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ULTRASTRUCTURAL ALTERATIONS OF THE GREY MATTER STRUCTURES OF THE BRAIN DUE TO EXPERIMENTAL MANGANESE INTOXICATION

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Pathomorphological observations concerning experimental manganese encephalopathy vary to a great extent from no abnormalities whatsoever to severe tissue impairment. The latter, as a rule, appears after prolonged intoxication, lasting for numerous weeks and months (Makarczenko 1956; Pentschew et al. 1963; Chandra, Srivastava 1970; Jonderko 1970; Chandra 1972; Singh et al. 1974). The most common for all descriptions is damage of the grey cerebral structures, either generalized, prevailing in the cerebral and cerebellar cortex or selectively limited to the subcortical structures including globus pallidus, striatum, thalamus, subthalamic nuclei, substantia innominata and substantia nigra. It consists in neuronal degeneration and/or loss with secondary glial reaction and good preservation of the white matter. All the above mentioned observations were carried out at the light microscopic level.

In a series of our own observations (Śmiałek, Mossakowski 1981; Mossakowski et al. 1982, 1983) white matter alteration, consisting in tissue spongiosis and severe damage to the axonal mitochondria, dominated the pathomorphology of the experimental manganese encephalopathy. The grey matter abnormalities, as seen in the light microscope, were slight and not significant. They took the form of nonspecific degeneration of individual or grouped neurons of the cerebral or cerebellar cortex. The only finding consistent with the other observations was the severe neuronal damage and loss in the substantia nigra, appearing in animals surviving 4 weeks after the end of intoxication. This inclined us to study systematically the nature and evolution of the ultrastructural abnormalities in the brain grey structures at various stages of the postintoxication period.

MATERIAL AND METHODS

The experiments were carried out on 6-week-old male albino rats (weighing ± 150 g at the beginning of experiment), which were given, in the course of 4 weeks, seven subsequent intravenous injections of manganese chloride, dissolved in physiological salt solution. Two initial injections, each containing a dose of 20 mg/kg of Mn^{++} were given every third day, the following 3 injections with a dose of 40 mg/kg body weight of Mn^{++} each, were administered in the course of one week at two day intervals. The last 2 injections containing the same doses of metal were applied at one week intervals. The intravenous way of manganese administration was chosen to avoid poor intestinal metal absorption and its dependance on alimentary factors (Aston 1980). Control animals were given intravenously physiological salt solution according to the same scheme.

The experimental animals were divided into three groups: group I — consisted of animals killed one day after the last injection, group II — comprised those sacrificed one week after the last injection, while those of group III were permitted to survive for the next four weeks, for allowing metal excretion from the body organs (Hietanen et al. 1981). The mortality rate in all experimental groups amounted to 43%. The animals died either at the time of injection or immediately after it. The survivers, during the whole time of observation, showed no neurological symptoms. However, their motor activity was obviously reduced. They lost their appetite and their hair was lusterless.

Both experimental and control animals were sacrificed by intracardiac perfusion with 2 percent solution of glutaraldehyde in cacodylate buffer, pH 7.4. The brains after removal from the skull were kept overnight in the same fixative at the temperature of 4°C and then sliced coronally. Tissue blocks, 1 mm³ in size were taken from the neocortex, Ammon's horn, striatum, substantia nigra and upper medulla. They were processed in a routine way up to embedding in Epon 812.

Ultrathin sections were counterstained on grids with uranyl acetate and lead citrate and examined under a JEM A7 electron microscope.

RESULTS

The general pattern of ultrastructural tissue abnormalities was similar in all the examined areas of the central nervous system, although their intensity was greatest in the substantia nigra and striatum. As documented by studies carried out on subsequent experimental groups these changes evolved significantly in time.

In experimental group I all the examined areas of the brain contained neurons with focally rarefied cytoplasm, impoverished in sub-
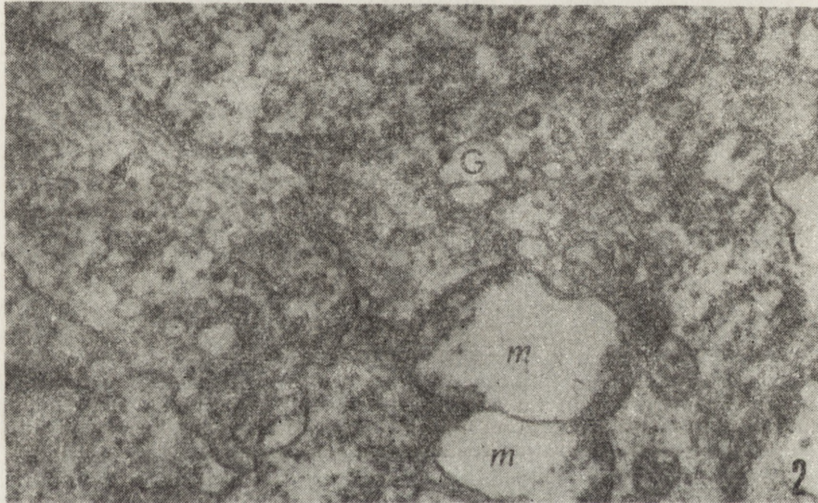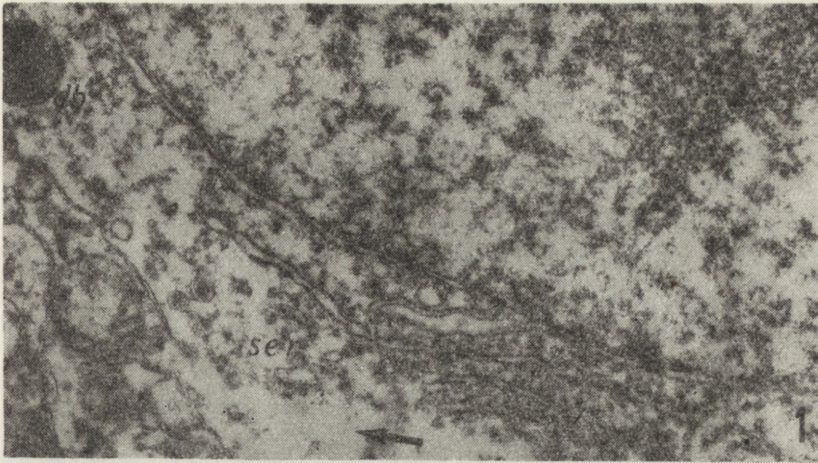
Fig. 1. Group I. Fragment of the motor cortex. Neuron showing a focal decrease of electron density of cytoplasm (arrow) with wide cisternae of smooth endoplasmic reticulum (ser) and a dense body (db). × 15 500

