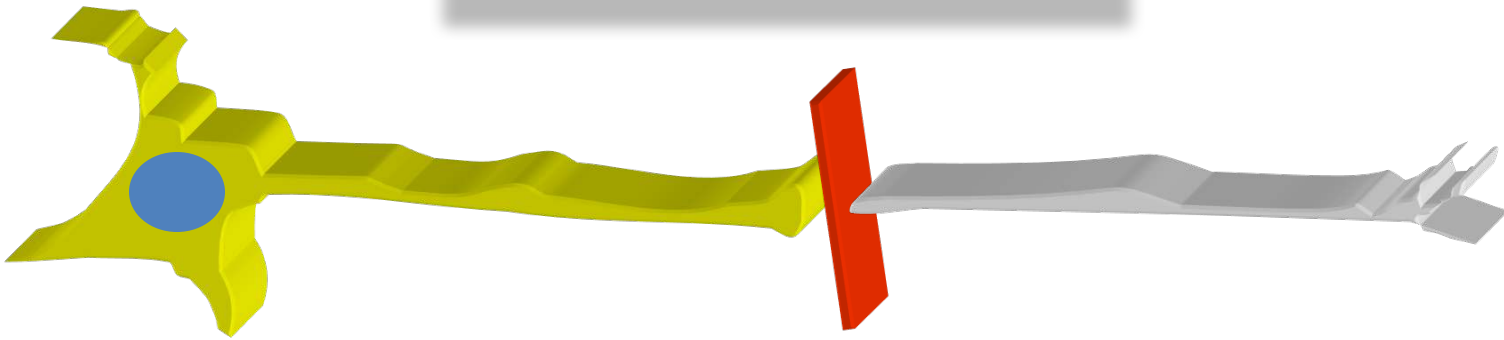


BASICS OF NEUROBIOLOGY

NEURODEGENERATION

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VULNERABILITY OF THE NERVOUS SYSTEM

AFTER COMPLETION OF THE DEVELOPMENT OF THE BRAIN, THE BASIC NEURONAL NETWORKS SERVING BRAIN FUNCTIONS GET ESTABLISHED

THE CONNECTIONS FORMED AMONG NEURONAL ASSEMBLIES MAINTAIN A REMARKABLE FUNCTION-DEPENDENT PLASTICITY AND THE ABILITY OF STRUCTURAL AND FUNCTIONAL REMODELING

IN THE MATURE BRAIN, NEURONS DO NOT DIVIDE ANYMORE, THEREFORE, THE ORIGINAL NEURON SETUP SERVES FOR LIFE SPAN

FROM STEM CELLS, HOWEVER, A LIMITED SUPPLY OF CERTAIN NEURON TYPES OCCURS IN THE CNS

THE COMPLEX ARCHITECTURE, THE CHARACTERISTIC NETWORKING, THE HIGH METABOLIC NEEDS AND THE LACK OF A SUBSTANTIAL REGENERATIVE SUPPLY OF NEURONS MAKE THE BRAIN EXTREMELY VULNERABLE

