Wang and Brown[8] were the first to describe the terminal rebound and, except for the fact that it is seen after stimulation of purely muscular nerves, the present experiments confirm theirs in essence. It is agreed that afferent C fibers must be active for the effect to appear. Another condition seems to be that the C fiber reflex must fall during the course of the A fiber reflex; otherwise, the C fiber reflex is inhibited as in the last record of Figure 4.

Wang and Brown[8] discuss the terminal rebound effect in terms of inhibition of the C fiber reflex during the period of stimulation by activity of larger cold-receptive fibers. However, as here shown, the effect is present when stimulation is confined to muscular afferent fibers (Figure 4), which means at the least that it is not specifically related to the action of cold-receptive fibers.

In the classical view, terminal rebound is a sign of concealed inhibition with excitatory effects outlasting the inhibitory to produce a response at the close of stimulation. As this seems the only explanation, it is probably correct to conclude, with Wang and Brown, that there exists an inhibitory reflex although one cannot specify the executant afferent pathway.

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NEURONAL EXTENSION AND GLIAL SUPPLY: FUNCTIONAL SIGNIFICANCE OF GLIA

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Our knowledge concerning the functional significance of glia cells is still insufficient. The present study represents an attempt to correlate the number of glia cells with known morphological features (length of axon) of neurons. Clark's column in the spinal cord provided an opportunity to compare the glial supply of

nerve cells which are functionally identical but have different length axons. The number of perineuronal glia cells in Clark's column shows a linear relationship to the length of the axons. Additional counts of the glia index (number of glia cells per nerve cell) indicate less glial supply in nuclei with very short connections than in nuclei with long connections.

Glia cells, particularly oligodendroglia, are considered "auxiliary metabolic units" attached to nerve cells wherever the morphological extension of the neuron renders the maintenance of metabolism difficult. Increased functional demands on a nerve cell apparently are not met with hypertrophy but with the attachment of glia cells to the nerve cell.

Observation.—The relative number of glia cells per one nerve cell (glia-index) in the cerebral cortex has been shown to increase in the following order: frog, chicken, mouse, rabbit, pig, cow, horse, man.[5] This increase has been considered an index

TABLE 1

NUMBERS OF PERINEURONAL GLIA CELLS AS COMPARED WITH PROBABLE AXON LENGTH

Length of cord in cm	Relative number of satellite cells	Total count
25	5.6 ± 3	141
30	5.3 ± 2	134
40	8.7 ± 3	219
45	7.2 ± 3	180
50	8.3 ± 4	209
55	10.0 ± 3	252
60	8.7 ± 3	218
65	9.0 ± 3	227
70	10.0 ± 4	251
75	10.6 ± 3	267
80	15.2 ± 4	378
85	11.9 ± 5	298
90	16.8 ± 6	421
100	14.0 ± 5	351
105	15.5 ± 5	389
110	16.2 ± 4	407
115	18.2 ± 6	457

of brain metabolism or brain development, respectively;[7, 8] however, Hawkins and Olszewski[9] showed still higher indices in the whale brain and concluded that the index depends on the size of the brain. They suggested, as a working theory, that nerve cells with longer processes may require more assistance from the supportive tissue to meet their metabolic needs.

This theory could be proved in a center with nerve cells of identical function and metabolism, but with different length of axons. The most appropriate nucleus for such a study, perhaps the only one in the nervous system, is Clark's column. Here the large cells can be considered of uniform functional significance; yet, since their axons terminate at approximately the same level (cerebellum), the length of their processes varies according to the segment in which the perikarya reside. Marchi degeneration[2-4, 12] as well as electrophysiological data evidence that at least a major fraction of the fibers pass the cord without relays. These fibers evidently originate from the large nerve cells, since only these cells showed chromatolysis following section of the tracts.[14] The differences of necessary axonal length are quite impressive in larger species, ranging in the cow approximately from 40 to 180 cm while the size of the perikarya do not change significantly.

The perineuronal satellite cells were counted at various levels of the cow's spinal cord in 10 μ paraffin sections, stained with chrom alum-gallocyanin. An arbitrary method was used to define perineuronal glia cells: Large nerve cells were centered in a square measuring 76 $\times$ 76 μ; all glia cells within this square were counted. The size of the nerve cells did not change significantly; the count thus reflected changes of glial density in the perineuronal tissue. Such counts were made at 5 cm intervals in 25 to 115 cm lengths of the cord measured from the caudal termination of the fourth ventricle. Only large nerve cells were selected for the counts, since only these cells exhibit chromatolysis following sections of the spinocerebellar fasciculus.

Table 1 shows the number of glia cells surrounding the perikarya of the large cells in the cow Clark's column, in comparison with the approximate length of the axons.

The cells in the cervical segments of Clark's column showed few attached satellite cells, and there were also few glia cells in the adjacent tissue. In contrast, the cells in the caudal segments of Clark's column exhibited numerous satellite cells often resembling pathological neuronphagias. Table 1 indicates a linear relationship between the number of pericellular glial cells and the length of the axons.

These findings suggest a more general correlation between axon length and the relative glial density of various centers. Glia indices were accordingly counted in six regions, each in five species. These data are recorded in Table 2.

