observed mitotic divisions which they postulated were due to injury. However, in the occasional instance of endothelial cell proliferation observed here, mitosis was not prominent, either.

Although the mechanisms involved in cellular proliferation in these experiments could not be ascertained, it is clear from the incidence of epithelialization in control as well as carrageenan injected corneas that the phenomenon was related to the production of a wound in the epithelial surface, and perhaps in the basement membrane and/or Bowman's membrane, rather than to the development of a collagenous carrageenan granuloma in the underlying stroma. Presumably this epithelialization represents an

exaggeration of part of the healing process of the wound caused by the act of injection into the cornea.

Zusammenfassung. Die Schädigung der Basalmembran durch eine Stichverletzung hat eine Proliferation und Einwanderung von Corneaepithelien zur Folge. Eigenartigerweise sind bei diesem Prozess keine Mitosen nachweisbar, was darauf hinzuweisen scheint, dass Amitosen experimentell verfolgt werden können.

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McMaster University, Hamilton (Ontario, Canada), 1 July 1968.

## Axo-Axonic Synapses in the Main Sensory Trigeminal Nucleus

Axo-axonic synapses have been found between the outer surfaces of axonal boutons in several locations in the central nervous system, including the spinal cord <sup>1,2</sup>, the cuneate nucleus<sup>3</sup>, spinal trigeminal nucleus<sup>4</sup> and the lateral geniculate body <sup>5,8</sup>. The purpose of this communication is to report the presence of axo-axonic synapses on unusual interdigitations of some axonal boutons in the main sensory trigeminal nucleus at the level of the motor trigeminal nucleus.

Adult cats and rats were perfused through the heart with potassium dichromate-buffered osmium tetroxide. In some instances, the brainstem blocks were placed in 2% uranyl acetate before dehydration (Figure 1b). Maraglas was used as the embedding medium. Thin sections were stained with lead citrate for electron microscopy.

Throughout the main sensory trigeminal nucleus, axonal boutons of different size have been found which relate to each other by small evaginations. In Figure 1a, a large bouton receives an evagination from a smaller bouton. The synaptic vesicles in the bouton receiving the evagination appear larger than those in the evaginating one. The reverse relationship is shown in Figure 1b; a bouton with small synaptic vesicles receives an evagination containing large synaptic vesicles.

One synapse is usually seen on small evaginations (Figure 1b); however, 2 may be seen on some larger ones (Figure 2a). Such axo-axonic synapses are rather short and characteristically occupy a small part of the apposed axonal plasma membranes. For this reason synapses are not seen in all sections through the axonal evaginations. It is our interpretation however, that at least 1 axo-axonic synapse is present on some part of the circumference of these evaginations. The axo-axonic synapses are charac-

terized by a widening of the intercellular space and the presence of electron dense material within the synaptic cleft (Figures 1b and 2b). The boutons containing small synaptic vesicles usually show small clusters of synaptic vesicles near the axo-axonic synapse (Figures 1b and 2b).

In some instances 3 axonal processes have been seen related to each other by evaginations. In Figure 3 a large bouton surrounds a smaller axonal process which in turn surrounds a third axonal process (AX 3). Axon 3 may

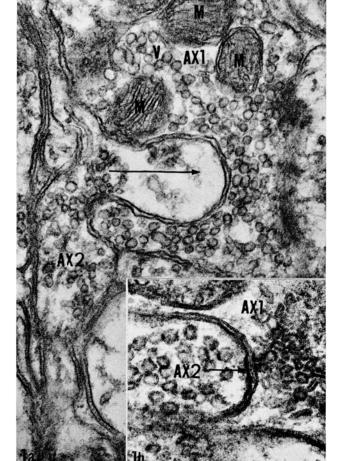


Fig. 1 (a) An axonal bouton en passant (AX 2) sends a projection (arrow) into a larger axonal bouton (AX 1). The synaptic vesicles (V) in AX 1 appear larger than those in AX 2. Mitochondria (M).  $\times$  60,000. (b) An axon containing small vesicles (AX 1) receives an axonal evagination containing large vesicles (AX 2). An axo-axonic synapse is seen at the arrow. At the synapse, note the widened intercellular space containing dense material. Synaptic vesicles in AX 1 are accumulated in the vicinity of the synapse.  $\times$  70,000.

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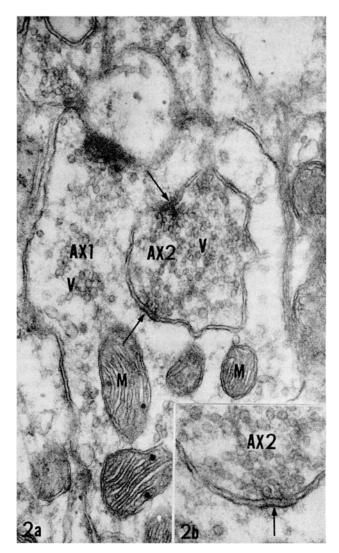


Fig. 2 (a) A large axonal bouton (AX 1) receives a polygonal axonal evagination (AX 2). 2 axo-axonic synapses (arrows) occur between these axons. Synaptic vesicles (V) are seen in both axons. Mitochondria (M).  $\times$  50,000. (b) The lower synapse in Figure 2a is shown at higher magnification. The intercellular space widens at the synapse (arrow) and is filled with dense material. Synaptic vesicles in AX 2 are accumulated in the vicinity of the synapse.  $\times$  70,000.

originate from axon 1 or it may arise from a third axon located outside the plane of section.

In addition to axo-axonic synapses found on axonal evaginations, synapses frequently occur on the outer surfaces of adjacent boutons, similar to the axo-axonic synapses reported in other areas of the central nervous system.

Apparently axonal evaginations are not limited to the main sensory trigeminal nucleus. Small axonal evaginations were reported in the lateral geniculate nucleus 8.9, although no synapses were demonstrated.

Physiologic evidence indicates that presynaptic depolarization of trigeminal afferent fibers occurs at the level of the main sensory trigeminal nucleus and can be evoked by stimulation of trigeminal nerve branches, the brainstem and cerebral cortex <sup>10-12</sup>. The axo-axonic synaptic interactions demonstrated in this report may represent a part of the morphologic basis for this axonal presynaptic depolarization. The identification of the

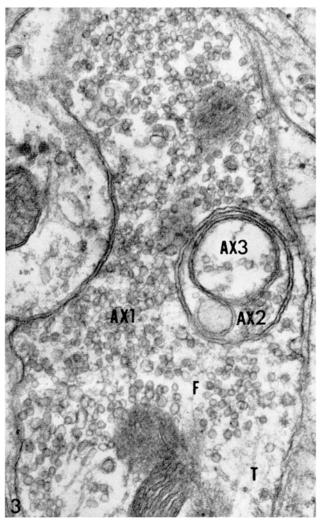


Fig. 3. A large axonal bouton (AX 1) contains a spherical axonal process (AX 2). This axonal process (AX 2) is in turn invaginated by a third axonal process (AX 3). Synaptic vesicles are seen in each of the 3 axonal processes. Neurotubule (T). Neurofilament (F).  $\times$  34,500.

source of the axons involved in these axo-axonic synapses will allow a more precise correlation between morphological and physiological findings.

Résumé. Des petites projections, provenant de boutons axoniques, sont émises dans un certain nombre de boutons axoniques adjacents au niveau du principal noyau sensoriel trijumeau.

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