References and Notes

1. C. E. Shannon and W. Weaver, *The Mathematical Theory of Communication* (Univ. of Illinois Press, Urbana, 1949).
2. E. R. F. W. Crossman, *Quart. J. Exp. Psychol.* **5**, 41 (1953); W. E. Hick, *ibid.* **4**, 11 (1952); R. Hyman, *J. Exp. Psychol.* **45**, 188 (1953).
3. An important exception is Hyman's observation (*2*) that the only nonlinear variance in his data is completely accounted for by sequence containing no repetitions of the signal. This and his subsequent observations in this regard completely accord with my findings.
4. P. Bertelson, *Quart. J. Exp. Psychol.* **13**, 91 (1961); S. Kornblum, in *Attention and Performance*, A. F. Sanders, Ed. (North-Holland, Amsterdam, 1967) [special issue of *Acta Psychol.* (1967)], p. 27.
5. The results for individual subjects show essentially the same patterns: in every instance the RT for the high-p_{nr} sequence is longer than for the low-p_{nr} sequence (matched on information).
6. The difference between the high- and low-p_{nr} points is, of course, highly significant ($t_{(7)} = 5.03$, $P < .001$).
7. At this point I estimate that results would be similar with considerably longer response-to-signal intervals (longer than 140 msec) if the stimulus-response relations were made less compatible than mine. Such findings would extend my conclusions, beyond serial tasks, to encompass discrete-choice RT tasks.

8. Research aided by the University of Michigan's Office of Research Administration. I thank J. Alford, H. Hamburger, and J. E. K. Smith for help and cooperation. This is a preliminary and partial report; the results emphasized are those bearing most directly on the Information Hypothesis. A more complete report will be published elsewhere.

11 December 1967

Baroreceptors in the Adrenal Gland

Abstract. *Afferent activity from dissected filaments of nerves to the adrenal gland was recorded. Firing rates of single fibers followed changes in systemic blood pressure. Chemically and mechanically induced changes in blood pressure were reflected by an appropriate directional change in unit activity.*

The existence of baroreceptors in the region of the carotid sinus and aortic arch has been well documented (*1*). There is also evidence that similar receptors are present in the pulmonary artery and in the heart (*2*). To our knowledge, baroreceptors in the smaller vessels of the arterial system have not been described. We now present neurophysiological evidence which suggests the existence of baroreceptors located in the vessels of the adrenal gland.

Experiments (24) with different nerve preparations were performed on six rabbits and two cats anesthetized with sodium pentobarbitone. Arterial blood pressure was recorded from polyethylene catheters in the cardiac end of the common carotid artery or the caudal portion of the abdominal aorta, or both.

We injected drugs into the jugular vein, recorded afferent nerve discharges with a negative-capacitance electrometer, and stored these records on magnetic tape. Single-fiber activity was converted into standard pulses by a discriminator and analyzed by a digital computer. Afferent discharge rate, blood pressure, electrocardiogram, and respirations were also recorded on a polygraph. The small nerves of the adrenal gland were located and isolated, and all branches which did not lead directly to the gland were cut. Recordings were taken from the peripheral portions of these nerves after their central connections were severed.

When a small filament was dissected from a nerve branch to the adrenal gland and placed on the recording electrode, spontaneous afferent discharges were observed frequently. Our study is only concerned with afferent firing related to changes in arterial blood pressure. As shown in the top line of Fig. 1, these units demonstrate some rhythmic activity with each pressure wave. After the epinephrine was injected (line 2), the discharge rate gradually increased, blood pressure increased, and rhythmical activity became more pronounced. After a maximum value was reached (line 3), the firing rate decreased and returned to that of the control (line 4). Firing rates closely paralleled the direction and magnitude of the changes in blood pressure.

In Fig. 2, results of experiments to determine the dependency of afferent firing rates on blood pressure levels are shown. The lower traces represent the number of spikes occurring each 0.1 second. This value, determined by the computer, is displayed on the polygraph record. The vertical axis represents firing frequency, and the horizontal axis represents time. Clamping the abdominal aorta proximal to the adrenal artery resulted in rapid cessation of firing of these fibers. Touch receptors, which responded to distension of the adrenal capsule, however, were readily excited during the brief