Ryc. 1. Grupa I. Fragment kory ruchowej. Komórka nerwowa z ogniskowym rozrzedzeniem cytoplazmy (strzałka), szerokimi zbiornikami gładkiej siateczki śródplazmatycznej (ser) i ciałem gęstym (db). Pow. 15 500 ×

Fig. 2. Group I. Fragment of striatum. In the cytoplasm of nerve cell, swollen mitochondria (m), large cisternae of Golgi apparatus (G) and abundant neurotubules (arrow) are visible. × 15 500

Ryc. 2. Grupa I. Fragment prążkowia. W cytoplazmie komórki nerwowej widoczne obrzmiałe mitochondria (m), szerokie zbiorniki układu Golgiego (G) i liczne neurotubule (strzałka). Pow. 15 500 ×

cellular organelles (Fig. 1). Numerous cisternae of smooth endoplasmic reticulum, some of them greatly distended, widened channels and cisterns of the Golgi system and swollen mitochondria with light matrix, peripherally displaced, shortened or broken down cristae were the most typical features of these neuronal abnormalities (Fig. 2). In numerous neurons, alongside with severely affected mitochondria normal ones

were present. In some nerve cells there was an increase of cytoplasmic tubular structures. Nerve cell nuclei were unchanged. Much less frequently neurons with condensed hyaloplasm, widened channels of rough endoplasmic reticulum and swollen mitocnondria were seen. Axons contained electron light cytoplasm with a reduced number of subcellular organelles and with enlarged cisternae of smooth endoplasmic reticulum. Their mitochondria were affected in the same manner as those in the neuronal perikarya (Fig. 3). Mitochondrial abnormalities were present in some nerve endings. In the latter, in addition, abnormalities in distribution of synaptic vesicles were observed, mostly in the form of irregular aggregations.
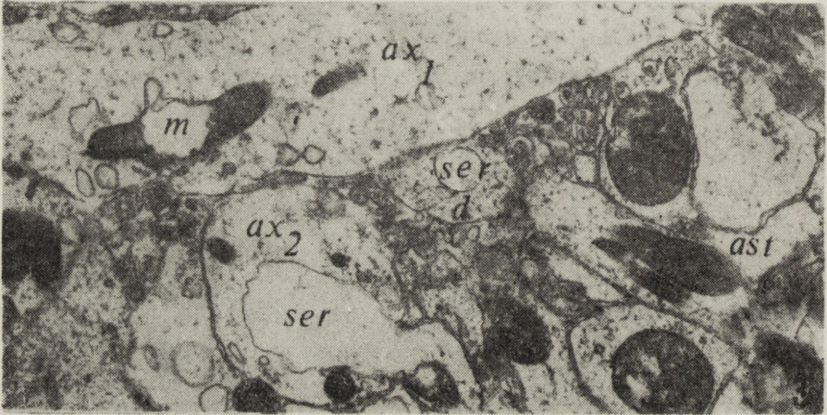
Fig. 3. Group I. Fragment of hippocampus. Swollen mitochondrium (m) with finger-like membrane protrusion in an axon (ax$_1$), vacuolization of smooth endoplasmic reticulum (ser) in another axon (ax$_2$) and dendrite (d) and mitochondrium with condensed configuration in an astrocytic process (ast). $\times$ 9 000

Ryc. 3. Grupa I. Fragment hipokampa. Obrzmiałe mitochondrium z palczastym wypukleniem błony (m) w aksonie (ax$_1$), wakuolizacja zbiorników gładkiej siateczki śródplazmatycznej (ser) w aksonie (ax$_2$) i w dendrycie (d), mitochondrium o konfiguracji skondensowanej w wypustce astrogleju (ast). Pow. 9 000 $\times$

