Table 1

Diet (per cent NaCl)	8 per cent		4 per cent		0·4 per cent	
Duration	6 Weeks		16 Weeks		6 Months	
	Control	Stress	Control	Stress	Control	Stress
n	5	5	5	5	4	5
Ave. blood pressure (mm Hg) (± *S.E.*)	230·0 (12·03)	228·4 (9·08)	206·6 (4·90)	194·8 (15·43)	144·5 (3·20)	143·6 (6·31)
Ave. weight (g) (± *S.E.*)	268 (11·9)	265 (7·6)	414 (10·6)	406 (5·4)	410 (10·2)	402 (20·9)
Shocks/day (ave.)	0	16	0	25	0	36

First experiment: effect of intermittent electroshocks on blood pressure of unconditioned rats on different intakes of NaCl. There was no statistically significant difference in average blood pressure or weight between any stress group and its control ($P > 0·05$). One rat in control (0·4 per cent NaCl) group died during the third month: blood pressure at end of second month was 133 mm Hg. The rate at which hypertension developed was the same among test rats and their respective controls.

Table 2

Diet	4 per cent NaCl	
Duration	6 Months	
	Control	Stress
n	6	6
Ave. blood pressure (mm Hg) (± *S.E.*)	174·7 (5·3)	174·7 (7·4)
Ave. weight (g) (± *S.E.*)	409 (9·2)	399 (6·6)

Second experiment: effect of intermittent electroshocks on blood pressure of conditioned rats on 4 per cent NaCl. Stress group received an average of 100 shocks/day. There was no statistically significant difference ($P > 0·05$) between the average blood pressure or weight in the two groups. Hypertension developed at the same rate in the two groups, as well.

Table 3

Diet	Low NaCl (0·4 per cent)			
Duration	5 Months			
	Control		Stress	
	Start	End	Start	End
n	8	8	7	7
Ave. blood pressure (mm Hg) (± *S.E.*)	183·0 (5·22)	156·4 (5·43)	183·4 (5·3)	169·4 (4·5)
Ave. weight (g) (± *S.E.*)	247 (6·0)	450 (7·2)	243 (7·0)	430 (13·7)

Third experiment: effect of intermittent electroshocks on recovery from early, mild NaCl-induced hypertension on conditioned rats. Stress group received an average of 100 shocks/day. The final average blood pressure and weights of control and stress groups were not significantly different although the blood pressure of the stress group remained suggestively higher than that of the controls (169·4 against 156·4 mm Hg, $0·1 > P > 0·05$). Three deaths occurred in first week (two test, one control); in each instance a new matched pair was added.

Table 4

Diet	4 per cent NaCl		Low NaCl (0·4 per cent)	
Duration (of crowding)	5 Months			
	Crowded	Control	Crowded	Control
n	16	9	15	10
Ave. blood pressure (mm Hg) (± *S.E.*)	166·8 (6·1)	175·1 (5·3)	136·8 (2·1)	147·2 (3·8)
Ave. weight (g) (± *S.E.*)	426 (7·7)	460 (7·0)	468 (6·5)	505 (7·9)

Fourth experiment: effect of crowding on blood pressure of rats. Average blood pressure of both crowded groups was lower than controls although only in the low NaCl groups was this statistically significant ($0·025 > P > 0·01$). Both groups of crowded animals weighed less than their respective controls ($P < 0·01$); each group on 4 per cent NaCl chow weighed less than the corresponding group on 0·4 per cent NaCl chow ($P < 0·01$). Ten animals that died from respiratory tract infection during the early weeks of the study have not been included in the analysis of results.

Table 3, suggests that stress may have impaired the expected improvement from a low salt diet: a larger sample might settle this question. The lower blood pressure of crowded rats compared with their respectiv controls could reflect smaller food intakes, for final weights were less in the crowded rats. It is known that increased population density diminishes growth primarily because of a reduction in food intake[11,12]. Food intakes were not measured here but, if the crowded rats ate less chow, their NaCl intakes decreased *pari passu*: this implies that restriction of NaCl was more important than any effect of crowding.

