DEGENERATE VERSUS MULTIPOLAR NEURONS IN SENSORY GANGLIA *

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Evidence has been presented for (Horton-Smith;¹ Kuré *et al.*;^{2,3,4} Okelberry;^{5,6} and Kahr and Sheehan⁷) and against (Duncan and Crocker;⁸ and Hinsey^{9,10}) the existence of spinal parasympathetic nerve fibers. Such attempts to challenge the Bell-Magendie law have been based on experimental degeneration of dorsal root fibers following root resection and on morphological studies of spinal ganglia under normal and experimental conditions.

Westbrook and Tower¹¹ have recently thrown new light upon the problem in their description of extraneous fibers which grow into the dorsal root following root resection and ganglionectomy. A detailed discussion of the recent literature can be found in their report.

The existence of parasympathetic fibers in the dorsal roots of spinal nerves would necessitate the presence of efferent (multipolar) neurons in either the spinal ganglia or within the spinal cord. Kuré, Saégusa, Kawaguchi and Shiraishi³ have described such cells of intraspinal origin as lying in the ventral portion of the dorsal horn, while Kiss¹² has described small, dark multipolar neurons in the spinal ganglia following prolonged osmification. Fisher and Ranson¹³ concluded that the stellate appearances of the dark cells described by Kiss were the result of cell injury and shrinkage.

In view of the above conflicting reports, a more extensive investigation with appropriate silver methods seemed desirable. By studying the finer ramifications of neuron processes in normal, senile and pathologic sensory ganglia one might expect to observe true multipolar neurons, should they exist.

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MATERIAL AND METHODS

Normal spinal and gasserian (semilunar) ganglia of 7 white leghorn chickens, 5 white rats, 10 adult cats and 3 rhesus monkeys were perfused with a neutral 4 per cent solution of formaldehyde and dissected for study. In addition, 57 human gasserian ganglia and 7 spinal ganglia from cervical, thoracic and lumbar levels were obtained at autopsy. The sources of the human specimens ranged from the newborn to 81 years of age and specimens were selected regardless of sex, clinical symptoms or autopsy findings. Celiac and lumbar sympathetic ganglia were obtained from 8 human bodies for purposes of comparison.

Fixation was in ammoniated absolute alcohol, 10 per cent alcoholic chloral hydrate, or neutral 4 per cent solution of formaldehyde. Following fixation the tissues were carried through the Ranson pyridine-silver, and the Cajal silver impregnation methods. Sections of silver preparations were cut in a cranio-caudal plane at 12 μ . The formaldehyde-fixed specimens were cut at 8, 10 and 12 μ and alternate sections stained by the Bodian protargol and cresyl-violet technics. Serial sections of each specimen were examined, using an oil immersion lens as needed.

OBSERVATIONS

Earlier investigations concerning structural changes in sensory neurons concomitant with senility in the chicken and man have been reported by me.^{14,15} During the course of these studies the atypical and degenerate neurons have constantly aroused interest, not only because of their numerous and complexly ramifying processes, but also because of their marked resemblance to true multipolar neurons. Such similarity is demonstrated by sensory cells possessing supernumerary processes, commonly designated as "frayed cells of Cajal." These alone are considered in this investigation.

It would not seem possible, to one examining the sensory ganglia for the first time, that a normal unipolar neuron (Fig. 1) could undergo extensive transfiguration and thereby be confused with the structure of a multipolar neuron (Fig. 2). Yet, if one compares the appearances of the degenerate sensory cells in Figures 3, 6, 9, 12, 15 and 18 with those of sympathetic neurons in

Figures 4, 5, 7, 8, 10, 11, 13, 14, 16, 17, 19 and 20, differentiation between the two cell types becomes progressively more difficult.

There appears to be no limitation on the number of such accessory processes of a unipolar cell, or on the complexity which each process may attain. With the addition of each new process, originating from either cell soma or undivided stem (axon), the sensory neuron more closely resembles the multipolar type.

In Figure 3 the accessory processes arise only from the axonic stump, and sensory neurons with this structure bear a likeness to the truncated multipolar cells of the sympathetic ganglia (Figs. 4 and 5). Sensory neurons demonstrating only a few short, thick radicles (Fig. 6) are similar to efferent neurons which possess a like number of processes (Figs. 7 and 8).

The degenerate unipolar cells in Figures 9, 12 and 15 are very common in senile and pathologic sensory ganglia of man. Due to the increase of processes and collateral branching, such neurons are easily confused with diverse sympathetic cells of closely parallel structure (Figs. 10, 11, 13, 14, 16 and 17).