The cytoplasm of astrocytic perikarya and processes was abundant poor in subcellular structures and contained enlarged cisterns of Golgi apparatus and of both rough and smooth endoplasmic reticulum as well as greatly swollen mitochondria with either light or granular matrix and peripherally displaced cristae (Fig. 4). The cytoplasm of some astrocytic cells was almost totally devoid of subcellular organelles, except some enlarged profiles of endoplasmic reticulum. This type of abnormalities concerned mostly perineuronal astrocytes accompanying neurons with greatly condensed cytoplasm (Fig. 5). The electron lucent cytoplasm of oligodendrocytes contained a great number of distended cisternae and channels of Golgi apparatus and rough and smooth endoplasmic reticulum (Fig. 6). Oligodendroglial mitochondria revealed the same abnormalities as those of neurons and astrocytes. Most of the capillaries and
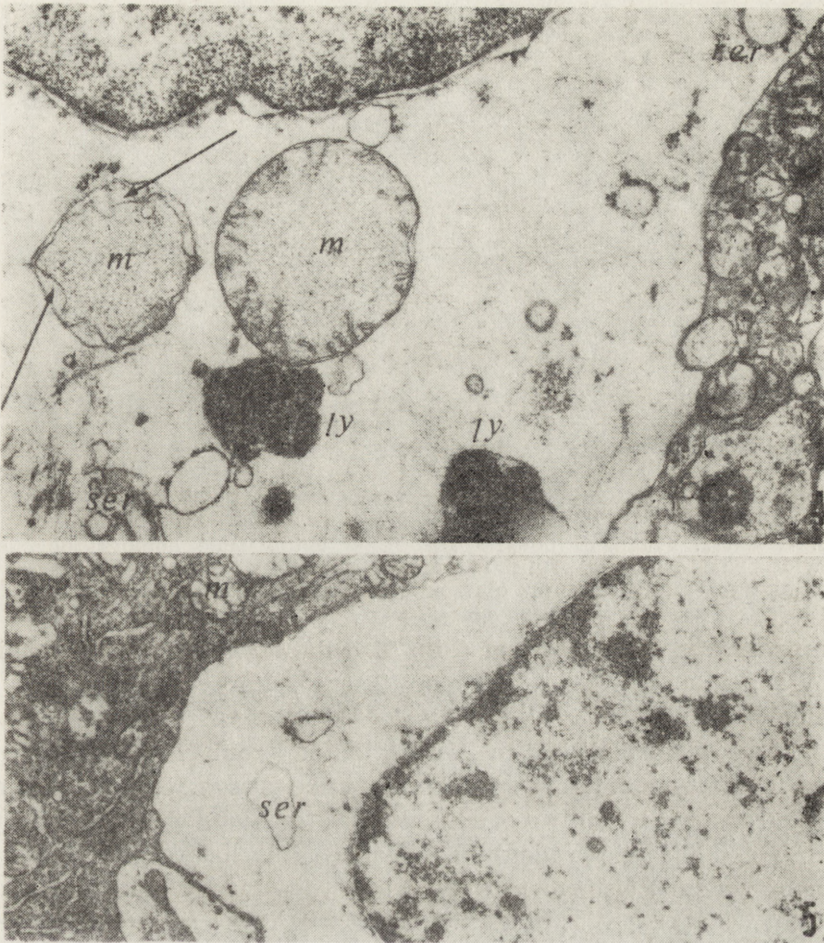
Fig. 4. Group I. Fragment of compact zone of substantia nigra. Astrocyte with greatly rarefied cytoplasm containing large mitochondria (m) with granular matrix and folded inner membrane (arrows), dense bodies (by) and widened cisternae of smooth (ser) and rough (rer) endoplasmic reticulum. × 12 500

Ryc. 4. Grupa I. Fragment zbitej warstwy istoty czarnej. Komórka astrogleju z cytoplazmą o małej gęstości elektronowej, w której widoczne są mitochondria z drobnoziarnistą macierzą (m) i sfałdowaną błoną wewnętrzną (strzałki), ciała gęste (ly), oraz szerokie zbiorniki szorstkiej (rer) i gładkiej (ser) siateczki śródplazmatycznej. Pow. 12 500 ×

Fig. 5. Group I. Fragment of motor cortex. Perineuronal satellite astrocyte with light cytoplasm containing wide cisterna of smooth endoplasmic reticulum (ser). Fragment of neuron with electron dense cytoplasm and swollen mitochondria. (m) × 7 500

Ryc. 5. Grupa I. Fragment kory ruchowej. Okołoneuronalny astrocyt satelitarny z cytoplazmą o małej gęstości elektronowej i z pojedynczym szerokim zbiornikiem gładkiej siateczki śródplazmatycznej (ser). Fragment komórki nerwowej z cytoplazmą o dużej gęstości elektronowej i obrzmiałymi mitochondriami (m). Pow. 7 500 ×

precapillaries had small, narrowed lumina. The capillary walls were ultrastructurally normal. In some of them there was a slight increase of pinocytotic vesicles. In some precapillaries thickening of the
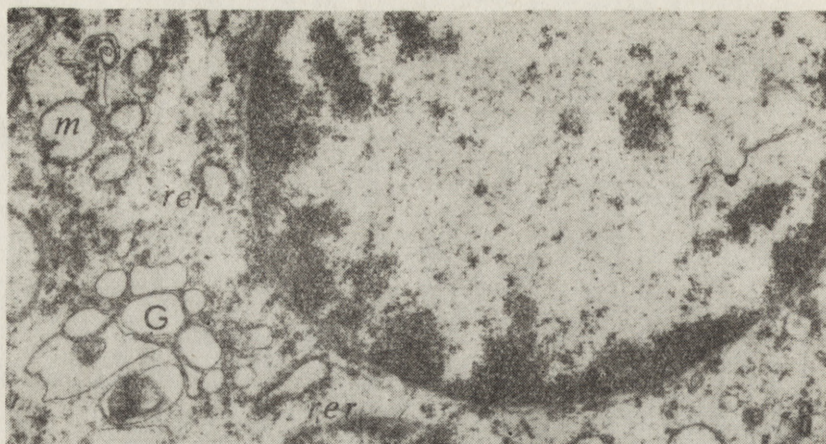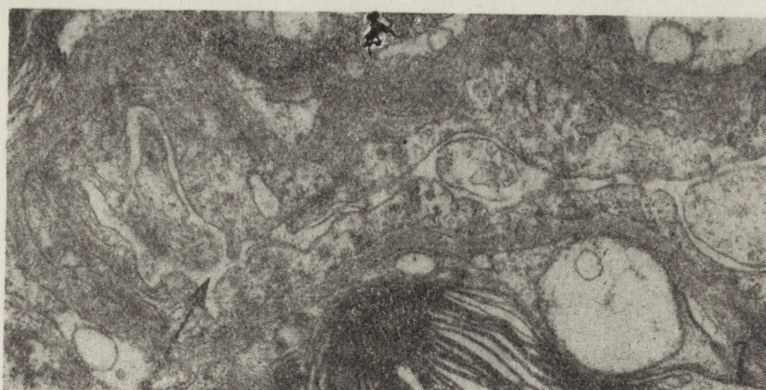
Fig. 6. Group I. Fragment of upper medulla. In the cytoplasm of oligodendrocyte distended cisternae of Golgi apparatus (G) and rough endoplasmic reticulum (rer) and swollen mitochondria (m) are visible. × 7 500

