increased from 5 to 55 mM (release stimulation). Radioactive products used were D,L-norepinephrine ^{3}H-7, 8-20 Ci/mmole, serotonin ^{14}C-1 40 mCi/mmole, and dopamine ^{3}H 1-2, 15-20 Ci/mmole (CEA Saclay).

Results. With concentrations higher than 10^{-8} M, SAH increased NE and 5HT uptake in the 3 parts of the brain, but did not affect DA uptake (figure 1). Increase was significant in cortex (32%) and brainstem (17%) for NE and in cortex (25%), midbrain (28%) and brainstem (18%) for 5HT. SAH (10^{-6} or 10^{-5} M) did not alter DA, NE and 5HT release, either spontaneous or induced by KCl.

Administered in vivo to the animal 1 h prior to sacrifice (7 mg/kg i.p.) it induced in vitro uptake increase for NE and 5HT, significant only in brainstem and midbrain (figure 2), but did not alter DA uptake.

Discussion. The above results are to be compared with the action of 2 drugs acting on the central nervous system: a) Diphenylhydantoïne, an anticonvulsant product, induces in vitro NE uptake increase in the whole brain (NE 10^{-6} M)[9], but its effect is clear with a concentration 10 times higher than concentration of SAH. An increase of NE and 5HT uptake, when discharging is generalized, might explain the anticonvulsant effect of both drugs. b) Methionine sulfoximine, a convulsant product[10], lowers SAH level in different parts of rat brain[11].

Therefore SAH seems to be involved in the regulation of the metabolism of 2 neurotransmitters NE and 5HT. The 1st point of impact of SAH might be located at the level of catechol-O-methyltransferase; it is possible that SAH inhibits the formation of uptake-inhibiting methylated products. This mechanism seems to be rather unlikely, as, in our experimental conditions, few methylated products are formed, and the main product, normetanephrine, is a very weak uptake inhibitor[12]. Administration of SAH in vivo and observation of the effect in vitro seems to show a strong affinity of SAH for NE and 5HT uptake system; thus a direct action of SAH on uptake mechanism at the membrane level is more credible.

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Possible mechanism of rubidium-induced hyperactivity in the rat

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Summary. This study suggests that replacement of intracellular potassium by rubidium ions might lower the resting membrane potential. Thus rubidium-treated rats were more responsive to depolarizing influences and generated more cyclic AMP in the brainstem and consequently the behavioral changes.

Meltzer and associates[2] reported that rubidium injection increased the prevalent frequency of the electroencephalogram in monkey and altered the behavior in the direction of increased activity. They further suggested that rubidium, like lithium, might have therapeutic application in the affective disorders. Stolk et al.[3] reported that treatment of rats for 10 days with rubidium caused an increase in the rate of disappearance of norepinephrine in the brainstem after the biosynthesis of norepinephrine was inhibited, suggesting the antidepressant potential of rubidium. The antidepressant properties of rubidium in humans is being investigated in the metabolic wards of several countries[4,5]. Johnson[6] demonstrated that rubidium-treated rats recorded an increase in both the vertical rearing and horizontal locomotor activity. The objective of this investigation was to gain some insights into the mechanism of rubidium-induced hyperactivity in the rat.

Methods. Male Sprague-Dawley rats with an average b. wt of 150 g were purchased from Spartan Research Animals, Inc., Haslett, Michigan. Upon arrival, rats were randomly paired and housed in stainless steel cages. The animal room was illuminated from 08.00 to 20.00 h, and the thermostat was set at 25 °C. Rats were allowed a week to acclimate to the laboratory environment, and food was available ad libitum. Experimental animals were given 50 mM rubidium chloride in their drinking water while control rats received equimolar sodium chloride solution. Motor activity was measured on an activity platform (Lafayette Instrument Company) each day at 16.00 h. Only 1 control and 1 experimental rat were tested each day. Animals were taken to a dark room and acclimated for 30 min in solitude under red light. The motor activity for the next 30 min were then measured. The sensitivity of the instrument was adjusted so that only large body movements of the rat were recorded. An electric timer was used to terminate the experiment at the end of 30 min.