Excessive proliferation of cytoplasmic outgrowths and cell excrescences results in the bizarre structure shown in Figure 18. The dichotomous branchings and profuse ramifications on these sensory neurons might readily lead one to assume that he was observing a motor neuron. The distinction is at times quite difficult in view of the similar structure and branching of the multipolar cells (Fig. 19). In addition, the so-called "comet-cells" of the sympathetic nervous system (Fig. 20) manifest a wealth of short branching processes, whereby they too simulate degenerate sensory components like those shown in Figure 18.

The features distinguishing between degenerate sensory and true multipolar neurons are shown in the accompanying figures. The short accessory processes of the sensory cell usually terminate within the limits of the surrounding capsule. The frequency of branching, the varicosities, and the terminal club-shaped expansions along the processes provide additional distinguishing criteria. Likewise, the abortive cell outgrowths stain more darkly with the usual silver impregnation methods than does the normal undivided stem of the sensory neuron.

In contrast to these features, the more lightly stained processes of the efferent cells pass through the confines of the cell capsule

as definite axon or dendrite radicles. They possess few or no club-shaped outgrowths or reticulated expansions. Branching of the true dendrites is more uniform and equal.

In sympathetic ganglia from older specimens, both animal and human, one frequently observes a definite thickening or hypertrophy of neuronic processes (Figs. 5 and 14). In other instances all of the dendritic processes do not penetrate the capsule (Figs. 11, 13, 14, 17, 19 and 20). As a result of these inconsistencies, the contrasting features as listed may be less clearly defined.

Serial examination of all the animal and human specimens revealed no cell which could be classified morphologically as a true multipolar neuron.

Distribution of Degenerate Neurons. Spinal and gasserian ganglia of the chicken, rat, cat, monkey and man possess the described degenerate neurons in variable numbers. Though relatively few in the spinal ganglia of the lower animals, they are more frequent in the animal gasserian and human spinal ganglia. Festooned sensory cells are abundant in human gasserian ganglia from patients of all ages. Their occurrence is particularly frequent following death from diabetes, chronic alcoholism, barbitol poisoning and prolonged infectious diseases.

COMMENT

Embryologically, it would be possible to account for the presence of multipolar neurons in the sensory ganglia since the primordia of the spinal ganglia lie along the course of migrating neuroblasts destined for the sympathetic ganglia. Decision whether such neuroblasts are derivatives of the neural crest, neural tube, or both, awaits further investigation. In any case the opportunity presents itself at this early stage for migrating neuroblasts destined to become efferent neurons to be retained within the definitive spinal ganglia. Subsequent differentiation of the retained neuroblasts into multipolar neurons, which were later reached by preganglionic fibers, might then offer a plausible explanation for the presence of so-called spinal parasympathetic fibers in the dorsal root of spinal nerves.

In a similar way the gasserian ganglion might be expected to manifest such retained neuroblasts, since the primordia of the ciliary, submaxillary, sublingual and sphenopalatine ganglia are

known to arise in close association with branches of the trigeminal nerve (Streeter,¹⁶ Stewart¹⁷).

This assumption or retention theory is not wholly free from justified criticism. However, it affords a legitimate explanation for, and understanding of the significance of, multipolar neurons should they be found to exist in sensory ganglia. From the study of serial silver preparations of spinal and gasserian ganglia designed to demonstrate such cells, no morphological evidence could be found to substantiate their existence. In the absence of efferent neurons within the sensory ganglia, the reality of preganglionic efferent fibers in the dorsal spinal root is questionable.

The presence of many degenerate sensory neurons, designated by Cajal¹⁸ as "frayed cells" in view of their ragged and cog-wheel appearance, might readily lead to confusion of neuron cell types. In addition, terminology becomes confusing if investigators classify ganglion cells with supernumerary processes as multipolar. Such cells are multipolar only in the sense that they possess more than two processes and in these instances the term cannot be applied with the intention of denoting a motor or efferent physiological nature.

It should be pointed out that no technic can be utilized in determining the multipolarity of a ganglion cell unless it is capable of staining the individual processes and demonstrating their capsular and extracapsular relationship. The classification of neuron cell types following the osmification method described by Kiss¹² has been found unreliable, as was pointed out by Fisher and Ranson¹³ and more recently by Levi and Meyer.¹⁹

Neurons herein described as atypical must be looked upon as degenerate cells. Due to clumping of the cytoplasmic tigroid bodies in senile sensory cells (Truex¹⁵), the cresyl-violet and Nissl technics cannot be relied upon to distinguish adequately between all sensory and motor neurons.