Ryc. 6. Grupa I. Fragment opuszki górnej. W cytoplazmie komórki oligodendrogleju widoczne szerokie zbiorniki układu Golgiego (G) i szorstkiej siateczki śródplazmatycznej (rer) oraz obrzmiałe mitochondria (m). Pow. 7 500 ×

basal membrane was observed (Fig. 7). Slight swelling of pericapillary astrocytic processes was a common feature. Intercellular spaces were unchanged.

Neuronal abnormalities in experimental group II were more intensive. Three types of nerve cell lesions were present. The most common were neurons with highly condensed cytoplasm and narrowed channels of rough endoplasmic reticulum. Against this background numerous groups of widened cisternae of Golgi apparatus and smooth endoplasmic reticulum were present. Mitochondria with light matrix and peripherally


Fig. 7. Group I. Fragment of upper medulla. Precapillary vessel with narrowed lumen (long arrow) and thickened basement membrane (short arrow). × 13 000

Ryc. 7. Grupa I. Fragment górnej opuszki. Naczynie przedwłosowate z wąskim światłem (długa strzałka) i pogrubiałą błoną podstawną (krótka strzałka). Pow. 13 000 ×
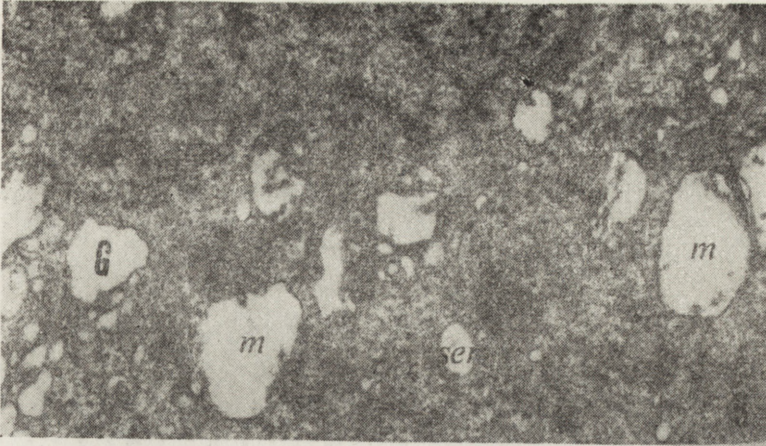
Fig. 8. Group II. Fragment of substantia nigra. In greatly condensed cytoplasm of nerve cell numerous swollen mitochondria (m), large cisternae of Golgi apparatus (G) and smooth endoplasmic reticulum (ser) are visible. Some narrow channels of rough endoplasmic reticulum (rer) are present. × 7 500

Ryc. 8. Grupa II. Fragment istoty czarnej. W cytoplazmie komórki nerwowej o dużej gęstości elektronowej widoczne obrzmiałe mitochondria (m), szerokie zbiorniki układu Golgiego (G) i gładkiej siateczki śródplazmatycznej (ser) i pojedyncze wąskie zbiorniki szorstkiej siateczki śródplazmatycznej (rer). Pow. 7 500 ×
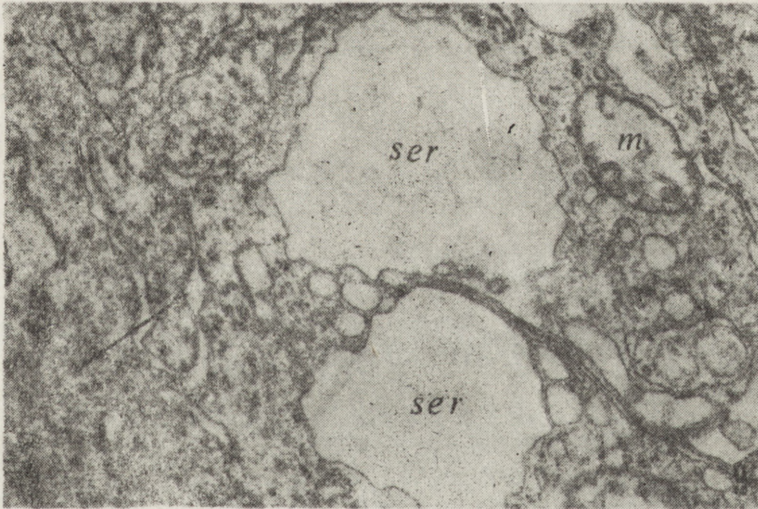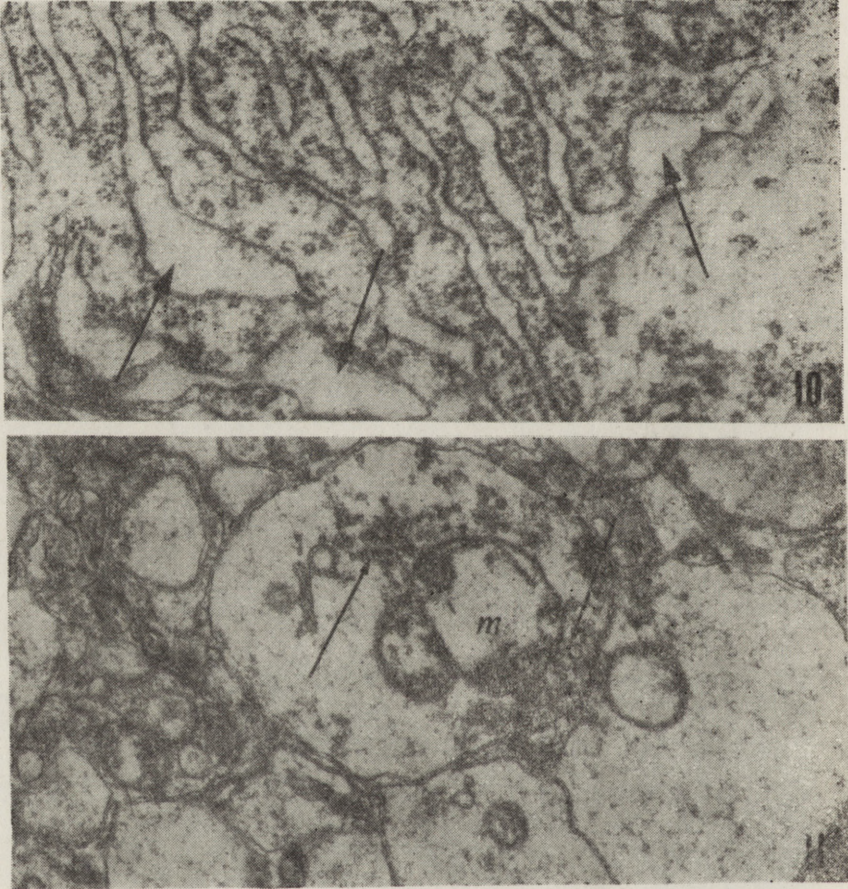

