tities, pre-empt a portion and, by substituting a weak for a strong action, subtract from and compete with the stronger action.

The parallelism between cerebral synaptic and behavioral actions, including reported clinical effects, of lysergic acid diethylamide and chlorpromazine and their competition lends support to the interpretation and confidence in the methods utilized.

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2. The effects of the injection procedure per se and of possible local actions at the site of injection were excluded by negative results with saline injection and with injections of LSD-25 during periods of high tolerance to this drug. The latter helps eliminate the possibility that a local irritant effect of LSD-25 might have been thought to be offset by an alleged local anesthetic action of chlorpromazine.

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Action of d-Tubocurarine Chloride on Net Flux of Water across Isolated Frog Skin

Abstract. *d*-Tubocurarine chloride, when added to the solution bathing the outside of the isolated frog skin, enhances the net flux of water which arises from the influence of an osmotic gradient. Although this effect appears to result from alteration in the pore size of the membrane, it is not accompanied by any consistent change in the resting potential.

Some years ago, Kirschner (*1*) showed that the addition of *d*-tubocurarine chloride (curare) to the solution bathing the outside of the skin of various species of frogs produces a reversible increase in the active transport of sodium. These results have been confirmed by others who observed a similar effect with a variety of neurotropic compounds (*2*). On the other hand, the lack of response of the skin of *Rana temporaria* L. to curare, already noted by Kirschner, was also confirmed and shown to result from hormonal variation (*3*).

In order to explain the enhancement of the active transport of sodium, it has been proposed that curare acts by increasing the passive permeability to sodium of the membrane of the skin epithelial cells which face the outside. This results in an increase in intracellular sodium concentration, which in turn stimulates the active transport mechanism for sodium. One way in which the passive permeability may be increased is by changing the pore size of the membrane. If this hypothesis is correct, one should also expect a modification of the net flux of water arising across the frog skin under the influence of an osmotic gradient. The purpose of the present study has been to test this hypothesis by measuring the net flux of water across the skin and to determine the effect of curare on such flux.

The apparatus used is similar in principle to the one described by Koefoed-Johnsen *et al.* (*4*). The experiments were performed on the isolated skin of *Rana temporaria temporaria* L. bathed with ordinary Ringer's solution on the inside and with Ringer's at a 10-fold dilution on the outside. After a control period of about 4 hours, curare was added to the outside solution at a concentration of 170 μg/ml. Table 1 shows the results obtained on the net flux of water as well as on the difference in electrical potential across the skin.

It can be seen that curare at the concentration used consistently enhanced the net flux of water. In some instances the flux rate was five times that of the control, although in most experiments the rate was enhanced two- to threefold. These results are consistent with the hypothesis that curare acts on the frog skin by increasing the diameter of membrane pores. However, it is important to note that, despite the apparent increase in membrane permeability to water, the membrane potential was not consistently altered.

The following conclusions may be drawn from these results. Although some of the results are contradictory to the proposed mechanism, it may be suggested that in these cases, for still obscure reasons, an intracellular increase of sodium concentration due to an increase in passive diffusion may not always enhance active transport. On the other hand, the hypothesis first proposed to explain the effect of curare on the active transport of sodium may not be correct, in that an increase in net flux of water and an increase in passive sodium permeability may result from two different mechanisms. Finally, the enhancement of active transport by curare cannot be explained in terms of an increase in the passive permeability to sodium (*5*).

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Table 1. Effect of curare on the potential difference and net flux of water across the isolated skin of *Rana temporaria temporaria* L. (Ringer's solution inside, Ringer at 1:10 outside). The time in hours indicates the duration of the control or experimental periods. Δ Potential difference is the maximum variation of the potential difference observed after application of 170 μg/ml of *d*-tubocurarine chloride in the outside solution. The minus sign indicates an increase in potential difference.

Experiment No.	Control		Curare		
	Time (hr)	Net flux of water (μl cm^{-2} h^{-1})	Time (hr)	Net flux of water (μl cm^{-2} h^{-1})	ΔPotential difference (mv)
1	4	5	4	8	—
2	4	3	3.5	7	4
3	4	3	4	4	11
4	4	3	3	16	6.5
5	4	3	3.5	15	7
6	3.5	3	3.5	9	4
7	3	5	1.5	12	−9.5
8	3	4	2.5	11	−1.5

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Excretion of Dopamine in Diseases of Basal Ganglia

Abstract. The urinary excretion of catecholamines has been measured in 32 patients with disorders of the basal ganglia. Sixteen patients with Parkinsonism (idiopathic, postencephalitic, and arteriosclerotic types) had a significantly lower amount of dopamine in the urine during a 24-hour period than a group of 24 normal control subjects. In a group of 16 patients with various striatal syndromes the excretion of dopamine and epinephrine was significantly higher than normal. Norepinephrine excretion was similar in the three groups. The lowest mean value of urinary dopamine was found in postencephalitic Parkinsonism; the highest occurred in Wilson's disease.

Recent chemical studies have revealed that 80 percent of the dopamine (3-hydroxytyramine) content of the brain is located within the corpus striatum (*1*). The differential concentration of norepinephrine and dopamine in

Table 1. Excretion of urinary catecholamines (μg/24 hr).

