Paradoxical Sleep and Avoidance Learning of Swiss White Mice after Early Undernutrition by Raising in Large Litters

In pure inbred strains of mice, there is a good correlation between conditioned avoidance learning ability and the amount of time spent each day in paradoxical sleep[1]. The best learners (e.g. DBA/2 and C57Br/cd) have a long duration of paradoxical sleep, whilst the poor learners, such as the CBA and C57B1/6 strains, have a much shorter duration.

If Swiss white mice are subjected to early malnutrition, either by rearing them in large litters or by allowing them to suckle from a malnourished foster-mother, they show marked deficits in conditioned avoidance performance, even after several months of nutritional rehabilitation[2,3]. In this experiment, we have compared paradoxical sleep patterns of mice reared in small or large litters, to test if this early treatment also has an influence on paradoxical sleep.

Materials and methods. Mouse pups were cross-fostered at birth to give litters of 5 or 20 pups per mother, in the ratio 4 males to 1 female. Only males were used for EEG recording. The mice were weaned at 21 days, housed 8 per cage and allowed unlimited access to stock diet (Nafag S.A. Gossau, Switzerland) until the end of the experiment. The temperature of the animal room was 23 ± 2°C and the light cycle was 12 h white light, beginning at 07.00 h, and 12 h darkness.

At 40 days of age, 4 mice from each group were chronically implanted with 4 cortical and 4 muscle electrodes using the technique described by VALATX[4]. After 5–10 day recovery period in individual glass cages, recording leads were attached and the animals were allowed 10 days to habituate to the recording conditions. Continuous EEG and EMG recordings were taken for 4 days beginning at 19.00 h. Recordings were taken from 4 animals during each session by means of an 8-channel polygraph. The paper speed was 5 mm/sec and the results classified in half-page intervals (30 sec) into waking, slow wave sleep and paradoxical sleep.

Results and discussion. At weaning, the mean weight of mice reared in large litters was 6.5 g and the mean for the small litter mice was 16.2 g, a weight deficit of nearly 60%. The animals used for EEG recording were chosen from a pool of mice with weaning weights within 0.5 g of the mean for their respective groups. At 40 days, the deficit was still 33% with the large litter mice weighing 38.2 g and the small litter ones 25.2 g.

Rearing in large litters had no apparent long-lasting effects on time spent in paradoxical or slow-wave sleep as, at 8 weeks of age, the 2 groups of mice had similar patterns of sleeping and waking with no significant differences in any of the parameters measured (Table). We have found that the level of brain serotonin and dopamine in previously malnourished mice was the same as in controls while the noradrenaline level was higher (LEATHWOOD, unpublished observation). However, whole brain biogenic amine levels do not always correlate well with sleep, although turnover rates do[5].

During the first 2 weeks of life young rodents normally have high levels of paradoxical sleep (15–17 h per day)[6]. In contrast, the pups reared in large litters spend long periods each day struggling for milk, so not only are they subjected to nutritional and maternal deprivation, they are also deprived of paradoxical sleep. The combination of these early stresses has profound effects on adult behaviour, and the mice from large litters learn a conditioned avoidance response in the shuttle-box more slowly than those from small litters[2].

Although experiments in behavioural genetics have shown that strains of mice which learn rapidly in the shuttle-box spend more time in paradoxical sleep than the poor learners[1], this general rule does not appear to hold for environmentally induced changes in performance of Swiss white mice. However, correlation between avoidance performance and paradoxical sleep levels was best in the fast learning strains[1,7], a group which does not include Swiss white mice. As Swiss white mice have rather low levels of paradoxical sleep, it is possible that they are so near the base level that they cannot drop further. In fact, it now seems that the increase in paradoxical sleep during the period following each avoidance session is more closely related to avoidance ability than is the total duration of paradoxical sleep each day[5]. A study using mice with high levels of paradoxical sleep and learning ability should resolve this question.

Résumé. La relation positive entre la durée du sommeil paradoxal et l'apprentissage dans un test d'évitement conditionnel, trouvée chez quelques souches génétiquement pures, n'a pas été confirmée chez les souris «White Swiss» malnouries pendant l'allaitement.

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Time (± S.E.M.) spent in slow wave and paradoxical sleep in Swiss white mice (%)

Group	Daytime (07.00–19.00 h)		Night (19.00–07.00 h)	
	Slow wave sleep	Paradoxical sleep	Slow wave sleep	Paradoxical sleep
5	53.2 ± 3.3	5.1 ± 0.43	39.3 ± 2.8	3.0 ± 0.41
20	57.0 ± 0.82	5.3 ± 0.23	46.0 ± 3.2	3.7 ± 0.20