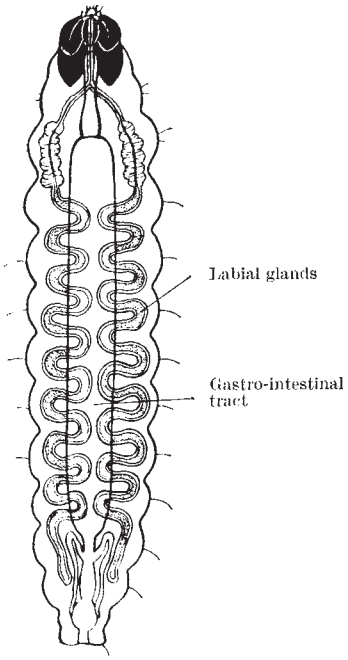
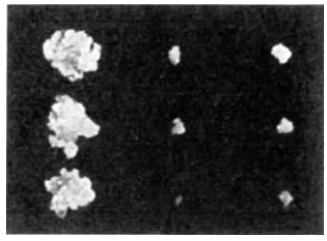


Fig. 3. Caterpillar of *St. argentipedella* (schematic drawing).



a *b* *c*

Fig. 4. Callus test from extracts of ten caterpillars of *St. argentipedella* collected October 23, 1968, and divided into (*a*) labial glands; (*b*) the gastro-intestinal tracts; (*c*) the rest of the bodies, and incubated in 12 ml. of medium for 25 days.

The thin layer chromatogram from the ethanolic extract of the labial glands of fifty caterpillars of *St. argyropeza* (collected on November 12) had twenty horizontal stripes, which were eluted and bioassayed in 25 ml. of medium for 24 days. This produced an active zone with R_F 0·65–0·8. Callus fresh weights of the three active stripes were 0·58 g, 0·47 g and 0·33 g. Average weights of controls were 0·05 g without kinetin, and 0·89 g for 0·01 mg/l. of kinetin. Table 2 shows the data we obtained from our results.

Total activity R_F was relatively low compared with corresponding assays of caterpillars or their secretions collected in September and October; and only one cytokinin could be detected in these glands in November while a more detailed study of green islands or even the intact caterpillars suggests that at least three active substances are involved. We estimated the labial glands to contain up to 0·5 per cent kinetin equivalents with relation to dry weight.

In summary we can say that under the influence of certain leaf-miners there is a large accumulation of cytokinins around the mines, which may be responsible for the preservation of chlorophyll, at a time when the metabolic activity of the plant is decreasing and the leaves are turning yellow. This is, of course, of considerable ecological value to the development of the larvae. The caterpillars themselves contain large quantities of cytokinin in their labial glands and in their excrements.

The problem of the origin of these cytokinins, however, remains to be investigated. Although it seems most probable that the labial glands of *Stigmella* larvae are a very active site of cytokinin biosynthesis, creating a zone of accumulated nutrients around the developing caterpillars, we cannot exclude two other possibilities. First, the cytokinins may be formed in the leaf under the influence of the caterpillars, and second, cytokinins may be attracted from other parts of the tree and accumulate near the holes, under the influence of the caterpillars.

Table 2

Material	Season of collection	Fresh weight (mg)	μg Kinetin equivalents
10 Caterpillars	Sept. + Oct.	100	2–5
100 Green islands	,, ,,	2,000	20–50
Old leaves	,, ,,	2,000	< 1
Young leaves	Early summer	2,000	1–3

L. Engelbrecht
U. Orban

Institute of Plant Biochemistry of the German Academy of Sciences, Halle/Saale.

W. Heese

Institute of Zoology of the Martin Luther University, Halle/Saale.

Received December 23, 1968; revised February 25, 1969.

[1] Hering, M., *Biology of the Leaf Miners* (Junck, 's-Gravenhage, 1951).
[2] Engelbrecht, L., *Flora*, A, **159**, 208 (1968).
[3] Linsmaier, E., and Skoog, F., *Physiol. Plant*, **18**, 100 (1965).
[4] Heide, O. M., and Skoog, F., *Physiol. Plant.*, **20**. 771 (1967).

Rubidium: a Potential Modifier of Affect and Behaviour

It has been generally recognized that sodium and potassium ions are essential to neural conduction and to the normal functioning of the nervous system. The role of lithium in nerve conduction is less understood. It does reduce manic hyperactivity and elation[2–5], however; thus its therapeutic use in the manic phase of manic depressive psychosis. A substance capable of producing similar improvements in the depressive phase remains to be discovered.