Fig. 9. Group II. Fragment of nerve cell from compact zone of substantia nigra. Vacuolization of smooth endoplasmic reticulum channels (ser), focal extension of rough endoplasmic reticulum channels (arrows) and swollen mitochondrion (m) are visible. × 15 500

Ryc. 9. Grupa II. Fragment komórki nerwowej zbitej warstwy istoty czarnej. Wakuolizacja zbiorników gładkiej siateczki śródplazmatycznej (ser), miejscowe poszerzenia zbiorników szorstkiej siateczki śródplazmatycznej (strzałki) i obrzmiałe mitochondrium (m.) Pow. 15 500 ×

displaced cristae were also enlarged (Fig. 8). Neurons with "dark" condensed cytoplasm and enlarged channels of rough endoplasmic reticulum were less common. The other neuronal abnormality consisted in a great

distension of the abundant cisternae of smooth endoplasmic reticulum, some of them forming large, irregular vacuolar structures, containing a small amount of light, floccular material (Fig. 9). Severe widening of channels of the rough endoplasmic reticulum was also a feature in these abnormal nerve cells (Fig. 10). A great number of axons, mostly those in substantia nigra and striatum were swollen and impoverished

Fig. 10. Group II. Fragment of nerve cell from compact zone of substantia nigra. Wide, focally extended channels and cisternae of rough endoplasmic reticulum (arrows). × 15 000

Ryc. 10. Grupa II. Fragment cytoplazmy komórki nerwowej zbitej warstwy istoty czarnej. Szerokie, miejscami rozdęte zbiorniki szorstkiej siateczki śródplazmatycznej (strzałki). Pow. 15 000 ×

Fig. 11. Froup II. Fragment of compact zone of substantia nigra. Axon terminal with light cytoplasm, containing aggregates of the synaptic vesicles (arrow) and swollen mitochondrion (m). Neighbouring dendrites with light swollen cytoplasm. × 15 000

Ryc. 11. Grupa II. Fragment zbitej warstwy istoty czarnej. Akson końcowy z cytoplazmą o małej gęstości elektronowej, z agregacją pęcherzyków synaptycznych (strzałki) i z obrzmiałym mitochondrium (m). Sąsiednie dendryty z jasną obrzmiałą cytoplazmą. Pow. 15 000 ×

in cytoplasmic organelles (Fig. 11). So were nerve endings, showing in addition an irregular distribution of synaptic vesicles and their abnormal aggregates (Fig. 11). Oligodendroglial alterations were of the same nature as in the previous group, although less intense. A great
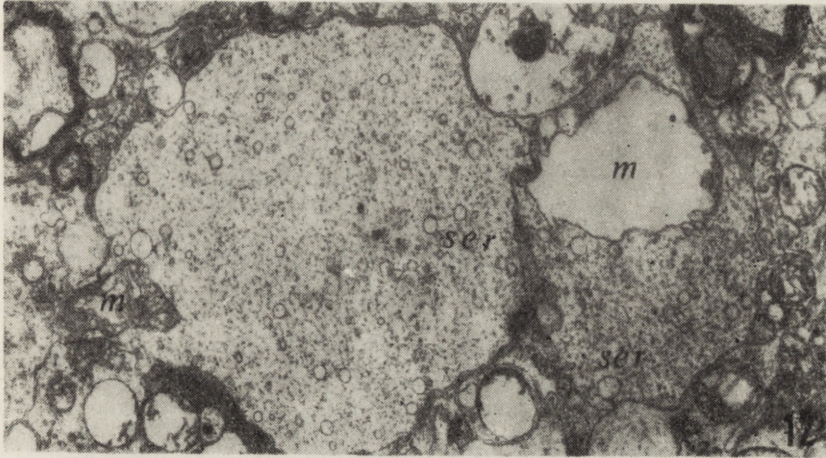
Fig. 12. Group II. Fragment of upper medulla. Astrocytic processes with swollen mitochondria (m), distended cisternae of smooth endoplasmic reticulum (ser) and abundant gliofilaments. × 7 000