SUMMARY

Serial silver preparations of the spinal and gasserian ganglia of the chicken, white rat, cat, monkey and man fail to demonstrate the presence of multipolar neurons. No morphological evidence has been presented to date which conclusively substantiates the existence of such neurons of parasympathetic function within

the spinal or gasserian ganglion. The reality of preganglionic efferent fibers terminating in spinal ganglia remains questionable.

Degenerate sensory neurons often simulate multipolar cells. These two cell types may be distinguished from each other by the length, branching, varicosities and staining of their respective processes.

Osmic acid and Nissl technics are inadequate methods with which to classify nerve cell types, due to structural variations of sensory neurons in senile and pathologic ganglia.

Recognition of cell types and variation in the appearances of degenerate neurons is essential for correct interpretation of sensory ganglionic structure.

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DESCRIPTION OF PLATES

PLATE 45

All figures are untouched photomicrographs from silver preparations of human material.

- FIG. 1. Normal unipolar neuron with capsule and process (axon). Gasserian ganglion. Male, 2½ years old. Cajal's technic. $\times 1000$.
- FIG. 2. Typical multipolar neuron with processes. Celiac ganglion. Female, 42 years old. Cajal's technic. $\times 1000$.
- FIG. 3. Degenerate unipolar neuron showing short extraneous outgrowths and a clublike expansion arising from its single process. Gasserian ganglion. Female, 66 years old. Cajal's technic. $\times 1000$.
- FIG. 4. Truncated multipolar neuron. Celiac ganglion. Female, 42 years old. Cajal's technic. $\times 1000$.
- FIG. 5. Truncated multipolar neuron with moderate hypertrophy of processes. Third lumbar sympathetic ganglion. Male, 59 years old. Bodian's technic. $\times 1000$.

Truex

Degenerate Versus Multipolar Neurons

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- FIG. 6. Degenerate unipolar neuron possessing three thick intracapsular processes. Gasserian ganglion. Male, 65 years old. Cajal's technic. $\times 800$.
- FIG. 7. Multipolar neuron with similar number of processes as cell in Figure 6. Celiac ganglion. Female, 42 years old. Cajal's technic. $\times 800$.
- FIG. 8. Multipolar neuron with three processes. Third lumbar sympathetic ganglion. Male, 34 years old. Bodian's technic. $\times 800$.
- FIG. 9. Degenerate sensory neuron with many short accessory processes arising from cell soma. Gasserian ganglion. Female, 66 years old. Cajal's technic. $\times 800$.
- FIG. 10. Multipolar cell with processes arising from cell soma. Celiac ganglion. Female, 42 years old. Cajal's technic. $\times 800$.
- FIG. 11. Multipolar neuron with short dendritic processes. Note that all processes do not penetrate the investing capsule. Third lumbar sympathetic ganglion. Male, 59 years old. Bodian's technic. $\times 800$.
- FIG. 12. Degenerate sensory neuron with supernumerary processes arising from entire circumference of cell. Note variation in thickness and terminal expansions of these radicles. Gasserian ganglion. Male, 65 years old. Cajal's technic. $\times 800$.
- FIG. 13. Multipolar neuron with branching processes. Third lumbar sympathetic ganglion. Male, 77 years old. Cajal's technic. $\times 800$.
- FIG. 14. Multipolar neuron with short branching processes. Note similarity to degenerate neuron in Figure 12. Third lumbar sympathetic ganglion. Male, 59 years old. Bodian's technic. $\times 800$.

Truex

Degenerate Versus Multipolar Neurons

PLATE 47

- FIG. 15. Degenerate unipolar neuron demonstrating short branching processes. Gasserian ganglion. Male. 65 years old. Cajal's technic. $\times 800$.
- FIG. 16. Multipolar neuron with process formation similar to the degenerate cell in Figure 15. Female. 42 years old. Cajal's technic. $\times 800$.
- FIG. 17. Multipolar neuron with short intracapsular processes. Third lumbar sympathetic ganglion. Male. 59 years old. Bodian's technic. $\times 800$.
- FIG. 18. Degenerate unipolar neuron with extreme branching of processes. Note the wealth of primary, secondary and tertiary rami on this cell. Gasserian ganglion. Female. 66 years old. Cajal's technic. $\times 800$.
- FIG. 19. Multipolar neuron with process formation similar to the degenerate sensory cell shown in Figure 18. Third lumbar sympathetic ganglion. Male. 77 years old. Cajal's technic. $\times 800$.
- FIG. 20. Multipolar neuron. Commonly designated as "comet-cell" of sympathetic nervous system. Note intracapsular branching of processes. Celiac ganglion. Male. 55 years old. Bodian's technic. $\times 800$.

Truex

Degenerate Versus Multipolar Neurons