Group	Cases (No.)	Samples (No.)	Mean ± standard error		
			Dopamine	Norepinephrine	Epinephrine
Normal	24	24	316 ± 14.6	42 ± 3.2	17 ± 1.1
Parkinsonism (all types)	16	16	241 ± 21.5*	40 ± 5.0	15 ± 0.4
Postencephalitic	6	6	177 ± 41.8*		
Idiopathic	8	8	297 ± 36.2		
Arteriosclerotic	2	2	212		
Striatal syndromes (all types)	16	32	377 ± 23.9*	36 ± 3.3	28 ± 3.7*
Wilson's disease	3	17	418 ± 24.8*		
Huntington's chorea	4	5	272 ± 45.8		
Dystonia	4	5	395 ± 45.8		
Sydenham's chorea	2	2	334		
Familial tremor	1	1	334		
Torticollis	1	1	328		
Choreoathetosis	1	1	308		

* Probability of difference from normal, $p < 0.01$.

various portions of the brain led Carlsson (*2*) to postulate a second role for the latter substance besides its established function as precursor of norepinephrine and epinephrine. This role has been related to the functioning of the extrapyramidal system (*3*). One of us (*4*) has reported the presence of a smooth muscle-stimulating substance, later identified as dopamine (*5*), in the urine of patients with diseases of the basal ganglia. The present report (*6*) concerns the differential urinary excretion of dopamine in Parkinsonian and some striatal syndromes.

Thirty-two patients and 24 normal control subjects (laboratory personnel) contributed 24-hour samples of urine for the determination of dopamine, norepinephrine, and epinephrine excretion. Epinephrine and norepinephrine were measured by the trihydroxyindole method (*7*, *8*), and dopamine by a modification of the Carlsson-Waldeck procedure (*8*). Fluorescence measurements were carried out with the Aminco-Bowman spectrophotofluorometer.

Urines were collected for periods of 24 hours in bottles containing 10 ml of 18 percent hydrochloric acid as a preservative. All medication was withheld for 24 hours before the collection period and during it. A total of 72 urines were analyzed.

The 32 patients represented the following diagnoses: postencephalitic, idiopathic, and arteriosclerotic Parkinsonism, Wilson's disease, Huntington's and Sydenham's choreas, dystonia musculorum deformans, torticollis, familial tremor, and choreoathetosis. The division into "Parkinsonian" and "striatal" syndromes was based mainly upon the known pathology of the particular diseases concerned.

The summary of the data for the three catecholamines in Table 1 shows that the daily excretion of dopamine in the two main diagnostic divisions departs significantly from normal. The means, arranged according to rank, are Parkinsonism < normal < striatal syndromes, and the ratio of the means is 0.76:1.00:1.20. Because of the large variation encountered in these series of cases, it was of interest to determine the extent to which this over-all distinction, based upon the urinary output of dopamine, carries over to the diagnostic entities mentioned. For this purpose the data were subjected to the analysis of variance (*9*), and the residual error, after accounting for variance between specific diagnostic categories, was used to calculate the standard errors shown. Inspection of Table 1 reveals that in postencephalitic Parkinsonism the dopamine excretion is significantly lower than normal, and that in Wilson's disease this excretion is higher than normal. Some of the categories contained too few cases to permit statistical evaluation.

Epinephrine excretion was also significantly greater than normal in the striatal syndromes considered as a whole (Table 1), but the variability within the diagnostic categories was so great that further analysis of the data did not seem warranted. Norepinephrine excretion did not vary significantly between the major groups.

The physiological significance of these findings is difficult to assess because of lack of knowledge about the actual function of dopamine and its metabolites in the brain. However, the results support the hypothesis that dopamine plays a role in extrapyramidal motor function. The association of gross differences in the urinary output of dopamine with certain neurological diseases indicates the importance of further studies of the metabolism of this catecholamine in these disorders. Such investigations should include analysis of the catecholamine content of the brains of patients who have died with basal ganglia disease, for such information can help determine whether the concentration of cerebral dopamine itself undergoes major changes in these disorders (*10*).

Note added in proof: Ehringer and Hornykiewicz (*11*) have shown that the concentration of dopamine in the neostriatum is significantly reduced in cases of Parkinsonism. The norepinephrine level in the hypothalmus is also low.

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Possible Physical Effect of Solar Particles on Meteorological Parameters in Alaska

Abstract. Statistical significance was found in the reception of solar-particle invasions to sea-level pressure and upper-flow pattern changes at 500 mb in Alaska during a period of high solar activity. Recent IGY findings suggest that a physical relation exists between such solar particles and atmospheric changes.

For a sample of ten weather stations in Alaska and northwestern Canada, enclosed within an area between 60° and 70°N and 170° and 120°W, the sea-level pressure was tabulated for 16 days after a day (the key day) in which the earth's magnetic field was particularly disturbed. A key day is defined as a day in which the daily magnitude of the A_p index was 20 or more with a daily change of +10 or more from the previous day. The values of this index for the fall through winter of 1956–57 were taken from the *Journal of Geophysical Research* (*1*). For each of the ten sample stations the 24-hr pressure change was obtained