Table 1. Distribution of taste thresholds for phenylthiourea among Ashkenazic Jews classified by sex.

Group	Taste thresholds																Total
	<1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	
Males	12	11	7	3	1	2		8	10	27	22	5	3					111
Females	14	5	9	3		1	2	5	16	31	29	13	2		1	1	1	133
Total	26	16	16	6	1	3	2	13	26	58	51	18	5		1	1	1	244

Table 2. Percentage of nontasters among Ashkenazic Jews as a whole, and among Polish Jews.

Sample	Total	Tasters (No.)	Nontasters (No.)	Nontasters (%)
Ashkenazic Jews (whole sample)	244	176	68	27.86 ± 2.87
Polish Jews	102	80	22	21.56 ± 4.07 } $\chi^2 = 3.46$
Remainder	142	96	46	32.39 ± 3.92 } $P = 0.06$

Table 3. Comparative data on the frequency of nontasters among Polish Jews and among Europeans and Mongoloids.

Group	Total	Tasters (No.)	Nontasters (No.)	Nontasters (%)
Europeans*	647	443	204	31.53 ± 1.82 } $\chi^2 = 4.15$
Polish Jews	102	80	22	21.56 ± 4.07 } $P \simeq 0.04$
Mongoloids	361	333	28	7.75 ± 1.40 } $\chi^2 = 15.75$, $P < 0.0001$

* Age range of the individuals: 10 to 39 years.

terraneans, the Ashkenazim have a typical CDe (R^1) frequency (about 53 percent) and a fairly high cDe (R^0) frequency (about 5 percent) as compared with Central European populations. This latter fact could indicate an African genetic component "probably received through Egypt" (*8*). Moreover, Ashkenazic Jews present a relatively low cde (r) frequency (about 36 percent) as compared with Central Europeans (*9*).

Table 3 presents a tentative comparison of the frequencies of nontasters among the Polish Jews and European populations, and among the Polish Jews and Mongoloids, investigated by means of the sorting technique. The combined data for English (*2*) and Danish (*4*) individuals were taken as representing the Europeans, and the combined data for Chinese (*3*) and Japanese (*1*) were taken as representing the Mongoloids. The difference in frequency of nontasters between Polish Jews and Europeans was significant ($\chi^2 = 4.15$; $P \simeq 0.04$), and that between Polish Jews and Mongoloids was highly significant ($\chi^2 = 15.75$; $P < 0.0001$).

The frequency of the "nontaster" gene among Mongoloids is about 30 percent and among Europeans, about 55 percent. The value of 46 percent found among Polish Jews suggests a Mongoloid admixture, but it could also represent an African component acquired before the dispersal of the Jews throughout Europe. This latter hypothesis is supported by a relatively high cDe (R^0) chromosome frequency among Jews from Central Europe (*8*). A further comparative investigation of the taste thresholds for phenylthiourea among Ashkenazic and Sephardic Jews from different areas of Central and Mediterranean Europe will probably be relevant to the problem.

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Newly Found Action of Cocaine

Abstract. Cocaine augments appreciably the effects of small doses of acetylcholine on the heart rate, blood pressure, and the nictitating membrane in intact, anesthetized animals. This phenomenon assigns cocaine, thus far only known as a potentiator of adrenergic stimulation, a more general role of potentiator of both adrenergic and cholinergic neurohumors.

Hitherto cocaine has been considered only as an adrenergic potentiator. A chance observation disclosed a completely new and entirely unexpected potentiating effect of cocaine on acetylcholine responses. It was found that cocaine in this series of experiments acted as an apparent in vivo cholinesterase inhibitor, augmenting various acetylcholine effects. It is known, however, that cocaine is not only devoid of anticholinesterase activity but that it actually activates in vitro pseudocholinesterase, and this only at concentrations well above pharmacological levels (*1*).

Cats under alpha-chloralose (80 mg/kg) anesthesia were used. Isotonic contractions of the nictitating membrane and arterial pressure from the carotid artery were recorded in the usual manner. All drugs were administered via the femoral vein. Maximal membrane contractions after preganglionic stimulation of the cervical sympathetic trunk through shielded electrodes were obtained with a square-wave electronic stimulator.

The duration of stimulation was 5 sec at a frequency of 20 per second; a pulse width of 0.5 msec was utilized. In each cat, three control responses of 1, 2, 4, 8, and 16 μg of acetylcholine (per kilogram) on the nictitating membrane, blood pressure, and the heart rate were recorded. After this, 3 mg of cocaine hydrochloride (per kilogram) was administered. Cocaine usually produced a primary vasodepressor and a secondary vasopressor effect. After a latency period of 60-sec duration, cocaine (3 mg/kg) itself caused the membrane to respond with a sustained, increased tension. The alteration of the baseline occurred whether or not the cervical sympathetic trunk was severed or the animals were adrenalectomized. The increased tension produced by cocaine is in itself an interesting phenomenon. If cocaine potentiates membrane contractions, this increased tension would militate against maximum potentiation. All the potentiations observed after cocaine injection are smaller than they would be if the membrane retained its normal tension.

Cocaine produced a potentiation of the acetylcholine-induced contractions of the nictitating membrane even when no acetylcholine response was observed on the nictitating membrane prior to the administration of cocaine (Fig. 1).

