in rats[9]. However, it is difficult to explain these positive inotropic and negative chronotropic actions of pantethine with respect to the quantity of endogenous co-enzyme A inside cardiac muscle. The mechanisms of these actions have not been elucidated as yet.

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Lead distribution in the nervous system of 8-month-old rats intoxicated since birth by lead

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Summary. Lead levels in the nervous system of rats intoxicated for 8 months by lead acetate (0.2% in drinking water) varied according to the region: the lowest levels were observed in sciatic nerve and the highest in hippocampus and cerebral neocortex, while intermediate levels were observed in pons medulla, cerebellum, midbrain, hypothalamus and striatum.

It has been shown that in immature rats intoxicated with high lead doses, the lead content was higher in the cerebellum than in other brain regions[2-4] and that this increase occurred before the appearance of morphological lesions[5]. The distribution of lead in the nervous system of immature or adult rats intoxicated with lower doses has been much less studied[6]. In intoxications with low doses, the morphological findings have been reported to occur only in discrete areas[7] and the various alterations in neurotransmitter levels or metabolism which have been observed varied according to the region of the nervous system[6]. We therefore measured the lead levels in several regions of the nervous system of chronically (35 weeks) intoxicated rats, as differences in lead content could possibly play a role in the development of functionnal abnormalities.

Methods. 48 rats of the Sprague Dawley strain were distributed at random on the first day after birth among the nursing dams (8 rats per dam). The dams were fed a commercial solid diet and, as drinking fluid, were given either a solution of 0.2% lead acetate (0.11% Pb) in freshly boiled deionized water (test animals) or freshly boiled deionized water only (control animals). During this period the test animals were thus intoxicated through the mother's milk. 21 days after birth, the pups were separated from the dams and grouped according to sex (7-9 animals in each group). They were given the same diet and drinking fluid as the mothers had previously received. The mean daily lead intake during the last month of intoxication was 30 mg for females, 44 mg for males.

Eight months after birth, 5 test and 5 control animals were implanted with electrodes on the dura, and electroencephalographic recordings under basal conditions were carried out 1 week later. Nerve conduction velocities (motor and sensory) were determined on the sciatic nerve of 20 other animals. 1 week later, the latter animals were anesthetized with ether, blood samples were collected by cardiac puncture and blood was washed from the vasculature by a perfusion of saline with heparin. The rats were then decapitated, the brains were excised and dissected out into: pons medulla, cerebellum, hypothalamus, midbrain, striatum, hippocampus and parietal cortex. The sciatic nerves were excised bilaterally, giving a length of about 1.5 cm. All the glassware (quartz or plastic) was nitric acid-washed and great care was taken to avoid contamination by atmospheric lead. Plasma, red cells and nervous system samples were digested in concentrated nitric acid at 100 °C in a multiblock heater (Labline Instruments). They were then diluted to 5 ml and analyzed by flameless atomic absorption spectrometry (Varian AA-1275 atomic absorption spectrophotometer fitted with a CRA-90 graphite furnace). The lead concentration was determined by adding aliquots of lead solutions of known concentration to each sample.

Results and discussion. The main features concerning test and control animals are given in table 1. Plasma, red cells, brain areas and sciatic nerve lead levels are shown in table 2. In control animals, lead levels in the blood and all nervous system regions were below the limit of detection given the technique used (0.05 µg/ml for fluid and 0.10 µg/g for solid samples. This high limit does not allow a comparison of our results with those published on lead distribution in normal brain[8,9]; however, our results are more in agreement with the studies reporting low lead contents[8-10] than with those reporting a very high content in some areas[11,12].