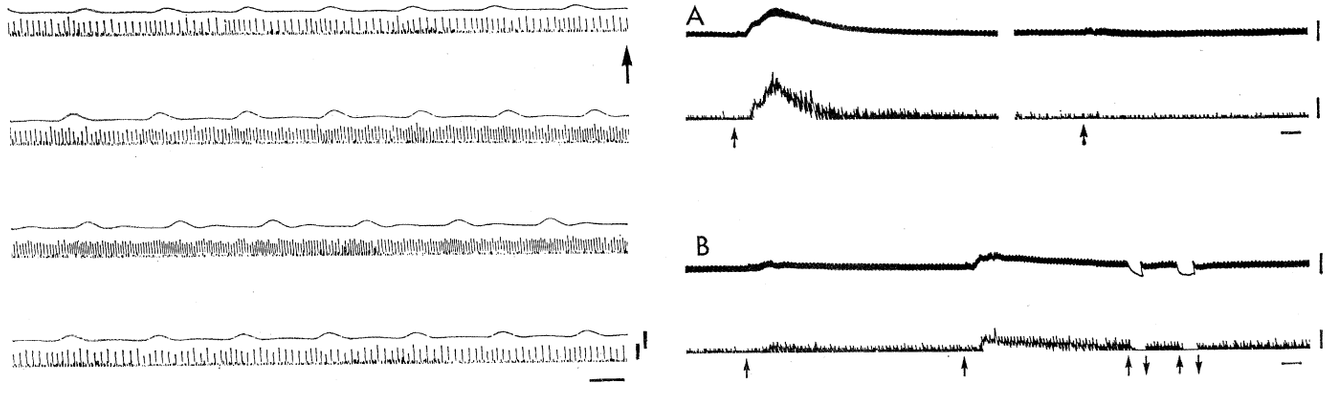

Fig. 1 (left). Effect of an intravenous injection of epinephrine (30 μg) on blood pressure (upper beam) and discharge rate of a single afferent fiber (lower beam) from the adrenal gland in rabbit. Calibrations: upper vertical bar, 0 to 100 mm-Hg; lower vertical bar, 1 mv; horizontal bar, 0.1 second. Fig. 2 (right). (A) Effect of 10 μg of epinephrine (left) and 100 μg of isoproternol (right) on blood pressure (upper trace) and firing rate (lower trace) of adrenal afferent. (B) Effect of 300 μg of metaraminol (left), 10 μg of norepinephrine (center), and repeated clamping of the abdominal aorta (right) on blood pressure and firing rate of adrenal afferent. Calibrations: vertical bars, 0 to 100 mm-Hg (blood pressure); spikes, 0.1 second (afferent discharge). Horizontal bars, 10 seconds.

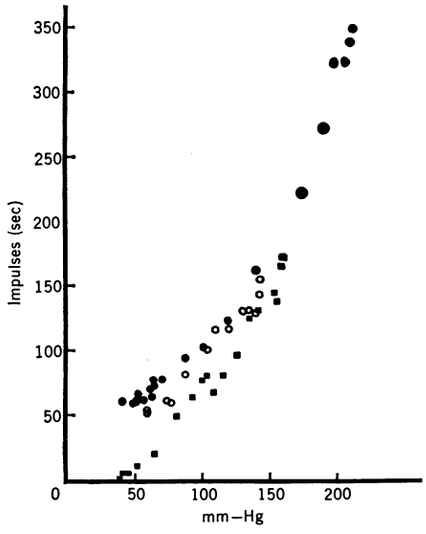

Fig. 3. Relation between afferent discharge rate and mean blood pressure. Values taken during short periods of constant pressure. Filled circles and squares, different trials on the same unit. Open circles, trials on a different unit.

periods of aortic clamping in our experiments.

Figure 3 shows the relationship between mean systemic blood pressure and firing rate from isolated afferent nerve fibers. The filled circles represent the response to intravenous injection of 100 μg of epinephrine; the filled squares represent the response to abdominal aorta clamping above the level of the adrenal artery, both recorded from the same afferent fiber. The open circles represent the response to intravenous injection of 30 μg of epinephrine in another afferent unit in a different animal. The high mean arterial blood pressure followed the injection of large amounts of epinephrine used to test the limits of the response. The relations between pressure and firing rate in these experiments are quite similar to those found for the carotid sinus (*3*).

We suggest that in the adrenal gland there are baroreceptors which send to the central nervous system information related to blood pressure within the gland. These receptors and those (*4*) in the rabbit kidney may represent the afferent limb of a set of reflex systems involved in the control of regional blood flow.