Ryc. 12. Grupa II. Fragment górnej opuszki. Wypustki astrocytarne z obrzmiałymi mitochondriami (m), poszerzonymi zbiornikami gładkiej siateczki śródplazmatycznej (ser) i obfitymi gliofilamentami. Pow. 7 000 ×
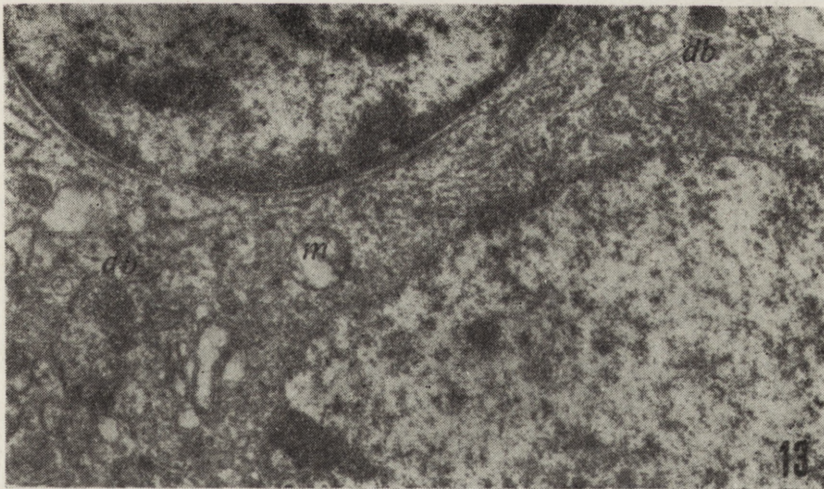
Fig. 13. Group III. Fragment of striatum. Neuron with some swollen mitochondria (m) and dense bodies (db). Unchanged satellite oligodendroglial cell. × 7 500

Ryc. 13. Grupa III. Fragment prążkowia. Komórka nerwowa z obrzmiałymi mitochondriami (m) i ciałami gęstymi (db) w cytoplazmie i niezmieniona komórka satelitarnego oligodendrogleju. Pow. 7 500 ×
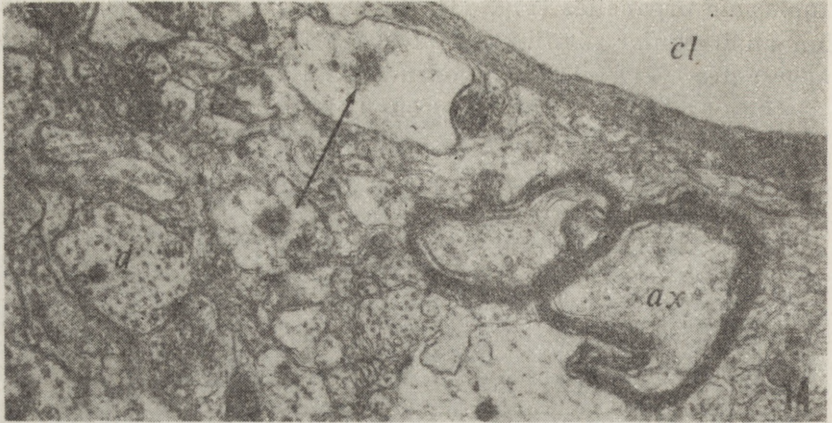
Fig. 14. Group III. Fragment of striatum. In the perivascular area terminal axon with light cytoplasm, containing an aggregate of the synaptic vesicles (arrow) is visible. Unchanged neuropil elements and capillary wall. cl — capillary lumen, ax — myelinated axon, d — dendrite. × 13 000

Ryc. 14. Grupa III. Fragment prążkowia. Fragment naczynia włosowatego z szerokim światłem (cl). W okolicy przynaczyniowej widoczne zakończenie aksonalne z cytoplazmą o małej gęstości elektronowej i agregacją pęcherzyków synaptycznych (strzałka). Niezmienione aksony (ax) i dendryty (d). Pow. 13 000 ×
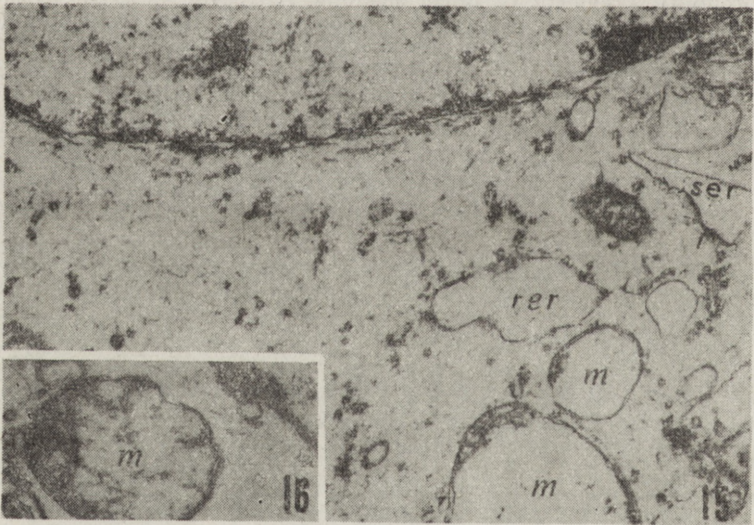
Fig. 15. Group III. Fragment of hippocampus. Astrocyte with light cytoplasm containing swollen mitochondria (m) and extended cisternae of rough (rer) and smooth (ser) endoplasmic reticulum. × 8 500

Ryc. 15. Grupa III. Fragment hipokampa. Komórka astrogleju z cytoplazmą o małej gęstości elektronowej, z szerokimi zbiornikami szorstkiej (rer) i gładkiej (ser) siateczki śródplazmatycznej i z obrzmiałymi mitochondriami (m). Pow. 8 500 ×

Fig. 16. Group III. Fragment of hippocampus. Swollen mitochondrion (m) from an astrocytic process with the cytoplasm of low electron density. × 11 000

Ryc. 16. Grupa III. Fragment hipokampa. Obrzmiałe mitochondrium (m) w wypustce astrogleju o małej gęstości elektronowej. Pow. 11 000 ×