Our findings do not support the popular concept that stress is a usual or common aetiological factor of hypertension. The experiments were designed to avoid bodily harm yet produce environments which are considered in experimental psychology to be strongly stress-producing. The observation times were long compared with those of the other accepted procedures we have tested[6–9] and we therefore consider it unlikely that further prolongation would have modified the conclusions. The ineffectiveness of these powerful stresses in highly susceptible animals should suggest caution in attributing to "stress" a general or primary role in inducing chronic hypertension.

This work was supported by the US Atomic Energy Commission.

L. K. Dahl
K. D. Knudsen
M. Heine
G. Leitl

Medical Research Center,
Brookhaven National Laboratory,
Upton, New York.

Received May 6; revised June 7, 1968.

1 Wolf, S., Cordon, jun., P. V., Shepard, E. M., and Wolff, H. G., *Life Stress and Essential Hypertension* (Williams and Wilkins, Baltimore, 1955).
2 Simonson, E., and Brožek, J., *Ann. Intern. Med.*, **50**, 129 (1957).
3 Shapiro, A. P., *Ann. Intern. Med.*, **53**, 64 (1960).
4 *Proc. Joint WHO-Czechoslovak Cardiological Soc. Symp. on Pathogenesis of Essential Hypertension*, Prague, 1960 (edit. by Cort, C. H., Fencl, V., Hejl, Z., and Jirka, J.) (State Medical Publishing House, Prague, 1961).
5 Page, I. H., and McCubbin, J. W., *Handbook of Physiology*, Section 2, Circulation, **3** (edit. by Hamilton, W. F.), 2163 (Amer. Physiol. Soc., Washington, 1965).
6 Dahl, L. K., Heine, M., and Tassinari, L., *J. Exp. Med.*, **115**, 1173 (1962).
7 Dahl, L. K., Heine, M., and Tassinari, L., *Nature*, **194**, 480 (1962).
8 Dahl, L. K., Heine, M., and Tassinari, L., *J. Exp. Med.*, **118**, 605 (1963).
9 Dahl, L. K., Heine, M., and Tassinari, L., *J. Exp. Med.*, **122**, 533 (1965).
10 Dahl, L. K., Knudsen, K. D., Heine, M. A., and Leitl, G. J., *Circulation Res.*, **22**, 11 (1968).
11 Benardis, L. L., and Skelton, F. R., *Proc. Soc. Exp. Biol. and Med.*, **113**, 952 (1963).
12 Adolph, E. F., *Biol. Bull.*, **61**, 350 (1931).

Cortical Synapses and Reinforcement: a Hypothesis

Most theories of learning assume some change in the synaptic conductivity of cortical pathways[1,2]. Facilitation by use alone, however, will not account for the most characteristic feature of learning—that what is learned are those motor responses which lead to a satisfactory or adaptive state of affairs for the organism[3–5].

A theory of cortical function which seems to overcome this difficulty has been proposed by Beurle[6,7]. In this theory, waves of neuronal activity are conducted across the cortical mass from sensory input to motor output. Use of particular pathways is assumed to lead to synaptic potentiation, but a "discriminator" or sensor of satisfactory states of affairs, comparable perhaps with the hypothalamus, is postulated to distribute its output to the cortex in general and to facilitate the passage of waves associated with biologically advantageous situations. It appears to have been overlooked, however, that information about the results of motor action can be available only after the passage of the activity leading to the motor output. The mechanism as postulated will select those patterns of behaviour succeeding rather than leading to beneficial responses, and there seems to be no reason to think that this result would be adaptive for the organism.

