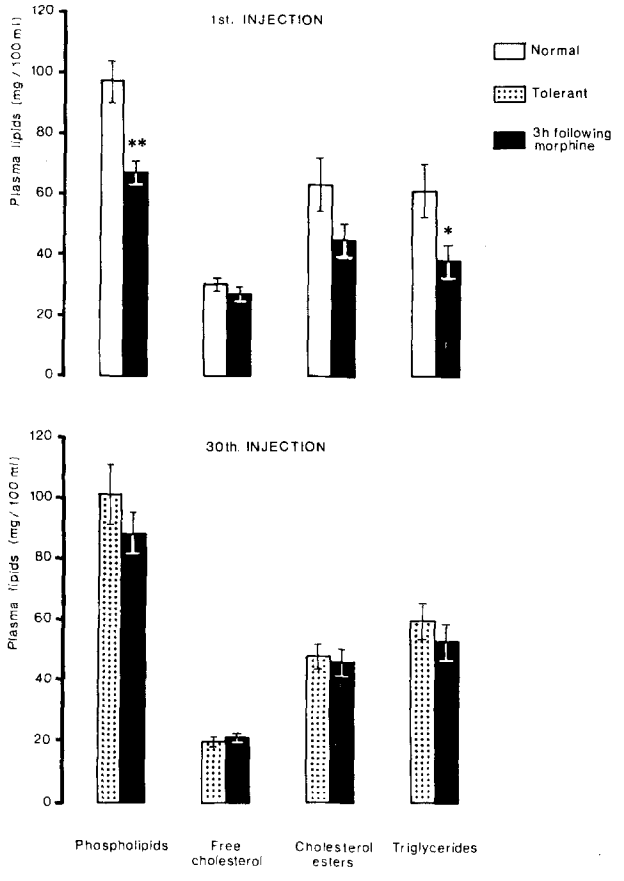

Fig. 2. Changes in morphine effects in various lipid fractions of rabbits plasma during chronic intoxication. Mean values ± SE, p is given by Student's t-test. * $p < 0.01$. ** $p < 0.05$.

tions are clearly higher than in controls. Finally, in animals withdrawn from morphine for several days or even weeks, the FFA concentration remains elevated, as does the immediate hypolipemic effect of the drug.

It is difficult to explain the effects on plasma lipids by changes in endocrine activity even though these effects occur simultaneously with changes in hormonal secretion. The initial injection of morphine elicits ACTH secretion as well as that of glucagon[4]. It is known that these 2 hormones mobilize fatty acids; however, we have observed the opposite effect on FFA. A single dose of morphine also causes a secretion of corticosteroids[2] whose immediate effects in rabbits are to lower plasma lipids[7]. It is possible that under these conditions the postmorphinic hypolipemia results from a hypersecretion of corticosterone. Nevertheless this explanation is not very satisfying when one considers the case of chronically treated animals in which morphine retains its depressive effect on plasma FFA and in which the drug actually depresses rather than increases the secretion of corticosterone[2]. In chronically morphinized rabbits, the FFA level in blood withdrawn 24 h after a given injection is abnormally high. At the present time we have no explanations for this.

To conclude, it is very difficult to supply a purely endocrinological explanation for the effects of morphine on blood lipids. Other experiments are necessary to elucidate the actions of morphine as well as the changes in action during chronic intoxication and withdrawal.

Résumé. Chez le Lapin, 1 h après une injection de morphine on note une baisse du taux des phospholipides, des triglycérides et des acides gras libres (AGL) du sang. Au cours du traitement chronique cet effet dépressif ne s'observe plus qu'au niveau des AGL dont le taux est anormalement élevé 24 h après la dernière injection.

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Effect of Long Term Lithium Treatment on Brain Fumarase Activity

The specificity of lithium therapy for manic-depressive psychosis is by now undisputed[1,2]; however the mechanism of this remarkable effect is still far from a satisfactory explanation[3,4]. Inspite of there being little or no effect on most enzymes studied[4], our previous communications reported the activation of succinate dehydrogenase[5] and the inhibition of aconitase[6] in the brains of mice treated with Li_2CO_3. These results led us to study the effect of Li^+ on brain fumarase (fumarate hydratase, E.C. 4.2.1.2)activity.