Fig. 17. Group III. Fragment of compact zone of the substantia nigra. Precapillary vessel with a large lumen (vl). Perivascular astrocytic process (ast) with cytoplasm of low electron density, containing swollen mitochondrion (m) and remnants of a disintegrated mitochondrion (arrow). × 13 000

Ryc. 17. Grupa III. Fragment zbitej warstwy istoty czarnej. Naczynie przedwłosowate z szerokim światłem (vl). Przynaczyniowa wypustka astrogleju (ast) z cytoplazmą o małej gęstości elektronowej, z obrzmiałym mitochondrium (m) i z resztkami rozpadłego mitochondrium (strzałka). Pow. 13 000 ×

number of astrocytes showed remarkable swelling of cytoplasm. In some of their processes an increased amount of fibrils was present (Fig. 12).

In experimental group III the neuronal and oligodendroglial lesions were least advanced. In the majority of them both nuclei and cytoplasm were ultrastructurally normal (Fig. 13). The only persistent ultrastructural abnormality was mitochondrial swelling. However, in both substantia nigra and striatum numerous nerve endings with abnormally light cytoplasm and aggregation of synaptic vesicles were still present (Fig. 14). Astrocytic abnormalities dominated the electron microscopic picture of the grey structures examined. They consisted in cytoplasmic swelling, poor content of subcellular cytoplasmic structures, irregular, vacuolar distension of smooth and rough endoplasmic reticulum and abnormal mitochondria (Figs 15, 16). In the substantia nigra a great number of astrocytes contained an excess of gliofilaments. Perivascular astrocytic processes were either normal (Fig. 14) or greatly distended (Fig. 17). The structural components of capillary walls showed no abnormalities (Figs 14, 17).

DISCUSSION

Our previous studies on experimental manganese intoxication were strongly suggestive of the predominance of the lesions in the white matter over those involving the grey matter brain structures (Śmiałek, Mossakowski 1981; Mossakowski et al. 1982; 1983). As far as the neuropathology of the grey matter damages due to manganese intoxication is concerned, they were based exclusively on light microscopic observations. They contradicted most of the data known from the literature, concerning the subject, based also on light microscopic observations, according to which the leading feature of experimental manganese encephalopathy was severe involvement of grey matter structures (Chandra, Srivastava 1970; Chandra 1971; Singh et al. 1974). The only finding consistent with some literature data (Makarczenko 1956; Pentschew et al. 1963; Jonderko 1970) was severe damage of substantia nigra, in which progressive degeneration of nerve cells and their loss with subsequent fibrogliosis was present.

The present studies, concerning ultrastructural abnormalities of the grey brain structures induced by manganese intoxication confirmed in general our previous observations, although the grey matter lesions were more generalized and severe than seen in light microscopy.

The pathological process involved all cellular elements of the grey matter: neurons with their processes and endings, oligodendrocytes and astroglia. Brain capillaries were least changed. The general pattern of electron microscopic alterations was similar in all the examined structures and in all experimental groups. However, there existed also some essential differences between them which permitted to speculate both on the topographic selectivity of lesions and on the dynamics of the pathological process and its time sequences.

Despite of the above mentioned similarity of pathological changes there were two structures of the brain in which the tissue alterations were more severe, generalized and persistent. These were substantia nigra and striatum. In the former both neuronal, synaptic and glial abnormalities were most generalized and severe and they evolved to neuronal disintegration with their subsequent replacement by astrocytes with a distinct increase of gliofilaments content. This could be considered as electron microscopic equivalent of neuronal loss and fibrogliosis seen in light microscopy (Śmiałek, Mossakowski 1981). The most noticeable and persistent ultrastructural abnormalities in the striatum consisted in degeneration of nerve endings, with less obvious neuronal damage. This selective involvement of nigral neurons and their synaptic system corresponded well with observations concerning the noxious effects of manganese on the dopaminergic system (Neff et al. 1969; Mustafa, Chandra 1971; Chandra, Shukla 1981; Hietanen et al. 1981).

In other brain structures, most tissue abnormalities seemed to be reversible, as indicated by the fact that neuronal and oligodendroglial changes, being most advanced and generalized in the second experimental group, i.e. in animals surviving one week after the end of intoxication, almost completely disappeared in the last experimental group. It has to be proven to what extent this reversibility of changes (if real) may be connected with the reduction of the tissue content of the toxic agent after exposure to it has been ceased, as postulated by Hietanen et al. (1981). Two factors may be involved in the normalization of the electron microscopic picture of most grey structures, observed in the last experimental group. The first is a real reversibility of cellular changes. Such a situation has been noticed in many other lesions to nerve and glial cells under experimental conditions. The second one is total disintegration and disappearance of irreversibly damaged cells. This is usually accompanied by either the presence of cellular residua or appearance of glial replacement with gliofilaments proliferation. Both these factors can also operate together. This seems more probable, as some of the observed neuronal changes have been proven to be irreversible (Brierley et al. 1973; Garcia et al. 1978).

The astrocytic abnormalities were most persistent. They were still present in the last experimental group, while at that time neuronal and oligodendroglial alterations were practically absent in most of the brain areas, except substantia nigra. However, a distinct evolution of astrocytic changes was seen. In the two earlier experimental groups they consisted in remarkable cytoplasmic swelling of perikarya and processes, while in the latest group this was replaced in most instances by gliofilaments proliferation. The same time sequences were noticed in the white matter under identical experimental conditions (Mossakowski et al. 1982; 1983).