A simple modification of Beurle's theory which would overcome this difficulty at the expense of introducing a further postulate is as follows: (1) input and output are connected by travelling waves of cortical neural activity as in Beurle's theory; (2) by itself the passage of a wave does not lead to any permanent change in synaptic conductivity (by contrast with the original theory) but leads to a short-term change in the cells involved in the wave such that they are picked out from a background of cells not so activated; (3) such cells are rendered sensitive by the short-term change to a reward signal (that is, discriminator output) in such a way that if such a signal occurs before the end of the decay time of the change the synaptic connexions between the cells are made more effective.

The function of the discriminator in this theory is to select[8,9] from the traces made available in short-term form those which lead to an adaptive outcome. Such a function can only be performed, however, given the existence of the postulated short-term trace mechanism.

© 1968 Nature Publishing Group

It may be thought that reverberating circuits could fulfil this role[10–12]. That this is not so can be seen by considering the effect of a reward signal on such a circuit. This will be to establish the synaptic connexions leading to reverberation (that is to say, those involved in activity at the time of the reward signal) and not those on the path which led to the adaptive motor output.

Some evidence for the existence of a short-term trace mechanism in the cortex may be adduced from experiments on the effects of positive d.c. polarization of the cortex[13,14]. Such effects are presumably related to the specific orientation of the pyramidal cell dendrites; a more discrete and patterned change occurring as a result of wave activity might have a shorter time course and could conceivably correspond to the short-term trace mechanism postulated.

The reward system (that is, discriminator output) as conceived here converts a configuration of cells identified by the postulated short-term change into a pattern of cells more permanently established by an increase in their synaptic interconnectedness. Such a system must have a distribution to all parts of the cortex. A fibre bundle with this characteristic has recently been demonstrated[15] by the fluorescence technique for catecholamines, and it is also of interest that, on the basis of a pharmacological analysis of the self-stimulation phenomenon originally described by Olds and Milner[16], Stein[17] had previously proposed that a noradrenergic system was involved.

A theoretical analysis of learning such as this implies two further features. The short-term mechanism would constitute a process through which all memory traces would have passed before reaching a long-term or permanent store, and would therefore be a measure of "rate of change of memory", a possible defining feature of consciousness[18,19]. It will also follow that new sensory inputs will lead in general to short-term trace patterns of cells the synaptic inter-connexions of which have previously been strengthened by the discriminator. An organism with such a mechanism will learn to perceive[11].

The principal suggestions which arise from this analysis are: (1) that travelling waves of neural activity in a randomly connected cell mass can form the basis of a learning mechanism as proposed by Beurle, only given the existence of a short-term characteristic of cortical cells such as that postulated in (2) and (3) earlier; (2) that reinforcement (in Skinner's sense[4]) could be a function of a distinct neural fibre system for transforming cortical synaptic connexions from a short into a long-term form.

T. J. Crow

Department of Physiology,
University of Aberdeen.

Received April 1; revised June 21, 1968.

[1] Kandel, E. R., and Spencer, W. A., *Physiol. Rev.*, **48**, 65 (1968).
[2] Burns, B. D., *The Uncertain Nervous System* (Edward Arnold, London, 1968).
[3] Thorndike, E. R., *Animal Intelligence* (Macmillan, New York, 1911).
[4] Skinner, B. F., *The Behaviour of Organisms* (Appleton-Century-Crofts, New York, 1938).
[5] Young, J. Z., *A Model of the Brain* (Oxford University Press, Oxford, 1964).
[6] Beurle, R. L., *Phil. Trans. Roy. Soc.*, B, **240**, 55 (1957).
[7] Beurle, R. L., in *Principles of Self-Organization* (Pergamon Press, Oxford, 1961).
[8] Pringle, J. W. S., *Behaviour*, **3**, 174 (1951).
[9] Broadbent, D. E., *Behaviour* (Eyre and Spottiswoode, London, 1961).
[10] Konorski, J., *Conditioned Reflexes and Neuron Organisation* (Cambridge University Press, London, 1948).
[11] Hebb, D. O., *The Organization of Behaviour* (Wiley, New York, 1949).
[12] Gerard, R. W., *Amer. J. Psychiat.*, **106**, 161 (1949).
[13] Rusinov, V. S., *Abstr. Nineteenth Intern. Physiol. Congr., Montreal* (1953).
[14] Morrell, F., *Ann. NY Acad. Sci.*, **92**, 860 (1961).
[15] Anden, N. E., Dahlström, A., Fuxe, K., Larsson, K., Olson, L., and Ungerstedt, U., *Acta Physiol. Scand.*, **67**, 313 (1966).
[16] Olds, J., and Milner, P. M., *J. Comp. Physiol. Psychol.*, **47**, 419 (1954).
[17] Stein, L., *Fed. Proc.*, **23**, 836 (1964).
[18] Schrödinger, E., *Mind and Matter* (Cambridge University Press, London, 1958).
[19] Griffith, J. S., *The Neural Basis of Conscious Decision* (Bedford College, London, 1967).

