Lithium lowers renal, cardiac and splenic ornithine decarboxylase activity in mice[1]

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Summary. A single i.p. injection of lithium chloride (5–7.5 μmoles/g b.wt) in mice caused a 70–80% decrease in renal, cardiac and splenic ornithine decarboxylase (ODC) activity within 1 h, whereas pulmonary ODC activity was unaffected. Lithium chloride did not have any effect on ODC activity in vitro when added to homogenates of the tissues studied. We suggest that the effect of lithium on ODC activity is not direct, but mediated via e.g. hormonal or nervous influence.
Key words. Lithium; ornithine decarboxylase activity; polyamines.

In a previous study[2] we have shown that the activity of ornithine decarboxylase (ODC, E.C. 4.1.1.17), the rate-limiting enzyme for formation of putrescine, spermidine and spermine, decreases in rat kidney after partial obstruction of the renal artery. The renin excretion of such kidneys is higher than normal[3] and is concomitant with a rapid development of systemic arterial hypertension[3,4]. It has recently been reported[5] that lithium ions increase renin release from rabbit kidney slices in vitro. It could then be expected that lithium might decrease renal ODC activity. In the present study ODC activity was determined in kidneys from male mice after administration of a single dose of lithium chloride. In order to elucidate whether possible effects of lithium on ODC activity were limited to the kidneys, or whether the ion had a systemic effect, ODC activity was also determined in heart, spleen and lung.

Materials and methods. Male mice (NMRI strain) weighing 35 g, and with an age of about 15 weeks were used. The animals were given a single i.p. injection of lithium chloride either 7.5 or 5 μmoles/g b.wt (which seems to be well below that giving toxic effects[6]). The control animals obtained corresponding injections of saline. After 1, 3, or 24 h the animals were killed, and the organs to be studied were rapidly removed and cooled on ice. The tissues were then homogenized, and assays of ODC activity as well as concentration of putrescine, spermidine and spermine were performed as described previously[7]. In a separate series of experiments lithium chloride was added to homogenates of organs from control animals and ODC activity was determined in order to see whether lithium had a direct effect on ODC activity. Results are expressed as mean±SE, with number of animals in parentheses. Statistical comparisons were performed using Student's t-test (two-tailed) for unpaired data.

Results. All animals became sedated but not unconscious after administration of 7.5 μmoles lithium chloride/g b.wt. In a separate series of experiments only 5 μmoles/g was given, as the sedation following this dose was less pronounced.

The kidneys had high ODC activity when compared with heart, lung and spleen (see table). 1 h after the injection of 7.5 μmoles lithium chloride/g, a marked reduction in renal ODC activity was noted. It then rose but was still significantly lower than the control level 3 h after the injection. After 24 h the activity had normalized (not shown in the table). In the heart, the relative decrease in ODC activity was similar to that in the kidney. No effect of lithium chloride was seen on pulmonar ODC activity. The effects on the spleen (studied only at the 1-h period) were similar to those on heart and kidney.

After injection of 5 μmoles lithium chloride/g b.wt the following ODC activity (nmoles/g × h) was obtained 1 h after the administration; heart 0.19±0.02 (n = 7), lung 0.84±0.14 (n = 7), spleen 0.79±0.14 (n = 7) and kidney 521±168 (n = 7). The activities did not differ significantly from those obtained after 7.5 μmoles lithium chloride/g (see table).

To elucidate whether lithium ions have a directly inhibiting effect on ODC, tissue homogenates were incubated for determination of ODC activity without and with lithium up to very high concentrations (five specimens of each organ). Lithium was found not to possess any directly inhibiting effect whatever.

Contents of putrescine, spermidine and spermine were not significantly altered after lithium administration (7.5 μmoles/g; 7 animals in each group) in any of the tissues examined.

Discussion. In a previous study[2] we have found that ODC activity in rat kidney decreases after experimental renal artery stenosis; a procedure known to induce arterial hypertension by renin release from the ischemic kidney[3]. Lithium ions have been shown to increase renin release from rabbit kidney in vitro[5]. It could be possible that there exists an inverse relation between ODC activity and renin release. If such a relationship exists, lithium would then be expected to decrease renal ODC activity. The present study on mice supports this assumption as i.p. injections of lithium chloride resulted in a 80% decrease in ODC activity within 1 h (see table). The effect of lithium chloride on ODC activity was not limited to the kidney but was found also in heart (80% decrease) and spleen (70% decrease), whereas pulmonary ODC was unaffected. The variations in lithium sensitivity might have several explantions; the ion might be unevenly distributed in the body, or the action of lithium on ODC activity might be indirectly mediated via e.g. hormonal or neural mechanisms. In accordance with an indirect action is the lack of effect of lithium on ODC activity in vitro.

ODC activity (nmoles/g × h) in kidney, heart, lung and spleen in control mice, and at 1 h and 3 h after i.p. injection of lithium chloride in a dose of 7.5 moles/g b.wt

	Controls	1 h	3 h
Kidney	1938 ± 257 (6)	354 ± 103*** (14)	1007 ± 287* (13)
Heart	1.65 ± 0.12 (9)	0.31 ± 0.16*** (6)	0.34 ± 0.02*** (6)
Lung	0.63 ± 0.09 (9)	1.20 ± 0.45 (6)	0.95 ± 0.12 (6)
Spleen	2.41 ± 0.48 (6)	0.65 ± 0.17** (6)	–

Number of animals in parenthesis. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, when compared with the controls.

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2 Uvelius, B., and Rosengren, E., Acta physiol. scand. *124* (1985) 11.
3 Leenen, F., and de Jong, W., Circulation Res. *36–37*, suppl. 1 (1975) 179.
4 Lundgren, Y., Acta physiol. scand., suppl. 408 (1974).
5 Ginesi, L.M., Munday, K.A., and Noble, A.R., Br. J. Pharmac. *78* (1983) 3.
6 DeFeudis, F.V., and Delgado, J.M.R., Nature *225* (1970) 749.
7 Henningsson, S., Persson, L., and Rosengren, E., Acta physiol. scand. *102* (1978) 385.

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