

HISTOLOGICAL CHANGES INDUCED BY OTOTOXICITY IN RATS. II. ULTRASTRUCTURE OF SPIRAL GANGLION CELLS. Sandra Rodríguez(1), Odelsa Ancheta(1), Tania Valdés(1), Yahima Harvey(1), Rosa María Coro(2), Armando Alvaré(3), Valia Rodríguez(3) and Pavel Prado(3). (1)Electron Microscopy Department, Biotechnology Division, National Center for Scientific Research; (2)Pathology Laboratory, Institute of Neurology and Neurosurgery; (3)Cognitive Neuroscience Department, Cuban Neuroscience Center. Havana, Cuba. E-mail: abundia67@yahoo.com

Introduction. Spiral ganglion (SG) cells are afferent neurons which convey information from the cochlea to the central auditory system. In normal cochleae, two types of SG cells have been described within the Rosenthal's canal [1]. Type I SG cells represent approximately 95% of SG cells in rat cochleae [2]. As they are more susceptible to injury than type II [3] and are considered of primary relevance in the application of cochlear implants [4] the present work focuses its attention on them. In a previous light microscopy (LM) study, degeneration of SG cells was observed following damage of hair cells induced by ototoxic drugs in rats [5]. Although hair cells showed pathological changes since the second week of deafness, loss of SG cells and their peripheral processes was not significant until the eighth week [5]. **Objective:** Cochleae were studied by TEM in order to ascertain the onset of degenerative changes at the ultrastructural level. **Methods.** Ten adult male Wistar rats were used. Two animals were healthy controls and the rest were deafened with a single dose of kanamycin (400 mg/kg) and frusemide (150 mg/kg). Deafened rats were sacrificed 2, 4, 8 and 16 weeks after the ototoxic treatment. Cochleae were fixed on glutaraldehyde and paraformaldehyde, decalcified in EDTA, post-fixed in OsO₄ and embedded in Spurr resin. Semithin sections at the level of the midmodiolar plane were used to locate the medial cochlear turn by LM [6]. Ultrathin sections stained with lead citrate and uranyl acetate were studied under a JEOL JEM 100S TEM. **Results.** In normal cochleae, SG cells were myelinated neurons with round nuclei, narrow channels of rough endoplasmic reticulum (Nissl bodies), apposed Golgi vesicles and mitochondria with normal cristae (Fig. 1 A). Signs of damage were observed in SG cells since the second week of deafness: some points of cytoplasmic retraction from the myelin sheath surrounding the cell and slight undulations of the nuclear envelope (Fig. 1B). Four weeks after deafness, prominent irregularities in both the myelin sheath and the nuclear envelope were observed (Fig. 1C) together with loss of the normal appearance of the cytoplasmic matrix, scarce Nissl bodies and dilated Golgi vesicles (Fig. 1D). After eight weeks of deafness, the remaining type I SG cells showed cytoplasm shrinkage from the myelin sheath and conspicuous cytoplasmic inclusions (Fig. 1E); invaginations of the nuclear envelope, dilated Nissl bodies and cytoplasmic vacuolization were also evident (Fig. 1F). Sixteen weeks after deafness, most of the remaining type I SG cells exhibited complete demyelination, resulting in the so called type III SG cells [3], showing dense mitochondria and scarce Nissl bodies (Fig. 1G). **Discussion.** Signs of damage induced by ototoxicity on SG cells were ultrastructurally detected 6 weeks before LM revealed the loss of SG cells and peripheral processes [2]. Progressive degenerative changes of Type I SG cells after deafness result in the emergence of Type III neurons, exclusive of pathological conditions [4]. **Conclusion.** An 8-week therapeutic window was determined according to LM findings, but ultrastructurally detected pathomorphological changes undermining further, more severe damage, are already evident since the second week.