Lithium may produce these changes in behaviour by preventing the binding of sodium and potassium by strandin in neuronal membranes *in vivo* as it has been shown to do *in vitro*[1]. Because rubidium has an effect, in a sense, "opposite" to the effect of lithium *in vitro* on strandin constrained in an artificial "membrane", it is possible that it may, likewise, have an "opposite" effect on naturally occurring neuronal strandin. Such an *in vivo* effect might be observed in animals by changes in overall behaviour and in EEG.

EEGs were recorded monopolarly from six macacus rhesus monkeys using needle electrodes inserted subcutaneously in the following locations: frontal, central ("motor") occipital and anterior temporal, bilaterally. The monkeys were conscious, unmedicated and seated upright, the head immobilized and the eyes blindfolded. Cations were administered in solution in the femoral vein of either leg. As a control, EEG recordings were taken for 15–20 min before IV injection. As a further control, 2–4 ml. physiological saline was injected, at a rate of 0·015 mequiv./min. Subsequently, the chlorides, either of sodium, potassium, lithium or rubidium, were injected at concentrations ranging from 0·5 to 2·0 mequiv./ml. into the inflowing saline from a branch tube located near the needle. Serum sodium and potassium were determined by conventional flame photometry, serum (and brain) rubidium by atomic absorption spectrometry.

Before injection the EEG showed chiefly 6–7 H_3 waves with slight transitory spiking over central ("motor")

Table 1. CONCENTRATIONS OF MONOVALENT CATIONS IN MONKEY WHO RECEIVED A FATAL 12 MEQUIV. DOSE OF RUBIDIUM CHLORIDE*

Brain area	Rubidium	Sodium	Potassium
Mixed†	1·48	65	94
Cerebellum	1·45	53	89
Left motor	1·77	57	91
Left anterior temporal and superior medial	1·46	64	98
Blood			
Cells	9·1	49	97
Serum	12·9	142	19

* mequiv./kg wet weight.

† Frontal, premotor and right motor.

no respiratory or cardiac distress. The most prevalent frequency (8–9 Hz) changed during the first half hour to 6–7 Hz, and then increased to 10–11 Hz.

Follow-up behavioural and EEG observations on monkeys that had received rubidium showed a complete return to their pre-treatment state.

The chronic effects of rubidium chloride were studied as follows. Two monkeys were each given a daily orange which had been injected with rubidium chloride (see Table 2) until they refused it. One monkey, which initially

Table 2. ACCUMULATION AND EXCRETION OF RUBIDIUM IN THE MACACUS MONKEY

Monkey	Date	Intake mm/day	Rubidium Cells mequiv./l.	Rubidium Serum mequiv./l.	Rubidium Cell serum	Potassium Cells mequiv./l.	Potassium Serum mequiv./l.	Potassium Cell serum	Sodium Serum mequiv./l.	Haematocrit per cent
No. 17	4/3	4·0	9·60	0·62	15·5	74	3·5	21·1	157	51
	4/10	Trace	9·36	0·53	17·7	66	3·4	19·4	150	42
	4/18	—	8·32	0·55	15·1	72	3·9	18·5	153	—
	4/26	—	7·36	0·40	18·4	92	3·6	25·6	154	49
	5/8	—	4·40	0·24	18·3	86	4·6	18·7	157	52
No. 18	3/14	0·5	2·40	0·12	20·0	81	4·5	18·0	143	45
	3/19	1·0	3·60	0·25	14·4	94	4·5	20·9	147	45
	3·26	2·0	6·40	0·32	20·0	86	4·0	21·5	142	41
	4/3	4·0	9·08	0·48	18·4	70	3·2	21·9	152	53
	4/10	Trace	11·60	0·70	16·5	90	4·7	19·1	148	46
	4/18	—	7·72	0·49	15·6	64	3·9	16·4	148	—
	4/26	—	7·72	0·42	18·4	90	4·1	22·0	152	42
	5/8	—	4·80	0·24	20·0	84	4·7	18·3	149	45

