that surface-positive polarization decreases the arousal level in the ipsilateral cortex and enhances it in the contralateral cortex, whereas surface-negative polarization enhances arousal in the ipsilateral and, within a limited current range, depresses it in the contralateral cortex. A similar interpretation is justified for experiments on the peripherally evoked somatosensory response.

We also may interpret the reciprocal changes in amplitude in the two hemispheres as representing reciprocal changes in excitability. If we use identical stimuli to evoke the potentials in homologous areas of the two hemispheres, and thus activate two homologous populations of neural elements, we can expect that reciprocal changes in the overall excitability in the two populations are likely to produce reciprocal changes in the amplitude of the evoked response.

Unilateral transcortical polarization or unilateral destruction of the cortex then brings about changes which are compatible with the proposed mechanism of a diverging negative feedback system operating between the subcortex and the two cortices. Although we do not have sufficient data to quantitatively and temporally define the operational characteristics of this system, we conclude from the present results that, within a limited range, changes produced in one hemisphere are compensated for by opposite changes in the other hemisphere. This points to one important function of this hypothetical negative feedback system, namely, to keep the "mean excitability" or the "mean arousal level" of the whole cerebral cortex at a constant level, whose actual value at a given time would depend upon a "preset" homeostatic magnitude.

The homogeneous distribution of excitability level over both hemispheres would be the function of the callosal "equalizer mechanism." According to Bremer (*13*), the two-way conduction channels in the callosal system are tonically active. Bremer also claimed that these commissural fibers are predominantly excitatory in nature, whereas Chang (*14*) came to the conclusion that the callosum exerts mainly inhibitory effects. Recently it has been shown that "phenomena of both excitatory and inhibitory nature follow the arrival of a transcallosal volley" (*15*). The "equalizing function" proposed here could be subserved by excitatory and/or inhibitory elements: a facilitatory influence would be the result of increased excitatory activity and/or a decreased inhibitory activity and, conversely, depression would result from a drop in excitatory activity and/or an increase in inhibitory activity (*16*).

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Canine Antiserums Analogous to Human Allergic and "Blocking" Antiserums

Abstract. *The serums of dogs that are allergic to ragweeed can passively sensitize normal dogs. Cutaneous reactions or systemic anaphylaxis may be produced by appropriate challenge with ragweed extract. Canine antiserum produced by immunization of normal dogs with ragweed extract is shown to inhibit these reactions of the passively sensitized dogs.*

Human reagin (allergic antibody, skin-sensitizing antibody) is an antibody believed responsible for certain reactions which occur in allergic individuals after exposure to the antigen (*1*). Antiserums produced by the injection of pollen extracts in man have been shown to modify the passive cutaneous reaction, the Prausnitz-Küstner reaction (*2*), of reagin and allergen (*3*). The antibody so produced is believed responsible for this modification and has been termed "blocking" antibody. Experimental studies in clinical pollinosis demonstrating a protective effect of "blocking" antibody against the passive production of asthma and anaphylaxis in man are not feasible.

Canine hypersensitivity provides a laboratory model of allergic disease (*4*). Canine reagin (allergic antibody, skin-sensitizing antibody) in sufficient quantity transfers cutaneous, bronchial, and anaphylactic sensitivity to normal dogs (*5*). The present studies report the production of an antibody to ragweed-pollen extract in normal dogs which modifies the reaction of dogs passively sensitized with canine anti-ragweed reagin and challenged with ragweed antigen.

Normal dogs received six biweekly injections of a 15-percent pollen extract of short ragweed (*Ambrosia elatior*) in incomplete Freund's adjuvant (*6*). The dogs were bled prior to each injection. The pooled serums of dogs immunized with ragweed (IDS) were tested for antibody by hemagglutination (*7*) of tanned red blood cells coated with ragweed antigen, and by ring and gel-diffusion precipitin tests (*6*). The hemagglutination titer of the pooled serums was 1:400. Ring and gel-diffusion precipitin reactions with 5 percent ragweed antigen were negative, although four of the twelve individual serums composing the pool were weakly positive.

Two separate pools of canine reaginic serums (CRS) were collected by bimonthly bleedings for 12 months from each of two dogs proven to be spontaneously sensitive to ragweed pollen (*8*). The highest serial five-fold dilution of each CRS pool eliciting a positive passive cutaneous reaction (*5*) after an intravenous challenge injection of 1 ml of a 3 percent concentration of ragweed extract was determined in two recipient normal dogs. The two CRS pools elicited positive passive cutaneous reactions at dilutions of 1:25 and 1:125, respectively. When the same amount of ragweed antigen was incubated with 10 ml IDS for 1 hour at 37°C prior to intravenous challenge, the mixture of ragweed and IDS did not result in any positive cutaneous reactions in the recipient dogs. This experiment suggested that the ragweed antigen was neutralized by the IDS and

did not react with the CRS implanted in the skin.

The intravenous injection of 10 ml of the reaginic serum passively sensitized normal dogs for anaphylaxis resulting from subsequent injection of 1 ml of a 3 percent extract of ragweed pollen. Twenty ml of the IDS, given simultaneously with sensitizing reaginic serum or after incubation with the challenge dose of ragweed antigen, showed that the normal dogs were protected from anaphylaxis. Table 1 summarizes the results of the sensitization and protection experiments.

