Effect of ouabain on Drosophila melanogaster

Concentration of ouabain (mM/l)	Dead parent flies (out of 30) in 10 tubes after 6 days		Living F_1 flies in 10 tubes after 12 days		
	Males	Females	Males	Females	Total
0	2	–	266	288	554
3.0	–	13	72	42	114
3.5	–	9	12	19	31
4.0	–	17	12	10	22
4.5	–	13	11	9	20
5.0	–	18	6	5	11
5.5	2	21	7	10	17
6.0	2	21	2	2	4

if the induction of resistance against ouabain can be achieved in Drosophila. Some questions remain open. It is not clear if the decreased survival of the progeny after ouabain treatment is the result of an effect on the germ cells of the male parents, on the germ cells of the female parents or on the development of the progeny itself. There might be a more complex effect, too. This question might be answered by testing the fertility of adult flies after ouabain treatment.

A problem that should also be mentioned is the marked difference of the toxicity of the substance against adult flies. Female flies are killed by ouabain to a much higher extent than male ones. This might be overcome by taking an increased number of females in the test, but further investigations must clarify the sex difference of Drosophila melanogaster against ouabain.

Enhancement of barium- and cesium-induced adrenal catecholamine release by lidocaine[1]

J. L. Borowitz and I. Shanbaky

Department of Pharmacology and Toxicology, School of Pharmacy and Pharmacal Sciences, Purdue University, West Lafayette (Indiana 47907, USA), 27 September 1976

Summary. Catecholamine release evoked from isolated perfused bovine adrenals by Ba^{+2} or Cs^+ is enhanced by lidocaine or by a calcium-free medium. The action of Cs^+ therefore differs from that of K^+ or Rb^+ in adrenal medulla. Divalent and monovalent metallic cations of relatively large atomic weight like Ba^{+2} and Cs^+, probably penetrate the cell more easily than small highly charged ions and act intracellularly to cause adrenal catecholamine release. Local anesthetics and calcium-free media may allow greater influx of Ba^{+2} and Cs^+ into adrenomedullary cells.

In contrast to the diminished action of acetylcholine or K^+ in a calcium-free medium, Ba^{+2} is more effective in adrenal medulla in the absence of extra-cellular calcium[2]. Cesium ion is reported[3] to release adrenal catecholamines in a manner similar to K^+, and would appear to have a different mechanism than Ba^{+2} in this tissue. However, the present study shows that the actions of both these ions are enhanced by lidocaine in adrenal medulla and suggests that they have mechanisms in common.

Fresh bovine adrenals were perfused (10 ml/min) with an aerated tris buffered Lockes solution, 22 °C as previously described[4]. Addition of Ba^{+2} to the medium caused catecholamine release (figure 1). The perfusate was assayed for total catecholamines by the colorimetric method of von Euler and Hamberg[5]. When lidocaine, 0.1 mM, was added along with Ba^{+2}, an enhanced response was seen (figure 1). The table shows that adrenal catecholamine release by Cs^+ is also enhanced by 0.1 mM lidocaine. The stimulatory effect of Cd^{+2} on adrenal medulla[6] was not altered by 0.1 mM lidocaine (4 glands). Dose response curves to La^{+3} in 6 pairs of bovine adrenals showed a decreased catecholamine release (20%) when lidocaine, 0.1 mM, was also present but the difference was not statistically significant. Thus enhancement of adrenal catecholamine release by lidocaine occurs with only a few metal ions of relatively large atomic weight and relatively low charge density.

Since local anesthetics block calcium flux across adrenomedullary plasma membranes[7], it is not surprising that barium's action on adrenal medulla is enhanced both by lidocaine and by ommission of calcium from the perfusing fluid. Cesium's effect in rabbit adrenals however is reportedly not enhanced by a calcium-free medium[3]. This seemed illogical so the effect of calcium lack on cesium's action was retested in isolated bovine adrenals. Rubidium was studied for comparison. Adrenal catecholamine release by Rb^+ is largely dependent on extracellular calcium although a

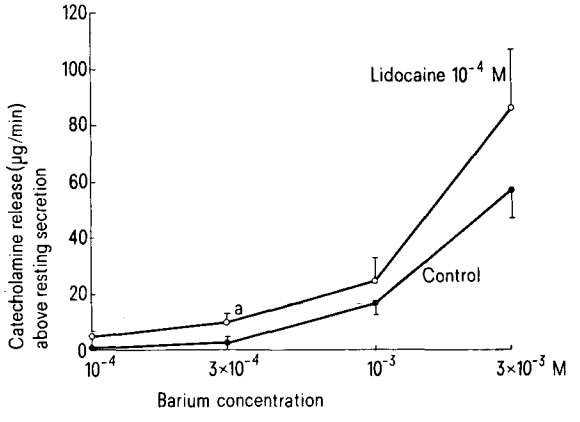

Fig. 1. Enhancement of Ba^{+2}-induced catecholamine release from bovine adrenals by 0.1 mM lidocaine. The barium solutions were infused (10 ml/min) one after the other. Each point is the mean of 4 experiments. a = $p < 0.05$ compared to control. Lidocaine alone has no effect on adrenal catecholamine release.