The most striking abnormality in all cellular compartments of the grey matter consisted in severe damage to mitochondria. The high affinity of the metal to these cytoplasmic organelles is very well known (Cotzias 1958; Autissier 1974). Ultrastructural mitochondrial lesions were consistent with biochemical and histochemical data, indicating severe impairment of the activity of mitochondrial enzymes in experimental manganese encephalopathy (Chandra 1972; Seth, Husain 1974; Singh et al. 1974; Sitaramaya et al. 1974; Hietanen et al. 1981). The question of the molecular mechanism of mitochondrial damage remains open. Perhaps it is connected with the membrane stabilizing function of manganese (Aston 1980) or its role as enzymatic cofactor (Leach, Lilburn 1978). The damaging effect of the metal on mitochondrial calcium transport has also to be taken into consideration (Leach, Lilburn 1978). Unanswered is also the problem of the greater sensitivity to its damaging action of astrocytic and axonal mitochondria as compared with that of mitochon-

dria in the neuronal perikarya and oligodendrocytes (Mossakowski et al. 1982; 1983). Nevertheless it seems plausible to consider that primary mitochondrial structural lesions with their metabolic consequences may be responsible for the changes involving other subcellular elements, observed in our material.

Basing on our present and previous observations (Śmiałek, Mossakowski 1981; Mossakowski et al. 1982; 1983) it is justified to state that subchronic intoxication with manganese chloride, applied intravenously, can result in toxic encephalopathy, dominated by involvement of the white matter, revealing characteristic light- and electron-microscopic alterations with a relatively slight, reversible and mostly selective damage to the grey matter structures. The discrepancy of our observations with other descriptions, stressing predominance of grey matter damage remains unanswered. Perhaps it may be connected with the kind of manganese compound used, its dosage, duration of intoxication and species-dependent animal differences. Comparison of the electron-microscopic alterations is also necessary. To our knowledge all morphological studies on experimental manganese encephalopathy have been carried out hitherto at the light-microscopic level.

USZKODZENIA ULTRASTRUKTURALNE ISTOTY SZAREJ MÓZGU W DOŚWIADCZALNYM ZATRUCIU MANGANEM

Streszczenie

Przedstawiono wyniki mikroskopowo-elektronowych badań istoty szarej mózgu w doświadczalnym zatruciu chlorkiem manganowym. Zwierzęta doświadczalne otrzymywały dożylnie roztwór chlorku manganowego w łącznej dawce 240 mg Mn^{++}/kg masy ciała, rozdzielonej na 7 porcji podanych w okresie 4 tygodni. Zwierzęta zabijano w grupach po upływie 24 godz., 7 i 28 dni po zakończeniu zatruwania.

Stwierdzono, że w badanych strukturach ośrodkowego układu nerwowego występowały umiarkowane uszkodzenia wszystkich elementów komórkowych tkanki. Uszkodzenia komórek nerwowych najsilniejsze po upływie 7 dni od zakończenia zatruwania, cofały się w dalszym okresie obserwacji (z wyjątkiem istoty czarnej i prążkowia, w których wykazywały dalszą progresję). Podobnie zachowywały się nieprawidłowości oligodendrogleju, dotyczące głównie okołoneuronalnych komórek satelitarnych. Uszkodzenia astrocytów utrzymywały się we wszystkich grupach doświadczalnych, w ostatniej wyrażały się one postępującą hiperplazją elementów filamentarnych. We wszystkich strukturach przeważały nieprawidłowości mitochondrialne.

Autorzy podkreślają, że w przeciwieństwie do większości danych z piśmiennictwa, w zastosowanym modelu doświadczalnej encefalopatii manganowej, przeważają uszkodzenia istoty białej. Zmiany w istocie szarej są mniej nasilone i mają charakter w większości odwracalny. Wybiórcze uszkodzenia istoty czarnej i prążkowia stanowią morfologiczny wykładnik upośledzenia układu dopaminergicznego przez mangan. Wiodące uszkodzenia mitochondriów wiążą się z powinowactwem manganu do tych właśnie struktur subkomórkowych, występującym zarówno w warunkach prawidłowych, jak i w stanach chorobowych.

УЛЬТРАСТРУКТУРНЫЕ ПОВРЕЖДЕНИЯ СЕРОГО ВЕЩЕСТВА ГОЛОВНОГО МОЗГА В ЭКСПЕРИМЕНТАЛЬНОМ ОТРАВЛЕНИИ МАРГАНЦОМ

Резюме

Представлены результаты электронно-микроскопических исследований серого вещества головного мозга в экспериментальном отравлении хлористым марганцом. Экспериментальные животные получали внутренно раствор хлористого марганца в общей дозе 240 мг Mn^{++}/кг массы тела, разделенной на 7 порций вводимых в течение 4 недель. Животных убивали в группах по истечении 24 часов, 7 и 28 дней после окончания отравления.

Констатировано, что в исследуемых строениях центральной нервной системы выступали умеренные повреждения всех клеточных элементов ткани. Повреждения нервных клеток, самые сильные по истечении 7 дней от окончания отравления, отступали в дальнейшем периоде наблюдения, за исключением черного вещества и стриатума, в которых они проявляли дальнейшую прогрессию. Подобным образом вели себя неправильности олигодендроглии, относящиеся главным образом к околонейрональным сателлитарным клеткам. Повреждения астроцитов удерживались во всех экспериментальных группах, в последней они выражались в прогрессирующей гиперплазии филаментарных элементов. Во всех строениях преобладали митохондриальные неправильности.

Авторы подчеркивают, что в противоположность большинству данных из литературы в примененной экспериментальной модели марганцевой энцефалопатии преобладают повреждения белого вещества. Изменения в сером веществе менее интенсивны и имеют в большинстве обратимый характер. Селективные повреждения черного вещества и стриатума составляют морфологический показатель ослабления дофаминэргической системы марганцом. Ведущие повреждения митохондрий авторы связывают со сродством марганца к тем именно субклеточным строениям, выступающим как в нормальных условиях, так и в патологических состояниях.

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