provided by fluorescent tubes (220 Lux measured 50 cm above the floor) from 06.30–18.30 h. The dogs were exercised in groups for two hours in a separate room (between 9 and 12 h) and fed daily between 16.00

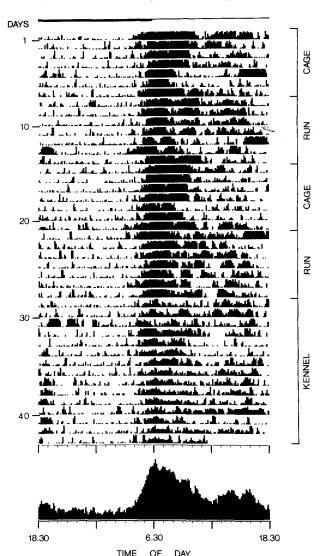


Figure 1. Long-term record (43 days) of motor activity of a dog. Activity is plotted at 11 levels with upper thresholds at 10, 30, 50, 70, 90, 110, 130, 150, 170, 190 and 230 counts (vertical bars). Mean activity (arbitrary units) during each consecutive 7.5-min recording episode is shown at the bottom. The 12-h dark period is indicated by the heavy bar at the top, the cage type on the right.

and 17.00 h. Working hours of the laboratory personnel were from 07.30 to 17.00 h.

Motor activity was measured continuously throughout the experimental period by an unobtrusive solid state monitor^{2,4} worn on the collar. The monitor integrated and stored motor activity values for 7.5-min episodes. Once a week the monitor was removed and the data were transferred into a PDP-11/34 computer for further analysis. A three way analysis of variance (ANOVA) was carried out to determine the influence of cage type, day of the week and dog. The effects of the three different enclosures on motor activity were reported elsewhere¹⁵. In a pilot study the behavior of several isolated dogs wearing the activity monitor was observed continuously for 24 h by time-lapse video recordings.

Sleep deprivation was carried out on Tuesdays or Wednesdays by keeping the kennel door open all day and by frequent visits to the kennel by laboratory personnel. During the normal 12-h dark period lights were left on and the dogs were disturbed as frequently as was necessary to keep them awake. During recovery the dogs remained under the same conditions as during control periods. Activity measures were obtained for one control day immediately preceeding the SD period, during SD and for one recovery day.

Results

The dogs exhibited a clear rest-activity rhythm in all enclosures, with activity predominating during the 12-h light period (figs 1–3, table 1). The amount of rest was quantified by the number of activity episodes ≤ 5 counts. During the 12-h light period several 'rest' episodes occurred (26.05% of total); however, a larger amount was present during the 12-h dark period (73.95%; table 2). A large interindividual variability was found in the amount of motor activity (fig. 2). The main activity bout began approximately 2 h before the lights were switched on, and continued for the first morning hours. A reduced activity period at noon was followed by moderate activity during

Table 1. Mean motor activity values expressed as a percentage of total daily activity (n=13; SEM in parenthesis) of three weeks in three different enclosures and of one week in the kennel where the SD experiments took place. D: mean motor activity based on mean hourly values for 12 h dark (18.30–06.30). L: mean values for 12 h light (06.30–18.30); missing data due to monitor change was replaced by mean values of other days. A: percentage of activity in the afternoon (13.30–18.30) of light time activity

	L	D	A
Three enclosures Kennel	76.11 (1.62) 75.40 (3.72)	23.89 (0.65) 24.60 (1.20)	37.58 (0.60) 41.22 (1.06)

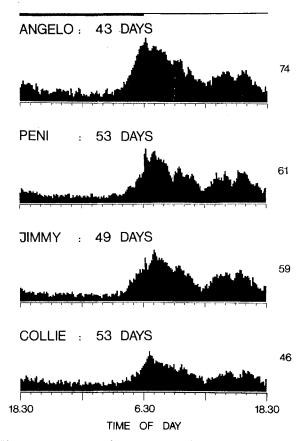


Figure 2. Mean activity of 4 dogs for the entire recording period (43–53 days; arbitrary units). The mean daily activity value is indicated on the right.

the afternoon (figs 1-3). The activity ratio afternoon/ total activity during the 12-h light period shows the predominance of activity during the morning hours (table 1). The activity pattern varied as a function of the day of the week (fig. 3). A two-way ANOVA with repeated measures revealed a significant influence of dog (p < 0.001) and weekday (p < 0.001). The effectiveness of the SD procedure was confirmed by the small percentage of rest episodes with ≤ 5 counts (L = 1.46% \pm 0.39 SEM, $D = 2.60\% \pm 0.38$). Interestingly, one animal with relatively high values of rest episodes during deprivation (L = 6, D = 8 compared to the mean values for the 10dogs L = 2.8 ± 0.74 SEM, D = 5.0 ± 0.72) exhibited no enhancement of rest during recovery. The effect of 24 h SD was a significant reduction of total activity in the first 6 h of the light period and a tendency to reduced activity during the entire 24 h of the recovery period (table 2,