The effects of small doses of acetylcholine cannot be due to either ganglionic stimulation or to catechol amine release from the adrenals. In the latter part of the experiment, every animal was administered hexamethonium ion (10 mg/kg), which abolished the preganglionic cervical sympathetic stimulation but did not abolish and occasionally even potentiated the height and duration of acetylcholine-induced contractions of the nictitating membrane. The last step in the experiment was the intravenous injection of 100 μg of atropine (per kilogram), which abolished the nictitating membrane-, vasodepressor-, and cardiac-effects and did not convert the acetylcholine responses into pressor effects. This proves beyond doubt that we are not dealing with "nicotinic" and allied effects of acetylcholine. The same dose of atropine did not abolish or diminish epinephrine-induced contractions after potentiation by cocaine. The vasodepressor response to epinephrine was usually, but not invariably, potentiated by cocaine. The effects of acetylcholine, before and after cocaine administration, on the nictitating membrane and blood pressure are summarized in Table 1.

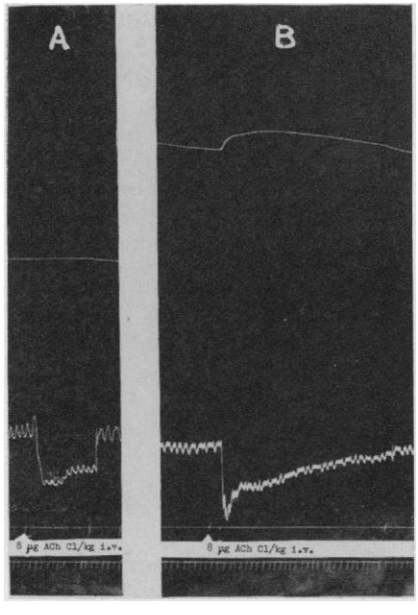

Fig. 1. Effect of intravenous injections of 8 μg of acetylcholine chloride (per kilogram) before (*A*) and after (*B*) cocaine administration (3 mg/kg); 2.8 kg cat. Top line, nictitating membrane response; second line, blood pressure and cardiac inhibition; third line, injection mark; fourth line, time: 10 sec. The time interval between the cocaine administration and the second acetylcholine injection was 12 min. Note the elevated baseline after cocaine administration (nictitating membrane).

Table 1. Cocaine potentiation of the typical effects of small intravenous doses of acetylcholine on the nictitating membrane and the mean arterial pressure responses of the cat (averages of data obtained from ten cats, including two adrenalectomized animals).

Acetylcholine dose (μg/kg)	Control		Experimental					
	Amt. (mm)	Range (mm)	Cocaine, 3 mg/kg		Cocaine, additional 3 mg/kg		Hexamethonium, 10 mg/kg	
			Amt. (mm)	Range (mm)	Amt. (mm)	Range (mm)	Amt. (mm)	Range (mm)
Height of contractions of nictitating membrane (mm)								
2	0.28	0–1	3.2	0–7	10.0	10	9.6	6–17
4	1.6	0–6	4.7	0–10	7.6	0–14	13.2	9–18
8	2.4	0–7	9.2	3–17	10.9	9–21	17.7	15–21
16	4.4	2–10	19.6	5–29	30.1	26–40	24.5	18–30
Vasodepressor effects (mm-Hg)								
2	40.5	10–60	56.0	20–70	60.0	60	26.0	2–50
4	53.8	12–82	57.6	20–92	79.8	64–90	38.4	14–50
8	43.9	8–70	59.8	20–90	58.1	45–80	53.5	18–70
16	49.4	8–70	69.4	18–110	79.0	64–90	48.8	20–80

Feeney *et al.* (*2*) have already differentiated between the effects of small and larger doses of acetylcholine on the nictitating membrane. These experiments have shown that the responses to small amounts of acetylcholine given are not due to ganglionic stimulation or to catechol amine release. Cocaine potentiation, as encountered in the currently reported investigation, is not related to the hypertension and contractions of the nictitating membrane in response to "nicotinic" doses of acetylcholine (*3*).

A positive explanation of the results reported in the present paper is not readily available. Several hypotheses, however, may yield fruitful information: Cannon and Rosenblueth (*4*) have proposed that facilitation of response results from increased permeability, thus enhancing the action of the stimulating agent. If this is the true explanation, it accounts for potentiation of both epinephrine and acetylcholine, since, under normal conditions, both of these agents cause the nictitating membrane to contract. It is well known that epinephrine potentiates the action of acetylcholine on skeletal muscle. Bulbring (*5*) found that the response of the nictitating membrane to a dose of acetylcholine was augmented by the presence of small amounts of epinephrine, and epinephrine is potentiated by cocaine. The possibility exists that cocaine may somehow enhance the response to small doses of acetylcholine by potentiating circulating epinephrine, which in turn acts on acetylcholine. The most likely explanation, which has been and will be further studied in this laboratory, is that cocaine changes the permeability of membrane to ions, since even in the case of sensitization of the sympathetic nervous system to epinephrine, inhibition of monamine oxidase or other enzymes is doubtful (*6*).

Note added in proof. Since this paper was submitted for publication, a paper by J. W. Thompson [*J. Physiol.* (*London*) **141**, 46 (1958)] has come to our attention, showing a figure from which it is obvious that in an isolated preparation of the muscle of the nictitating membrane, the addition of cocaine to the bath fluid raised the base line and increased the magnitude of acetylcholine contraction. We are, therefore, in a position to point out a close agreement between cocaine effect on acetylcholine *in situ* and in vitro.

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