electrophoresis, veronal buffer, as in zone electrophoresis, the mobility of *P* is slightly less than that of *G*.) In an attempt to sharpen this heterogeneity, an aliquot of hæmoglobin *A* was added to an equal amount of 'MTu's' hæmoglobin sample, and the mixture was analysed in free electrophoresis, veronal buffer, *p*H 8·6, 0·1 *M*. It was then resolved into two distinct peaks in both the ascending and descending patterns, and the areas of these peaks were in about the expected proportions (3*A* : 1*P*).

Hæmoglobin *P* may now be characterized as follows: in zone electrophoresis, veronal buffer, *p*H 8·6, the mobility of *P* lies between *G* and *S*, like that of hæmoglobin *L*[2]. In free electrophoresis in acid buffer (cacodylate *p*H 6·2–6·9, 0·1 *M* or phosphate, *p*H 6·4, 0·04 *M*) the mobility of *P* appears identical with that of *A*. However, in analyses of mixtures of *P*, *A* and *G* (cacodylate *p*H 6·5), there is indication that in this *p*H range the net charge of *P* is not precisely the same as that of *A*, but rather that *P* overlaps *A* and *G* in this respect. This is also suggested by the results of column chromatography with 'Amberlite', citrate buffer, *p*H 6·5 (ref. 8). In free electrophoresis in alkaline buffer (veronal, *p*H 8·6, 0·1 *M*) *P* does not separate clearly from *A* in a 1 : 1 mixture of these two types. However, in a mixture containing approximately three parts of *A* and one part of *P*, quantitative separation does occur, and the mobility of *P* (as in zone electrophoresis) is less than that of *A*. Finally, in free electrophoresis at *p*H 6·5 of mixtures of *P* with other types of hæmoglobin, the qualitative and quantitative resolutions of *P* are to a unique extent influenced by the nature of the companion proteins.

This work was aided by U.S. Public Health Service Grant *A*–780.

ROSE G. SCHNEIDER
MARY ELLEN HAGGARD

Tissue Metabolism Research Laboratory
and Department of Pediatrics,
University of Texas Medical Branch,
Galveston, Texas.
May 23.

[1] Schneider, R. G., and Haggard, M. E., *Nature*, **180**, 1486 (1957).
[2] Ager, J. A. M., and Lehmann, H., *Brit. Med. J.*, ii, 142 (1957).
[3] Schneider, R. G., and Genereaux, B., *Roy. Soc. Trop. Med. and Hyg.*, **50**, 614 (1956).
[4] Vella, F., Wells, R. H. C., Ager, J. A. M., and Lehmann, H., *Brit. Med. J.*, i, 752 (1958).
[5] Robinson, A. R., Robson, M., Harrison, A. P., and Zuelzer, W. W., *J. Lab. Clin. Med.*, **50**, 745 (1957).
[6] Shooter, E. M., and Skinner, E. R., *Biochem. J.*, **60**, 38 (1955).
[7] Morrison, M., and Cook, J. L., *Fed. Proc.*, **16**, 763 (1957).
[8] Huisman, T. H. J., and Prins, H. K., *J. Lab. Clin. Med.*, **46**, 255 (1955).
[9] Edington, G. M., Lehmann, H., and Schneider, R. G., *Nature*, **175**, 849 (1955).

Gamma-Amino-*n*-Butyric Acid and Spinal Synaptic Transmission

A MAJOR constituent of factor I isolated from mammalian brain has been shown to be γ-amino-*n*-butyric acid[1]. It has been assumed that this material, an inhibitor of the crayfish stretch receptor, is an inhibitory transmitter substance within the mammalian central nervous system[2]. Recent investigations indeed have shown that γ-amino-*n*-butyric acid reversibly depresses the potentials arising from the synaptic activation of cells within the cerebral cortex[3] but no precise differentiation as to the mode of action of γ-amino-*n*-butyric acid has been attempted.

In the present investigation, γ-amino-*n*-butyric acid has been passed electrophoretically, as a cation, from one barrel of a multi-barrelled electrode. The responses, both of single cells and of groups of cells within the spinal cord of the cat, have been recorded from another barrel of the electrode filled with 4 *M* sodium chloride solution.

In the dorsal horn and intermediate nucleus of the spinal cord, cells caused to discharge by volleys in skin or muscle afferent fibres are prevented from firing by γ-amino-*n*-butyric acid. Similarly in the ventral horn, motoneurones cannot be fired either orthodromically or antidromically under the influence of γ-amino-*n*-butyric acid. In addition, the antidromic responses of small motoneurones, and the responses of Renshaw cells both to synaptic stimulation and activation by ionophoretically applied acetylcholine, are prevented by γ-amino-*n*-butyric acid. All these effects of the acid are evoked by currents of 20–350 × 10^{-9} amp. and are of short latency and rapidly reversible.

In both the dorsal and ventral horns focal synaptic potentials, recorded extracellularly and evoked by simultaneous excitation or inhibition of groups of cells, are diminished or even abolished by γ-amino-*n*-butyric acid. This reduction of excitatory focal synaptic potentials is not altered by strychnine administered intravenously, and is not accompanied by any diminution in the size of potentials recorded simultaneously from the pre-synaptic fibres. Excitatory synaptic potentials, evoked in motoneurones by impulses in group *Ia* afferent fibres, and recorded extracellularly as negative potentials, could be converted into positive potentials, indicating that the membrane behaving as a sink for current had been converted into a source.

These results make it extremely unlikely that γ-amino-*n*-butyric acid is a transmitter substance in the mammalian spinal cord. In particular, the abolition of the excitatory post-synaptic potentials of motoneurones recorded extracellularly excludes the possibility that γ-amino-*n*-butyric acid is the inhibitory transmitter upon these cells. Although it might be expected that excess inhibitory transmitter would lead to hyperpolarization of the cell with abolition of inhibitory post-synaptic potentials, the actual alteration in the membrane conductance would be small[4]. Hence, post-synaptic excitatory potentials would not be abolished and focal synaptic potentials, consisting predominantly of extracellularly recorded excitatory potentials, would still be recorded.

Accordingly, it is probable that γ-amino-*n*-butyric acid has a depressant action on the whole soma-dendritic membrane of centrally located neurones, both the chemically activated subsynaptic membrane and the remaining electrically activated post-synaptic membrane.

D. R. CURTIS
J. W. PHILLIS

Department of Physiology,
Australian National University,
Canberra.
April 30.

[1] Bazemore, A., Elliott, K. A. C., and Florey, E., *Nature*, **178**, 1052 (1956).
[2] Florey, E., and McLennan, H., *J. Physiol.*, **130**, 446 (1955).
[3] Iwama, I., and Jasper, H. H., *J. Physiol.*, **138**, 365 (1957). Purpura, D. P., Guado, M., and Grundfest, H., *Science*, **125**, 1200 (1957). Marrazzi, A. S., Hart, E. R., and Rodriguez, J. M., *Science*, **127**, 284 (1958).
[4] Eccles, J. C., "The Physiology of Nerve Cells" (Johns Hopkins Press, 1957).