For these counts formalin-fixed brains of mouse, rat, pig, cow, and man were used. Cell counts were made in 10 μ paraffin sections stained with chrom alumgallocyanin, counterstained with eosin. An ocular net micrometer was used to count all glial nuclei and all neuronal nuclei in a given field, each field containing about 20 to 50 cells. No attempt was made to differentiate between the types of glia cells, but care was taken to avoid endothelial nuclei. An effort was made to count only the

TABLE 2

GLIA INDICES IN CENTERS WITH DIFFERENT AXON LENGTHS AND BRAINS OF VARIOUS SIZE

	Mouse	Rat	Pig	Man	Cow	Man (Friede, '54)	Man (Hawkins and Olszewski, '57)	Whale
Fascia dentata (short, intranuclear connections)	0.07 ± 0.02	0.06 ± 0.01	0.17 ± 0.05	0.14 ± 0.02	0.66 ± 0.22			
Lam. II, occipital (intracortical connections)	0.19 ± 0.07	0.41 ± 0.11	0.92 ± 0.20	0.72 ± 0.12	0.92 ± 0.25			
Cornu ammonis (extranuclear projection)	0.11 ± 0.03	0.16 ± 0.10	0.60 ± 0.08	0.94 ± 0.17	1.28 ± 0.37			
Lam. II, frontal (intracortical connections)	0.26 ± 0.11	0.35 ± 0.06	0.95 ± 0.11	1.54 ± 0.21	1.00 ± 0.22	Lam. II: 1.24	1.53	1.11–1.84
Lam. V, occipital (extracortical projection)	0.42 ± 0.12	0.67 ± 0.17	1.22 ± 0.06	1.21 ± 0.35	1.32 ± 0.30			
Lam. V, frontal (long projection)	0.73 ± 0.28	0.96 ± 0.18	1.68 ± 0.06	1.93 ± 0.46	1.98 ± 0.77	Lam. V: 1.93	1.27	4.47–7.89

nucleoli of neurons instead of the nuclei, but it was found difficult to distinguish the nucleoli in several centers, e.g., the fascia dentata, where the nuclear chromatin showed numerous dense aggregations.

In the counting of particles in sections, one has to take into consideration the size of particles as compared to the thickness of sections. Larger particles will be cut more often than smaller ones; thus, the true number of particles in the tissue is smaller, than that counted in sections.[1, 7, 13]

Since the nerve-cell nuclei were larger than glial nuclei, the number of nerve cells counted was actually an overestimation; therefore, the differences of the glia index among regions should be even greater than is shown in our data.

The data in Table 2 indicate that the glia index increases with brain size; the increase, moreover, being greater in regions with long axonal connections than in those with short connections (e.g., fascia dentata, second layer of the occipital cortex). This correlation seems logical, since increased size of the brain affects the spacing of centers more than it does their size. The indices exhibit considerable fluctuation in some of the regions, probably reflecting inhomogeneity of the material (mixed projections of fibers of different length?). An effort was made to count other regions characterized by extremely short axonal connections, such as the granular layers of the olfactory bulb and the cerebellar cortex, but these counts failed because of lack of a reliable method permitting one to distinguish neuronal and non-neuronal nuclei. It was estimated, however, that the glia index of these regions was about as low as that in the fascia dentata.

Comment.—The transmission of an impulse from one place to another requires a morphological extension of the nerve cell. This extension depends on the size of the animal and its nervous system, respectively. The physiological characteristics of a cortical cell in mouse and cow are similar, but the latter has to maintain an axon about 40 times longer. The data in this article support the concept that glial cells, particularly oligodendroglia, serve as auxiliary metabolic units, being attached to the nerve cells wherever the length or ramification of cell processes render their maintenance difficult. A nerve cell apparently cannot meet increased demands by simple hypertrophy, because this would disturb the functional microstructures. Instead, glial cells are attached to the neuron and serve as "auxiliary metabolic units." This is in accordance with the increased numbers of satellite cells following hyperactivity[11] and likewise with the intricate relationship between glial and neuronal metabolism.[10] Our study was concerned with the glial supply of the nerve cell only; the glia-neuron relationship is further complicated by the glial supply of axons in fiber tracts, showing the intricate correlation of glial and axonal enzyme activity. Activity of oxidative enzymes (DPN-diaphorase) in axons and oligodendroglia cells showed an inverse relationship in various human fiber tracts; this suggests that axon and glia cells share their enzymatic activity while the relative share taken by either axon or glia varies greatly among tracts.[6] Biochemical studies of glial metabolism may face a proteus-like problem, since the glial metabolism may represent different shares of the neuronal metabolism for different species or even nuclei; the nerve cells in the fascia dentata, for example, have minimal glial supply. It is strongly felt that all the data presented above apply to oligodendroglia and not to astrocytes, but this could not be proved without differential counts. This study represents a preliminary report of a continued project.

APPENDIX

BY RALPH W. GERARD

These findings are the most convincing ones I have seen, in fact, the first convincing ones, indicating a metabolic role of glia as "nursing" the neurons. There is a further important implication. The mere static existence of a longer axon would not demand any greater perikaryon metabolism than would a shorter axon. The greater metabolic activity implies a greater dynamic requirement in maintaining a longer axon, presumably by a more rapid material movement from soma into axon along the lines urged by Gerard,[15] Weiss,[16] and others.[17] Explicitly these results lead to the prediction that the rate of movement of materials in an axon varies as axon length—linearly as a first approximation. Experiments to test this are being initiated.

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INDETERMINISM IN INTERSPECIFIC COMPETITION

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The extensive experiments of Park and his associates[1–4] on competition between two species of flour beetles, *Tribolium castaneum* and *T. confusum*, have become one of the most-quoted examples of indeterminism in biology. When populations of the two species are kept together in cultures containing whole-wheat flour and yeast, one species invariably displaces the other. Under high temperature and high relative humidity, *T. castaneum* (hereafter designated *CS*) is the winner; when both temperature and humidity are low, *T. confusum* (designated *CF*) wins. At intermediate regimens, such as represented by 29°C and 70 per cent humidity, in