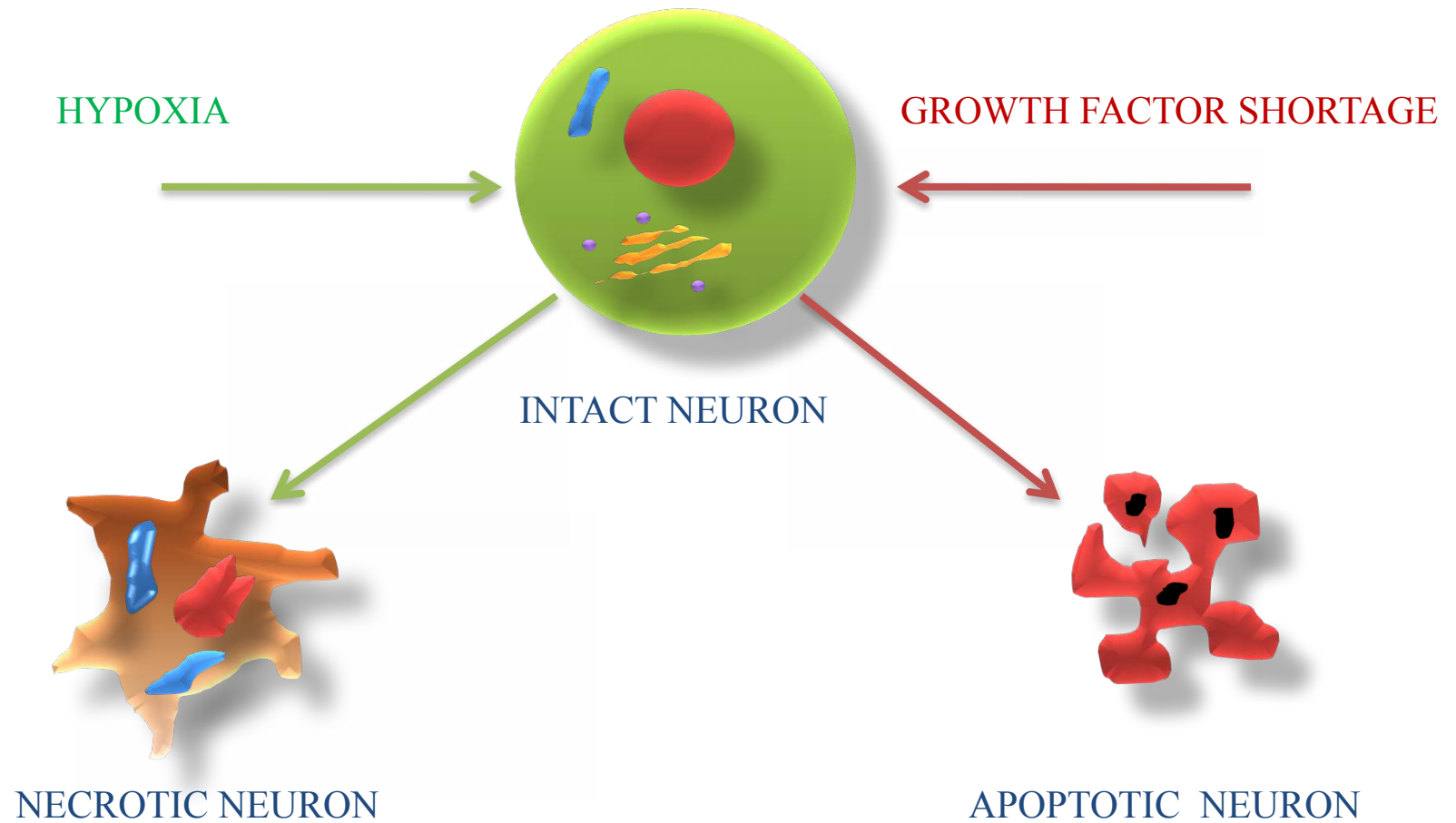
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CAUSES OF NEURAL TISSUE DAMAGE

- GENETIC MUTATIONS: TRINUCLEOTIDE (CAG) REPEAT EXPANSION DISORDERS (HUNTINGTON'S DISEASE)
- TRAUMATIC BRAIN INJURY: HEMORRHAGIC CONTUSIONS
- TUMOR: MALIGNANT AND BENIGNANT CELL PROLIFERATIONS
- INFECTION: INFLAMMATION CAUSED BY BACTERIA AND VIRUSES (ENCEPHALITIS)
- OXIDATIVE STRESS: SUPEROXIDE RADICAL, HYDROGEN PEROXIDE
- CHEMICAL DAMAGE: ALCOHOL, DRUG ABUSE, ORGANIC SOLVENTS
- ISCHEMIA: RESTRICTION IN BLOOD SUPPLY (ARTERIOSCLEROSIS)
- HYPOXIA: SHORTAGE IN OXYGEN SUPPLY
- AGING: STRUCTURAL AND NEUROCHEMICAL PROPERTIES OF NEURONS CHANGE

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NECROTIC AND APOPTOTIC DEGENERATION OF NEURONS



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APOPTOTIC DEATH OF NEURONS

NEURONS UNDERGOING APOPTOSIS SHOW A CHARACTERISTIC MORPHOLOGY:

CELL SHRINKAGE AND ROUNDING DUE TO THE BREAKDOWN OF THE CYTOSKELETON BY CASPASES

THE CYTOPLASM APPEARS DENSE, THE ORGANELLES APPEAR TIGHTLY PACKED

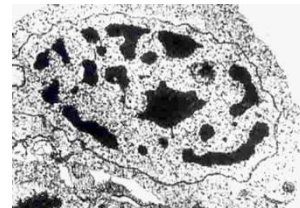
CHROMATIN UNDERGOES CONDENSATION INTO COMPACT PATCHES AGAINST THE NUCLEAR ENVELOPE. PYKNOSIS, A HALLMARK OF APOPTOSIS