areas, bilaterally. There was discernible change in behaviour or EEG during or immediately after the initial control injection of 2–4 ml. of physiological saline in any experiment. Repeated injections of 0·1 M NaCl (1 ml. in 80 s) produced no discernible change in behaviour or EEG. One ml. of 2 N potassium chloride was injected in 13 s and was followed by a transitory increase to 20 c H_3. There was no change in behaviour. Forty ml. (80 mequiv.) of lithium chloride, injected over a 1·6 h period, produced transitory laboured respiration, jerking of tail and left arm, and a slight increase in the incidence of 6–7 H_3 waves, but not of spikes. Behaviour and EEG returned to the control pattern after 40 s and remained so for 1·3 h of continuous recording. These minor transitory changes were in marked contrast to the effect of rubidium on this same monkey, who, 1 week previously, had been given 1 ml. containing 2 mequiv./ml. rubidium. This produced 2–3 H_3 waves of high amplitude, especially over frontal and central areas; these showed "mitten" patterns (Gibbs). At the same time there was marked twitching of the left side of the head lasting 40 s. Then, 3–6 Hz activity recurred in bursts over all areas. Repetition of the same dose produced a similar reaction, but more violent, with struggling, cyanosis, shrill crying, laboured breathing, clonic jerking of left shoulder and arm, and high amplitude 2–3 Hz slow waves. Six minutes later the behaviour and EEG had returned to their pre-treatment pattern.

A monkey which had received potassium chloride was given a sodium chloride injection; then, 2 min later, a slow injection of a total of 6 ml. of rubidium chloride (12 mequiv.). This produced spiking and increased 5–6 Hz activity especially over the central areas bilaterally, associated with severe facial twitching, crying, defaecation, opisthotonus, followed by a loss of EEG rhythms, cessation of respiration and, some 30 s later, cessation of heart beat. There was increased rubidium content in the left motor area of the brain (see Table 1).

Any effects of sodium and potassium in this unexpected fatality appear to be ruled out by the following observations. A monkey which had received no cations was given 2 ml. (4 mequiv.) of rubidium chloride intravenously. This produced behavioural and EEG changes similar to those previously observed in rubidium treated animals. In addition, there was a mild but generalized seizure accompanied by widespread EEG spiking followed by a loss of EEG activity, respiratory arrest, cessation of heart and death.

Subsequent injections of rubidium chloride of about one twentieth of the previous dosages in other monkeys produced phonation, struggling and facial twitching but retreated instantly when approached, eventually stood his ground. The second monkey, originally aggressive, became hyperactive and more aggressive. Both animals showed a gradual increase in the incidence of the higher frequencies, from 8–9 Hz to 11–12 Hz at the end of observation.

The biological half-life of serum rubidium in each monkey was estimated to be 20 days, based on serum measurements following removal of rubidium from the diet. Rubidium was without effect on serum sodium and potassium levels (see Table 2).

In a subsequent double blind experiment, four monkeys were given rubidium and two were used as controls. Those receiving rubidium showed such increased activity and aggressiveness that they were all identified correctly. None of the toxic effects noted after IV injections occurred as a result of these chronic experiments.

If rubidium chronically administered to increase its blood level produces increased activity and alertness in monkeys, and also produces a shift in the EEG to a preponderance of higher frequencies, this shift might be speculatively regarded as a prolonged "alerting" response similar to that observed in animals and humans. This might suggest that rubidium has the potential to increase the general level of alertness, activity and affect of humans, as contrasted with lithium, which tends to slow the EEG and reduce hyperactive behaviour and excessive affect.

In any projected trial of rubidium in humans, it would appear that intravenous administration is absolutely to be avoided due to the demonstrated toxicity with convulsive and even lethal results, consequent apparently on too rapid a rise in blood rubidium levels.

Gradual administration by mouth, however, would seem to present none of the above hazards and, in addition, seems to be more effective in producing a prolonged modification of behaviour.

H. L. MELTZER
R. M. TAYLOR
S. R. PLATMAN
R. R. FIEVE

New York State Psychiatric Institute,
722 West 168 Street,
New York, NY 10032.

Received April 21; revised May 27, 1969.

[1] Meltzer, H. L., *J. Neurochem.*, **13**, 423 (1966).
[2] Cade, J. J., *Med. J. Austral.*, **36**, 349 (1949).
[3] Gershon, S., and Yuwiler, A., *J. Neuropsychiat.*, **1**, 229 (1960).
[4] Schou, M., *et al.*, *J. Neurol. Psychiat.*, **17**, 250 (1954).
[5] Wharton, R. N., and Fieve, R. R., *Amer. J. Psychiat.*, **123**, 706 (1966).