References

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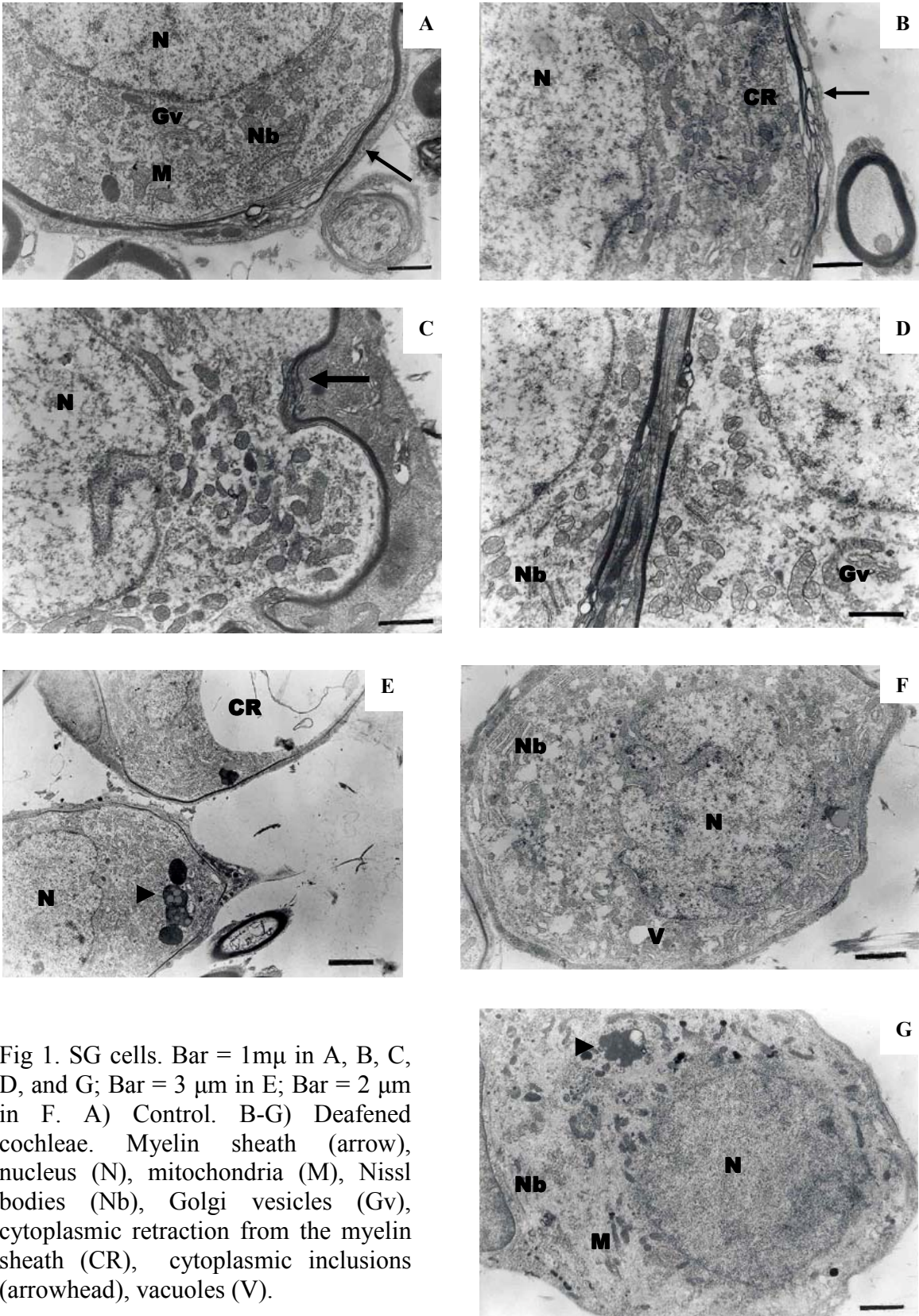


Fig 1. SG cells. Bar = 1 μ m in A, B, C, D, and G; Bar = 3 μ m in E; Bar = 2 μ m in F. A) Control. B-G) Deafened cochleae. Myelin sheath (arrow), nucleus (N), mitochondria (M), Nissl bodies (Nb), Golgi vesicles (Gv), cytoplasmic retraction from the myelin sheath (CR), cytoplasmic inclusions (arrowhead), vacuoles (V).