Material and methods. The experiments were carried out with male Swiss mice (mean initial body weight 20 g) maintained in a standard balanced diet ad libitum. To the control group of mice, distilled water was given. The other group of animals received as drinking water a solution containing 100 mg Li_2CO_3/l. After a period of 132 days of experimentation, the mice were killed by cervical dislocation and the brains removed quickly and stored at −20 °C until used. Brain homogenates (10%) were prepared in ice-cold 0.1 M phosphate buffer, pH 7.4, and the fumarase activity was determined by a modification of the spectrophotometric method of RACKER[7]. The final volume was 2.0 ml including 1.0 ml of 0.1 M sodium L-malate, pH 7.4, 0.95 ml of 0.1 M phosphate buffer, pH 7.4, and 0. 05 ml of brain homogenate to start the reaction. Incubation was carried out at 37 °C for 10 min and the reaction was stopped by the addition of 2.0 ml of 0.5 M $HClO_4$. A control was prepared for each sample by the addition of $HClO_4$ and homogenate to the buffered substrate at time zero. Spectrophotometric determinations in the supernatants were made at 240 nm in a Shimadzu QV-50 spectrophotometer equipped with cells of 10 mm light path. The enzymatic activity follows a zero order kinetics and it is proportional to concentrations of the homogenate up to 0.25 ml. One unit of enzymatic activity is equivalent to a change in optical density of 0.001 in 10 min at 37 °C. Total proteins in the homogenates

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Effect of Li^+ on mouse brain fumarase activity

Treatment	No. of mice	Body weight (g)	Fumarase (units/mg of protein)
Li_2CO_3	20	29.7 ± 0.8	1547 ± 29
Controls	20	28.8 ± 1.0	1414 ± 53

Each value represents the mean $\pm$ standard error of the mean.

were determined by the biuret method of GORNAL, BARDAILWL and DAVID[8], using crystalline bovine plasma albumin as standard and the specific activity of fumarase was expressed as units/mg of protein.

Results and discussion. The mean intakes of water or Li_2CO_3 solution throughout the period of experimentation were 6.3 and 6.4 ml/mouse/day, respectively. This volume is equivalent to 21.5 mg Li_2CO_3/kg body weight/day, which is in the range of the dose used in manic-depressive psychosis[1].

The final weights of mice and the brain fumarase specific activity are shown in the Table. Treatment with Li_2CO_3 does not influence the weights of the animals ($t = 0.703$, $P < 0.5$). A significant ($t = 2.201$, $P < 0.05$) increase of the specific fumarase activity was observed in Li^+ treated mice. Our experiments to demonstrate an in vitro effect of Li^+ were negative. Addition of Li_2CO_3 up to 0.5 mg/0.05 ml of the homogenate and incubation (37 °C, pH 7.4) for 15 min before fumarase determination did not change the enzyme activity.

FORN and VALDECASAS[9] reported the in vitro inhibition of rat and rabbit cerebral cortex adenyl cyclase by a wide range of Li^+ concentrations. On the other hand, the activation of fumarase by Li^+, as well as our previously reported effects of this ion on succinate dehydrogenase[5] (activation) and aconitase[6] (inhibition), were obtained after long term administration. These data suggest that the effects of lithium on those 3 enzymes of the Krebs cycle are indirect. The lack of knowledge of Li^+ mechanism of action precludes the exact evaluation of the role of these enzymes in manic-depressive psychosis.

Résumé. L'activité spécifique de la fumarase cérébrale des souris traitées pendant 132 jours au lithium (Li_2CO_3) a été déterminée. On a observé une activation significative de l'enzyme. Cependant, cet effet n'a pas été constaté in vitro.

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Effect of Carboxy- or Methemoglobinemia on Motor Conduction Velocity

There are several references to impairments of peripheral motoric nerve function after carbon monoxide (CO) intoxication: CO poisoning may produce peripheral neuropathy[1–10]; in dependence on CO partial pressure, the amplitude of action potential of isolated[11,12] or dissected[13] nerves decreased; and CO produces a retardation of the nerve conduction[3,13,14]. To determine whether the affection on the peripheral nerve is a hypoxic result only, we examined the motor conduction velocity of the N. ischiadicus after acute carboxy- or methemoglobinemia.

Methods. Male albino rats (outbred stock, about 200 g) in groups of 8–15 animals received s.c. injections of 0.5, 0.8, 2.4, and 12 mmol CO/kg or i.p. injections of 0.4, 0.8 and 1.2 mmol sodium nitrite ($NaNO_2$)/kg. Blood samples were taken after 30 min from the retro-orbital plexus. The rats were anaesthetized by hexobarbital (100 mg/kg i.p.) and the motor conduction velocity of N. ischiadicus determined according to the method of GLATZEL et al.[15]. Room temperature was 22 °C. The carboxyhemoglobin (CO-Hb) level was calculated from hemoglobin and CO level in blood. Hemoglobin was determined as cyanmethemoglobin. CO in blood was analysed according to the method of WENNESLAND[16] as modified by us[17,18]. The methemoglobin (Met-Hb) level in blood was assayed by the method of PFORDTE[19]. Student's t-test was used for statistical comparisons.

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