Table 2. Mean activity values per hour and number of rest episodes (activity ≤ 5 counts; n = 10; SEM in parenthesis) for the control day and for the recovery day following 24 h sleep deprivation. Activity is computed as the percentage of total daily activity. Asterisks indicate significant difference from control (*p < 0.02; °p < 0.1; Wilcoxon matched-pairs signed-ranks test, two-sided)

	Light First 6 h	Second 6 h	12 h	Dark First 6 h	Second 6 h	12 h	Total 24 h
Mean activity p	er hour				<u> </u>		
Control	84.32 (12.42)	69.58 (10.76)	76.13 (10.75)	20.57 (3.00)	23.85 (4.42)	22.22 (3.09)	49.18 (6.23)
Recovery	50.22* (8.37)	58.58 (7.90)	54.41 (6.31)	16.42 (2.64)	22.23 (2.72)	19.33 (2.27)	36.89° (3.84)
Number of rest	episodes per hour						
Control	0.92 (0.20)	1.98 (0.30)	1.45 (0.23)	4.30 (0.17)	4.20 (0.39)	4.12 (0.20)	2.78 (0.16)
Recovery	1.83° (0.35)	2.48 (0.31)	2.13* (0.27)	4.90 (0.37)	4.23 (0.26)	4.68° (0.31)	3.41* (0.23)

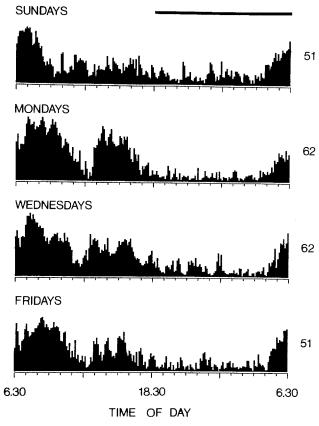


Figure 3. Activity for different days of the week. Mean values of 7 weeks obtained from one dog (arbitrary units).

fig. 4, left). The activity values per hour showed a reduction during the first morning hours when the animals were habitually very active, and an enhancement during feeding time (fig. 4, left). Activity values during most of the dark period after SD were higher than control. How-

ever, since only little activity habitually took place during this period, small differences could give rise to high percentages (fig. 4, left). In addition, a significant enhancement of rest, as indicated by the number of episodes with little activity (≤ 5 counts) was present in the 12-h light period as well as in the 24-h recovery period following the deprivation. Only a tendency to enhanced rest values was present in the 12-h dark period (table 2). The hourly values for rest episodes exceeded control values during most of the 24-h recovery period with the exception of the feeding hours (fig. 4, right).

Discussion

A clear rest-activity pattern was exhibited by all dogs. While the general pattern was similar, large individual differences were present for the amount of activity. Although motor activity was significantly influenced by the different cage types¹⁵, reflecting to some degree the influence of laboratory activities, a similar rest-activity pattern was found under isolated conditions (fig. 1, kennel). The dogs began to be active at 05.30, 1 h before the lights went on and 2 h before activity in the laboratory started. Therefore the activity pattern of the dogs did not merely reflect laboratory activity.

There are no reports of continuous long-term recordings of dogs under time-free or controlled conditions. In contrast to our results, where activity predominated during the day, intermittent activity measures in feral dogs revealed a predominance of activity at night¹⁴. Laboratory dogs may have largely adapted their rest-activity rhythm to human activities. This social dependence may account for some of the differences in the daily distribution of sleep and waking reported from different laboratories (see Introduction). Further recordings are being obtained from dogs living in private homes to examine the social

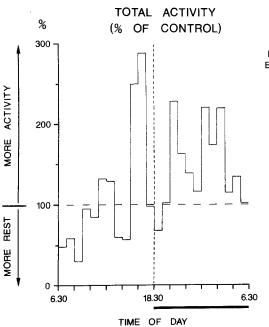
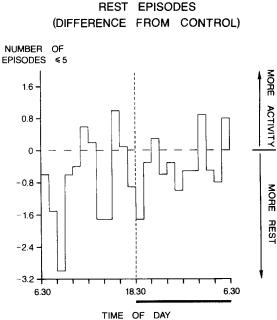


Figure 4. Mean hourly values of total activity and of rest episodes (number of activity episodes with activity ≤ 5 counts) during the recovery period after 24 h SD (n = 10). Total activity is expressed as a percentage



of the control (control = 100%), rest episodes as difference from control values. Black bars indicate the dark phase of the LD-cycle.

influence on activity and the degree of adaptation to human activities.

The results from this study show that the compensatory response to sleep loss can be recorded without measuring the EEG. Night-time immobility has been used as an index of sleep quality in drug studies². The same method was applied in the present study to measure the duration of sleep or rest. In dogs REMS is often accompanied by bouts of motor activity e.g. running activity and barking⁷. In the same study, frequent body movements were also reported during episodes of drowsiness. Our pilot study involving time-lapse video recordings confirmed this observation. Therefore, we arbitrarily allowed up to 5 counts for a rest episode in order not to include such 'agitated' sleep episodes. This measure proved not only appropriate for quantifying the effectiveness of SD but also to describe the effect of SD during recovery. Recoverv from SD was less evident from the reduction of motor activity than from the enhanced number of rest episodes. It has been previously demonstrated in the rat that the increase of slow-wave activity is not a consequence of locomotion but must be attributed to sleep loss^{3,9}. Particular attention was given in this study to avoiding unnecessary activation of the dogs during the deprivation. It is therefore not probable that the compensation after SD was only a consequence of enhanced motor activity.