After ingestion of rubidium chloride solution for 4 weeks, each rat was acclimated to the microwave oven for 3 consecutive days to minimize stress prior to sacrifice. At 14.00 h on the following day, 1 control and 1 experimental rat were subjected to microwave irradiation individually, as described by Schmidt et al.[7,8]. Animals were then decapitated and the heads were chilled in ice. The brain was

Ingestion of 50 mM rubidium chloride in the drinking water for 1 month on brain potassium concentration* in the rat

	Control	Experimental
Rubidium	0.2±0.1	32.5±1.9
Potassium	118.8±4.4	84.4±3.3
Rubidium+potassium	119.0	116.9

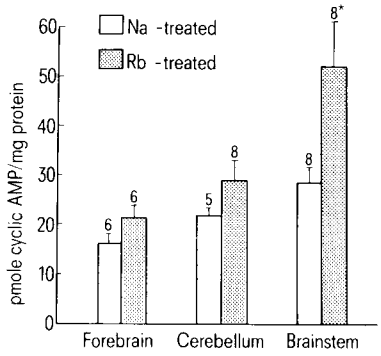
*Values, expressed as meq/kg wet wt, represent the mean±SE of 5-8 animals.

separated into brainstem, cerebellum and forebrain[9]. Cyclic AMP was assayed per procedure of Gilman[10], as modified by Weller et al.[11]. A Perkin-Elmer atomic absorption spectrophotometer (model 403) equipped with a 3-slot nebulizer burner was used for the determination of rubidium, sodium, potassium, calcium and magnesium ions[12].

Results. Rubidium-treated rats appeared more alert and aggressive relative to the sodium-treated controls. Hyperactivity was observed starting 2 weeks after rubidium ingestion. The activity meter reading (mean±SE) for rubidium-treated rats was 121±10 cpm as compared to 63±5 cpm for controls. Rubidium ingestion hat no effect on sodium, calcium and magnesium concentrations in the brain. However, rubidium was found to replace brain potassium approximately on a molar basis (table). The figure shows that ingestion of 50 mM rubidium chloride for 1 month lead to almost a doubling of the cyclic AMP concentration in the brainstem. There was also a general but statistically insignificant ($p > 0.05$) increase of cyclic AMP levels in the forebrains and cerebellums of rubidium-treated rats.

Discussion. The literature report that rubidium treatment increased locomotor activity in the rat[6] was also observed in this laboratory. In addition, this study demonstrated the replacement of brain potassium by rubidium in the rat. This may result in a less negative resting membrane potential[13], and rubidium-treated rats would be more responsive to depolarizing influences. It is therefore reasonable to predict that rubidium-treated rats may have a higher neuronal firing rate, which in turn releases more catecholamines at the nerve ending. This can explain the findings of Stolk et al.[3] that greater amount of neuronal stored norepinephrine were released to central adrenergic receptors in the rat after rubidium injections.

Cyclic AMP has been established to be the intracellular messenger mediating the biological effects of norepinephrine[14]. Increased levels of cyclic AMP would result in the activation of phosphorylase kinase in the synaptic region and phosphorylation of proteins in the plasma membrane[15,16]. Altered membrane permeability may then facilitate synaptic transmission[17], which could be expressed as hyperactivity in the affected animal.



Effect of ingestion of 50 mM rubidium chloride for 1 month on cyclic AMP levels in the rat; * $p < 0.05$.

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Radioprotective effect of a protein free parathyroid extract on the mitotic index of rat bone marrow cells

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Summary. The protective efficacy of an orally administered bovine protein-free parathyroid extract (PF-PTE) was studied on rat bone marrow cells in vivo with the mitotic index after 850 R irradiation. A remarkable decrease was found in the mitotic activity of bone marrow cells after irradiation in the non-protected animals. However, in the animals treated with PF-PTE after irradiation, a significantly smaller decrease and a faster recovery were found in the mitotic activity of the bone marrow cells.

We have demonstrated recently[1] that a bovine protein-free parathyroid extract (PF-PTE) increased the survival of 850 R and 1000 R whole-body X-ray irradiated rats. It was assumed that the radioprotective effect of the protein-free, and consequently calcium-inactive extract, was mainly due to a hitherto unknown water-soluble bioactive agent. The aim of this study was to investigate the mode of action of this agent. The preparation of PF-PTE was described previously[2]. The experiment was carried out in male CFE rats weighing 150–250 g. The whole-body irradiations were exposed by a Super Liliput 200 X-ray apparatus (Medicor, Budapest) 180 kV, 4 mA, filtered with 0.5 mm Cu, the focus-target distance: 50 cm, with a dose-rate of 7.8 R per min. The mitotic activity of bone marrow was studied after 850 R whole-body irradiation. 1 group of the irradiated animals ($n = 30$) received 0.1 ml physiological saline i.p. as the solvent of PF-PTE, on the day of X-ray exposure and on the 3 successive days thereafter. Another group of