The lead content in the nervous system of test rats varied according to the region: the lowest in the sciatic nerve, similar intermediate levels in pons medulla, cerebellum, hypothalamus, midbrain, striatum; a higher content in the hippocampus and the highest in the parietal cortex. This distribution differs from that observed in immature animals treated with high lead doses, for which the highest lead content was constantly oberserved in cerebellum[2-5], or treated with low doses for which the highest content was in hippocampus[13]. It also differs from that of animals treated up to 8 weeks[13] in which the distribution was more equal. The high content observed in the cortex in our experiments (35-week treatment) is closer to those observed in dogs treated for 12 weeks where the highest level was in the occipital cortex[14], and to those observed in human lead encephalopathies where the highest level was observed in the hippocampal and frontal cortex[15] and in the cortical gray matter[16]. It is thus possible that in young animals the

Table 1. Body weight, red cell count, nerve conduction velocities and EEG data in control and lead intoxicated, male and female 35-week-old rats

			Controls		Tests	
			Males	Females	Males	Females
Body weight (g)			582±71 (9)	312±17 (8)	524±44 (9)	303±24 (7)
Red cell count ($\times 10^{12}$/l)			7.4±0.3 (5)	5.8±1.1 (5)	7.7±0.5 (5)	6.4±0.3 (5)
Sciatic nerve conduction velocity (motor) (m/sec)			55±13 (5)	55±8 (5)	51±9 (5)	57±14 (5)
Sciatic nerve conduction velocity (sensory) (m/sec)			70±4 (5)	62±2 (5)	65±4 (5)	62±1 (5)
EEG	Arousal	NW	8-10 Hz (diffuse), β (frontal) (3)		8-10 Hz (diffuse), β (frontal) (3)	
		AW	7 Hz (parieto-occipital), β (frontal) (3)		7 Hz (parieto-occipital), β (frontal) (3)	
	Sleep	SW	2-5 Hz (diffuse) (3)		2-5 Hz (diffuse) (3)	
		SP	14 Hz, high voltage (diffuse) (3)		14 Hz, high voltage (diffuse) (3)	
		PS	7-8 Hz (diffuse) (3)		7-8 Hz (diffuse) (3)	

Values are mean±SD. The number of animals is indicated in parentheses. Differences between control and test group are in no case statistically significant ($p > 0.05$). Abbreviations: NW, normal waking; AM, active waking; SW, slow waves; SP, spindles; PS, paradoxical sleep.

Table 2. Plasma, red cells, brain areas and sciatic nerve lead levels in 8-month-old rats intoxicated by lead acetate (0.2% in drinking water) since birth

	Control rats		Test rats	
	a	b	a	b
Plasma	<0.05	<0.2	0.12±0.04	0.6±0.2
Red cells	<0.05	<0.2	2.26±0.26	10.9±1.2
Pons medulla	<0.1	<0.5	0.50±0.17	2.4±0.8
Cerebellum	<0.1	<0.5	0.56±0.06	2.7±0.3
Midbrain	<0.1	<0.5	0.50±0.07	2.4±0.3
Hypothalamus	<0.1	<0.5	0.48±0.19	2.3±0.9
Striatum	<0.1	<0.5	0.56±0.08	2.7±0.4
Hippocampus	<0.1	<0.5	1.00±0.27	4.8±1.3
Cerebral cortex	<0.1	<0.5	1.42±0.30	6.8±1.4
Sciatic nerve	<0.1	<0.5	0.22±0.13	1.1±0.6

a) Lead levels in µg/ml or µg/g fresh weight; b) lead levels in µM or nmoles/g fresh weight. Values are mean±SD. n=4 animals for each value.

lead content is higher in the less mature areas and that lead progressively accumulates in hippocampus and neocortex as the animal matures and the intoxication endures.

The reason for lead accumulation in those areas is not obvious. It has been reported that lead concentrates in capillaries[17-19] and it is known that the surface of endothelium is larger in cerebral neocortex than in other regions of the nervous system[20]. Therefore, the high lead content in cerebral cortex may in part be a consequence of a larger endothelial cell compartment with a high lead content. If lead has such a compartmentation, the total content in a given area will give little indication about the lead level to which brain cells are actually exposed.

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Regeneration and in vitro flowering of plants derived from callus cultures of opium poppy *(Papaver somniferum)*[1]

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Summary. From callus cultures of *Papaver somniferum* L., green buds and shoots were formed at a high rate under illumination at low temperatures, 16-18 °C. The shoots continued to grow and finally flowered in vitro and in soil.

The opium poppy, *Papaver somniferum* L., is an important medicinal plant, which contains morphinan alkaloids, such as morphine, codeine and thebaine. Various calluses have successfully been induced from the capsule and the other parts of the plant. However, it was shown from the chemical constituents[3] and by biotransformation experiments[4]