A. NIIJIMA*
D. L. WINTER
Department of Neurophysiology, Walter Reed Army Institute of Research, Walter Reed Army Medical Center, Washington, D.C. 20012

26 JANUARY 1968

References and Notes

1. D. W. Bronk and G. Stella, *J. Cell. Comp. Physiol.* **1**, 113 (1932); S. Landgren, *Acta Physiol. Scand.* **26**, 1 and 35 (1951); C. Heymans and E. Neil, *Reflexogenic Areas of the Cardiovascular System* (Churchill, London, 1958).
2. J. C. G. Coleridge, A. Hemingway, R. L. Holmes, R. J. Linden, *J. Physiol. London* **136**, 174 (1957); J. C. G. Coleridge and C. Kidd, *ibid.* **150**, 319 (1960); A. S. Paintal, *Ergeb. Physiol.* **52**, 74 (1963); S. Homma and S. Suzuki, *Jap. J. Physiol.* **16**, 31 (1966).
3. C. M. Bloor, *J. Physiol. London* **174**, 163 (1964); J. W. Spickler and P. Kezdi, *Amer. J. Physiol.* **212**, 471 (1967).
4. A. Niijima, in *Proc. Int. Congr. Physiol. Sci. 23rd* **1965**, 381 (1965).
5. A.N. was supported by a China Medical Board fellowship.
* Present address: Department of Physiology, Niigata University School of Medicine, Niigata City, Japan.

26 September 1967

Parathyroid Hormone Production in vitro by Human Parathyroid Cells Transformed by Simian Virus 40

Abstract. *Cells from a human parathyroid adenoma were infected with simian virus 40 and maintained through 13 subcultures in monolayer tissue culture. For more than 9 months, these "transformed" cells continued to produce parathyroid hormone which was identified by radioimmunoassay and density-gradient ultracentrifugation.*

The production of parathyroid hormone (PTH) by parathyroid glands maintained as organ cultures has been described (*1*), but production of hormone by parathyroid cells grown as monolayer tissue cultures has not been reported. Certain oncogenic viruses, such as simian virus 40 (SV40), can alter the growth characteristics of certain mammalian cells in vitro, and these "transformed" cells retain some of the biochemical functions of the original cells (*2*). Production of a melatonin-forming enzyme by pineal tissue infected with SV40 (*2*) and synthesis of pituitary hormones in monolayer culture (*3*) have been reported. Our report describes the transformation (by simian virus 40) of tissue from a human parathyroid adenoma into a monolayer cell culture that produced parathyroid hormone; this hormone was identified by radioimmunoassay and density-gradient ultracentrifugation.

Tissue cultures of a human parathyroid adenoma were begun in prescription bottles (60-ml) with surgical specimens (10 mg, wet weight) of the tumor. The methods used have been previously described (*2, 4*). After 2 days, one of the cultures was infected with 2×10^7 $TCID_{50}$ (tissue culture infective dose, 50 percent effective) of SV40. By the 8th day, the infected cells showed the morphological characteristics of human cells transformed by SV40 (*5*). Uninfected cells grew poorly. Cells were separated from the surface of the bottle with trypsin and subcultured when the monolayers became confluent. The transformed cultures (Fig. 1) continued to grow, but the uninfected cells did not survive the first subculture. The SV40 "T" antigen was detected in more than 90 percent of the infected cells by immunofluorescence (*6*). The virus itself could be isolated from the transformed cells by growing them in contact with green-monkey kidney cells (*7*).

Tissue culture medium was assayed directly for PTH. Tissue culture cells were separated from the medium by centrifugation and assayed after extraction with urea. Parathyroid hormone was measured by radioimmunoassay (*8, 9*); charcoal (*10*) was used to separate the free and antibody-bound fractions

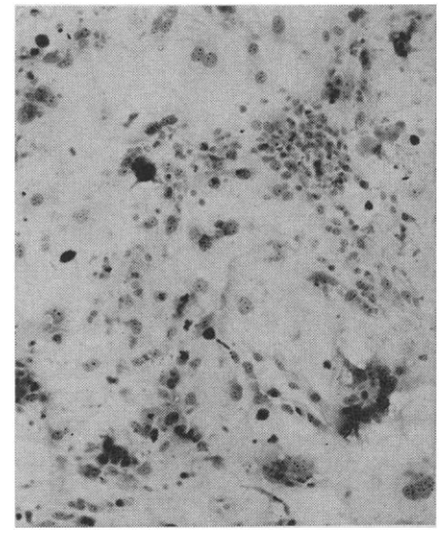

Fig. 1. Cell culture derived from human parathyroid adenoma and transformed in vitro by SV40 (tenth subculture, 8 months after infection). The cells are cuboidal and polygonal and vary considerably in size (fixed in formol-sublimate; stained with hematoxylin and eosin; magnification $\times$ 135).