Passive cutaneous reactions were eliminated by mixing IDS with the challenging ragweed antigen. This alteration in the cutaneous reaction occurred when the control reaction either preceded or followed the protection experiment. Thus, neutralization of reagin by persisting antigen after a control experiment was not responsible for the inhibition. A large increase in the quantity of ragweed antigen used for challenge resulted in reversal of inhibition of the cutaneous reaction by IDS. Dogs were not resensitized for anaphylaxis until a positive passive cutaneous reaction could be elicited.

Table 1. The effect of IDS (serum from dogs immunized against ragweed) in animals passively sensitized with CRS (canine reaginic serum) obtained from dogs spontaneously sensitive to ragweed pollen. The challenge dose of ragweed was 1 ml of 3 percent solution. The amount of IDS was 20 ml, and the amount of CRS was 10 ml.

Dog No.	Sensitizing material	Intravenous challenge after 24 hrs	Severity of symptoms after challenge*
1	CRS-1	RW	3+
	3-Day interval		
	CRS-1 + IDS	RW	None
	14-Day interval		
	CRS-1	RW	3+
	9-Day interval		
	CRS-1	RW + IDS	None
2	CRS-1	RW + IDS	±
3	CRS-1 + IDS	RW	None
4	CRS-1	RW + normal dog serum	3+
5	CRS-1 + 20 ml normal dog serum	RW	3+
	9-Day interval		
	CRS-1 + IDS	RW	None
6	CRS-2	RW	2+
	3-Day interval		
	CRS-2 + IDS	RW	None
7	CRS-2	RW + IDS	None
8	CRS-2	RW	2+

* 1+ = Ataxia, vomiting or diarrhea or both; 2+ = Ataxia, vomiting, diarrhea, and collapse; 3+ = Ataxia, vomiting, bloody diarrhea, collapse, dyspnea.

Thus, antibodies can be induced in normal dogs injected with pollen antigen which will protect dogs passively sensitized against ragweed antigen by canine reagin.

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Hepatic Glucokinase: A Direct Effect of Insulin

Abstract. *Particle-free extracts of the livers from rats on a normal diet were incubated with insulin for 4 minutes; during this time the glucokinase activity increased. This insulin effect is dependent upon the dose.*

The utilization of glucose by the liver of the alloxan-diabetic rat is profoundly impaired (*1*). This impairment is not due to a blocking of the transport of glucose into the hepatic cell (*2*). Since the glucokinase activity of the liver of the alloxan-diabetic rat is diminished (*3*), it is possible that this decrease in enzyme activity is responsible for the impairment in glucose utilization. In accord are our data, which show that, under specific conditions, insulin exerts an effect on hepatic glucokinase in vitro.

Male Holtzman rats weighing 150 to 250 g, maintained on a rat chow diet, were used. After the animals had been stunned and decapitated, the liver was perfused *in situ* with 40 ml of cold (4°C) 0.15*N* NaCl solution.. All procedures were conducted at 4°C. The liver was removed and blotted on filter paper, weighed, minced with scissors, and homogenized in 0.3*M* KCl in a Potter-Elvehjem Teflon-glass homogenizer. The homogenate was adjusted to a final volume of 4.0 ml per gram (wet weight) of liver. It was centrifuged for 10 minutes at 20,000*g* in a Servall SS-4 centrifuge to remove larger particles, and the supernatant was recentrifuged at 100,000*g* for 30 minutes in a Spinco model L preparative centrifuge.

Each supernatant was tested as follows: 0.05 ml of supernatant was added to each of four cuvettes. To two of these, water was added in a volume equal to that of the insulin solution used in the other pair—9 to 30 μl. To the other pair of cuvettes, insulin (25 units per milliliter) was added (*4*). Each pair of cuvettes was placed in a Beckman D-K double-beam recording spectrophotometer and incubated for 4 minutes. Solutions incubated in this fashion reach a temperature of 29° to 30°C within 1 minute and remain constant thereafter. At the end of the initial 4-minute interval, the glucokinase activity was determined by a modification of methods described elsewhere (*5*). Accordingly, the following reagents were added: 0.15*N* KCl in amount to make final volume 3.0 ml; 0.1*M* tris buffer (*p*H 7.6), 1.0 ml; $MgCl_2$, 16 μmole, 20 μl; hexokinase-free glucose-6-phosphate dehydrogenase from yeast, 0.3 Kornberg units (*6*), 10 μl; nicotinamide adenine dinucleotide phosphate (NADP), 2 μmole (*p*H 6.5), 20 μl; glucose, 75 μmole, 25μl.

The contents of the cuvettes were stirred after each addition, and the reaction was initiated in one cuvette by the addition of 10 μmole of adenosine triphosphate (the disodium salt) which had been adjusted previously to *p*H 6.5. The absorption difference between the two cuvettes was measured at 340

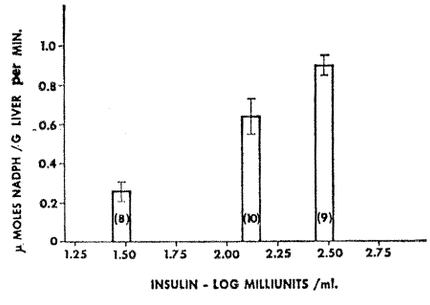

Fig. 1. The vertical bars indicate the mean (± S.E.) differences in glucokinase activity between untreated controls and supernatants treated with 30, 133, and 300 milliunits of insulin per milliliter. The numeral in each bar is the number of animals at that dosage. The mean rate of $NADPH_2$ production by the untreated controls (27) was 1.51 ± 0.15 μmole per gram of liver per minute. The ordinate is the increase in glucokinase activity attributable to insulin.