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Increased cesium-induced catecholamine release from isolated adrenals by lidocaine, 0.1 mM

Experiment	Total catecholamine µg/min above resting secretion Control	Lidocaine
1	78.2	119.3
2	224	235
3	75.6	165.7
4	87.5	76.6
5	24.5	36
6	28.1	69.3
7	92.7	119.3
8	126.6	213.6
Mean	92.2	129.4

Paired glands from the same animal were used for each experiment. 4 right glands and 4 left glands were used in each group. Release was measured during a 1-min-exposure to 56 mM Cs^+. Lidocaine significantly enhanced release by comparison of paired differences ($p<0.05$). Lidocaine alone has no effect on arenal catecholamine release.

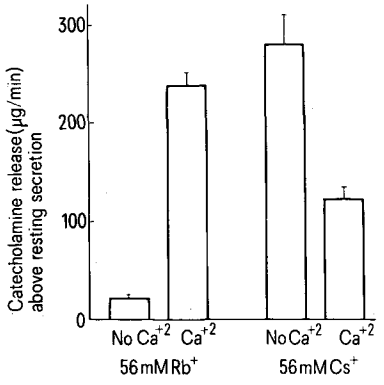

Fig. 2. Effect of a calcium-free medium on the response of bovine adrenal medulla to Rb^+ and Cs^+. Glands were infused for 20 min with calcium-free Lockes solution and then stimulated with 10 ml (1 min) of Rb^+ or Cs^+ containing solution (sodium content was decreased to maintain isotonicity) in the absence of calcium. 2 min after the initial stimulation, calcium was added back to the medium and the glands were restimulated with the same ion 18 min later. 4 glands were used for each ion.

small response is seen when calcium is absent from the medium (figure 2). The response to Cs^+, by contrast is greater without calcium in the medium (figure 2).

Thus, mechanism of adrenal catecholamine release by alkali metal varies with atomic weight. In the absence of extracellular calcium, the lightest ion K^+ is ineffective, Rb^+ is slightly active, and the heaviest ion Cs^+ shows greater effectiveness than in the presence of calcium. Potassium probably acts on adrenal medulla in the classical manner to depolarize the plasma membrane and admit extracellular calcium into the cell. Cesium as well as Ba^{+2} may act intracellularly since these ions are more potent under conditions of increased membrane permeability (calcium-free media). Lidocaine may increase membrane 'fluidity' or induce 'prelytic' changes, which allow increased penetration of Ba^{+2} and Cs^+ (see ref.[8]). Rubidium's effect appears to be a mixture of Cs^+-like and K^+-like actions. Many small metallic cations are essentially ineffective as agonists in adrenal medulla, e.g. Mg^{+2}, Co^{+2}, Ni^{+2}, Mn^{+2}, Zn^{+2}, Li^+ [3,6,8], whereas large metallic cations like Hg^{+2} are very good releasers of adrenal catecholamines[7]. Some metals may fail to release because they cannot activate the secretory apparatus[9]. Other ions e.g. Ba^{+2}, Cs^+ and possibly Sr^{+2} [9], may fail to release or release relatively small amounts because they cannot penetrate well into adrenomedullary cells. Plasma membrane surfaces of adrenomedullary cells may carry weak fixed negative charges which would favour penetration of ions of low charge density[10].

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Possible role of GABA in the development of tolerance to alcohol[1]

G. J. Leitch, D. J. Backes, F. S. Siegman and G. D. Guthrie

Indiana University School of Medicine, Evansville Center, 8600 University Blvd, Evansville (Indiana 47712, USA), 15 September 1976

Summary. Rat cerebellar GABA levels were reduced following 2 weeks alcohol administration. Animals also exhibited alcohol tolerance with an air righting reflex. This tolerance was mimiced by picrotoxin administration in control animals and was reduced in animals chronically administered alcohol by aminooxyacetic acid.

Acute exposure to ethanol appears to have a variable effect on central nervous system GABA (gamma amino butyric acid) levels. Both increases[2,3] and decreases[4,5] in the level of this putative transmitter have been reported. Chronic alcohol administration more generally causes a reduction in GABA levels[3], and such a reduction is greatest at that time when the signs of alcohol withdrawal are most severe[6]. Drugs that increase brain GABA levels reduce alcohol withdrawal convulsions[7]. The present communication deals with the question of whether or not GABA is involved in alcohol tolerance. The air righting reflex was used as the test procedure as it involves a cerebellar component, which includes GABAergic neurones[8].

Materials and methods. Male Sprague-Dawley rats, 200 g (CD outbred, Charles Rivers Breeding Labs., Inc., Wilmington, MA.) were divided into 3 groups. The control group was fed unsupplemented Purina lab chow meal and water ad lib. The alcohol group was fed one half the mean weight of food consumed by the control animals, and 10% ethanol was their only source of drinking water. The glucose group was fed the same amount of meal as the alcohol group, was given a glucose solution isocaloric with the mean daily alcohol consumption of the alcohol