The use of motor activity as a measure for compensatory processes after SD has formerly been applied in animal species where EEG measures are difficult or impossible to obtain. Thus rest deprivation in fish brought about by exposure to light prolonged rest during recovery²⁰. In cockroaches, rest deprivation by mechanical stimulation was also followed by a short period of enhanced rest¹⁸. The present results are consistent with the proposition that the reduction of motor activity after sleep loss reflects a homeostatic process of sleep regulation.

Acknowledgments. We thank Dr. A Borbély for his support and for comments on the manuscript. The study was supported by the Swiss National Science Foundation, Grant 3.518-0.83.

- 1 Borbély, A. A., Hum. Neurobiol. I (1982) 195.
- 2 Borbély, A. A., Br. J. clin. Pharmac. 18 (1984) 83S.
- 3 Borbély, A. A., and Neuhaus, H. U., J. comp. Physiol. 133 (1979) 71.
- 4 Borbély, A.A., Neuhaus, H.U., Mattmann, P., and Waser, P.G., Schweiz. med. Wschr. 111 (1981) 730.
- 5 Campbell, S.S., and Tobler, I., Neurosci. Biobehav. Rev. 8 (1984) 269.
- 6 Copley, M. P., Jennings, D. P., and Mitler, M. M., Sleep Res. 5 (1976)
- 7 Fox, M. W., J. small Anim. Med. 8 (1967) 77.
- 8 Gordon, C.R., and Lavie, P., Physiol. Behav. 32 (1984) 345.
- 9 Hanagasioglu, M., and Borbély, A.A., Behav. Brain Res. 4 (1982) 359–368.
- 10 Latash, L. P., and Shlyk, G. G., Sleep Res. 4 (1975) 145.
- 11 Lucas, E. A., Powell, E. W., and Murphree, O. D., Physiol. Behav. 19 (1977) 285.
- 12 Mitler, M.M., Boysen, B.G., Campbell, L., and Dement, W.C., Expl Neurol. 45 (1974) 332.
- 13 Royant-Parola, S., Borbély, A.A., Tobler, I., Benoit, O., and Widlöcher, D., Br. J. Psychiat., in press (1985).
- 14 Scott, M. D., and Causey, K., J. Wildl. Managt 37 (1973) 253.
- 15 Sigg, H., and Tobler, I., Z. Versuchstkde, in press (1986).
- 16 Takahashi, Y., Ebihara, S., Nakamura, Y., and Takahashi, K., Neurosci. Lett. 10 (1978) 329.
- 17 Takahashi, Y., Ebihara, S., Nakamura, Y., and Takahashi, K., Endocrinology 109 (1981) 262.
- 18 Tobler, I., Behav. Brain Res. 8 (1983) 351.
- 19 Tobler, I., in: Endogenous sleep substances and sleep regulation. Eds S. Inoué and A. A. Borbély. Japan Scientific Societies Press, Tokyo 8 (1985) 57.
- 20 Tobler, I., and Borbély, A. A., J. comp. Physiol. 157 (1985) 817.
- 21 Wauquier, A., Neuropsychobiology 10 (1983) 60.
- Wauquier, A., Verheyen, J.L., Van den Broeck, W.A.E., and Janssen, P.A.J., Electroenceph. clin. Neurophysiol. 46 (1979) 33.

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Luminous phenomena and earthquakes in southern Washington

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Summary. Luminous phenomena, mostly nocturnal lights, are associated with very small earthquakes in southern Washington state. The phenomena seem to be electrical in nature, related to earthquake lights, and tend to occur when the locus of earthquake activity moves across an active fault in an area of compressional stress.

Key words. Luminous phenomena; earthquake lights; nocturnal lights; earthquakes; Yakima Indian Reservation; Toppenish Ridge; Washington; seismicity; tectonic stress; geomagnetism; exoelectron; piezoelectric.

Introduction

Variable luminous events that occur during or just before some earthquakes have been reported for centuries $^{10, 16}$. Spherical, discrete sources of light of various colors and odd kinetics have also been paired with seismic activity $^{11, 15, 42}$. Statistical analyses suggest that large numbers of similar luminosities may be reported weeks to months before an increase in the number of low intensity ($\leq V$) earthquakes $^{27, 30}$. Several multivariate studies have shown

conversely that temporal patterns of earthquakes within a region can accurately forecast reports of these odd phenomena^{28, 31, 32}. Recently, miniature luminosities have been generated in laboratory experiments immediately before rock fractures. Rocks under uniaxial pressure produce light of 1–15 µs duration from exoelectron emission, independent of rock type and with a spectrum that of the ambient atmosphere^{6, 20}. All of these results are consistent