Affinity of Neurones in Regeneration

Classes of neurones which are capable of forming synapses with other classes (as distinct from those which actually do so in normal growth) can be defined only by allowing the neurones to show—by their growth in abnormal conditions—what anatomical patterns of connexions they will form and what they will not. It remains to be shown that the orderly connexions that are formed in the normal process of development are but a fraction of the possible connexions that can be revealed by transplantation. As a result of numerous transplantation experiments and the analysis of the resultant synaptic patterns it may one day be possible to delineate sets and subsets of neurones by their preferences and aversions for synaptic contact with other sets and subsets which are so revealed. Where a single neurone can be individually recognized again and again in different preparations, these experimental tests lead to conclusions about the determination of character of single cells, otherwise only groups of neurones can be distinguished.

Observations of this kind have been made on regeneration of the optic tract of lower vertebrates after rotation of the eye[1] and after operations on the retina[2]; on regeneration of axon terminals into sympathetic ganglia[3] or into muscle[4]; and upon the growth of Mauthner fibres in rotated or transplanted amphibian embryo tissue[5]. The general conclusion from these studies on vertebrates is that growing nerve fibres are sensitive to delicate chemical signals by means of which they grow towards and identify their post-synaptic cells with sufficient specificity to permit a gross functional, but not necessarily a detailed anatomical, recovery. Regenerating axons can find their approximate normal destinations when regenerating along an abnormal path, as in the regeneration of the optic tract of *Xenopus* along the track of the oculomotor nerve[6], or in the growth of an antennule in place of an eyestalk in the spiny crayfish, *Panulirus*[7].

Apart from the large number of experiments required, there are two outstanding barriers to progress in this field. In vertebrates only certain isolated examples of giant neurones are individually recognizable, either in the same animal after growth, or in different members of the same species. A normal anatomical connectivity pattern cannot therefore be worked out in sufficient detail to give information about single cells as distinct from types of cells.

Second, most of our information on synaptic patterns comes from physiological studies which reveal physiological pathways, not anatomical connectivity patterns. Usually there are numerous alternative explanations of physiological pathways in terms of anatomical connectivity and it is the latter which is of interest. It is therefore important to find preparations which have a constant and knowable anatomical connectivity pattern and also which can be tested functionally and by electrophysiological methods. The projection of the primary visual cells of insects upon the second order cells closely approaches this ideal.

The compound eye of an insect consists of an array of several thousand facets: behind each facet lies the group of retinal cells which comprise the ommatidium. The primary photoreceptors, of which there are usually two kinds, totalling eight in each ommatidium, have axons which run to the first optic lobe (called the lamina) immediately below. The lamina is a regular array of synaptic structures which from their shape are called optic cartridges. Here one group of primary retinula fibres (the short fibres) terminate and form synapses with the second order neurones. Each optic cartridge corresponds to one ommatidium, but the retinula fibres of an ommatidium do not necessarily all terminate in the same cartridge. In Diptera (flies), fibres of six of the retinula cells of a single ommatidium run to six

© 1968 Nature Publishing Group