THE NUCLEAR ENVELOPE BECOMES DISCONTINUOUS AND THE DNA FRAGMENTED

THE CELL MEMBRANE SHOWS IRREGULAR BUDS KNOWN AS BLEBS

THE CELL BREAKS APART INTO SEVERAL VESICLES CALLED APOPTOTIC BODIES WHICH BECOME PHAGOCYTOSED

PYCNOTIC NUCLEUS IN AN APOPTOTIC CELL



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NECROSIS OF NEURONS

NEURONS UNDERGOING NECROSIS SHOW SPECIFIC MORPHOLOGICAL SIGNS:

INCREASED ACIDOPHILIC STAINING IN LM PREPARATIONS

INCREASED AND INTENSE ARGYROPHILIA

MAJOR DARKENING AND SHRINKAGE OF THE NUCLEUS AND CYTOPLASM

PLASMA MEMBRANE AND THE NUCLEAR MEMBRANE BECOME IRREGULAR

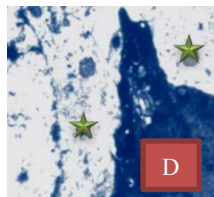
THE CYTOPLASM GENERALLY CONTAINS MANY LARGE VACUOLES

SWOLLEN MITOCHONDRIA WITH DISRUPTED CRISTAE

PLENTY AUTOPHAGIC VACUOLES

INCREASED ASTROCYTE AND MICROGLIA ACTIVITY IN THE VICINITY

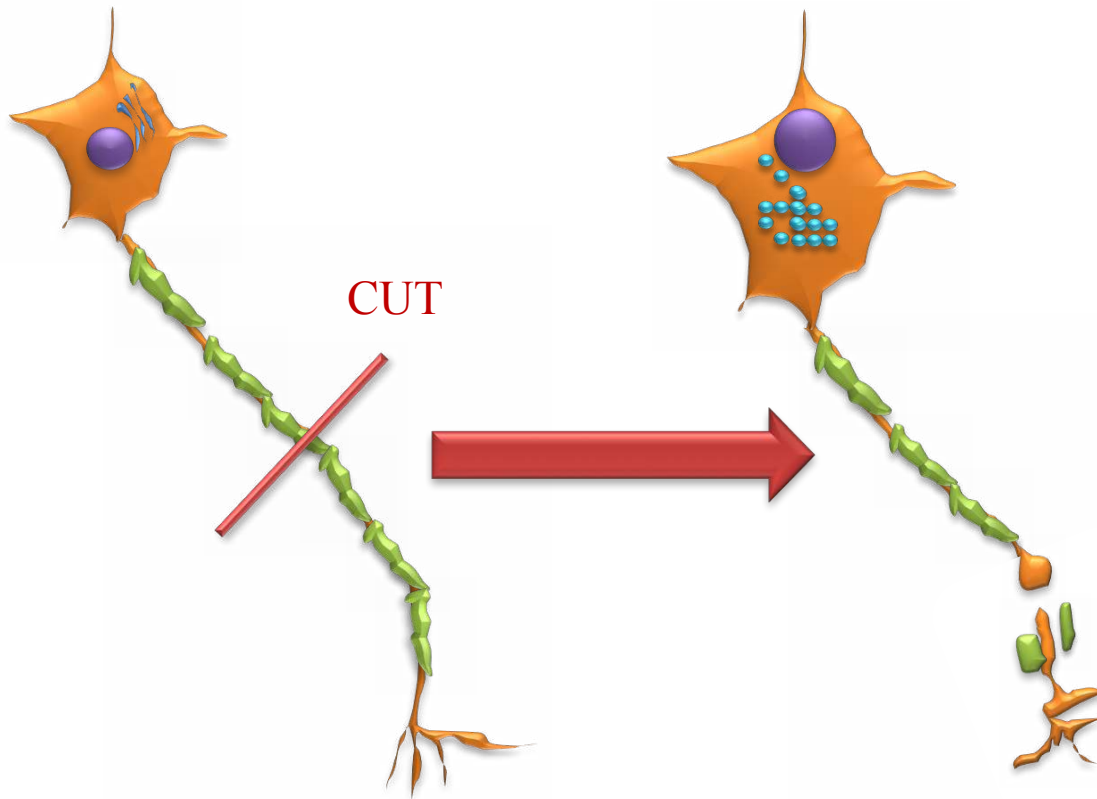
THE NEURONS FALL APART AND GET PHAGOCYTOSED



DEGENERATING, NECROTIC NEURON (D) SHOWS HIGH ELECTRON DENSITY IN THE VICINITY OF NORMAL NEURONS (STARS)

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WALLERIAN DEGENERATION OF NEURONS AFTER AXON TRANSECTION



MAIN FEATURES:

EXCENTRIC NUCLEUS

ENLARGED PERIKARYON

CHROMATOLYSIS

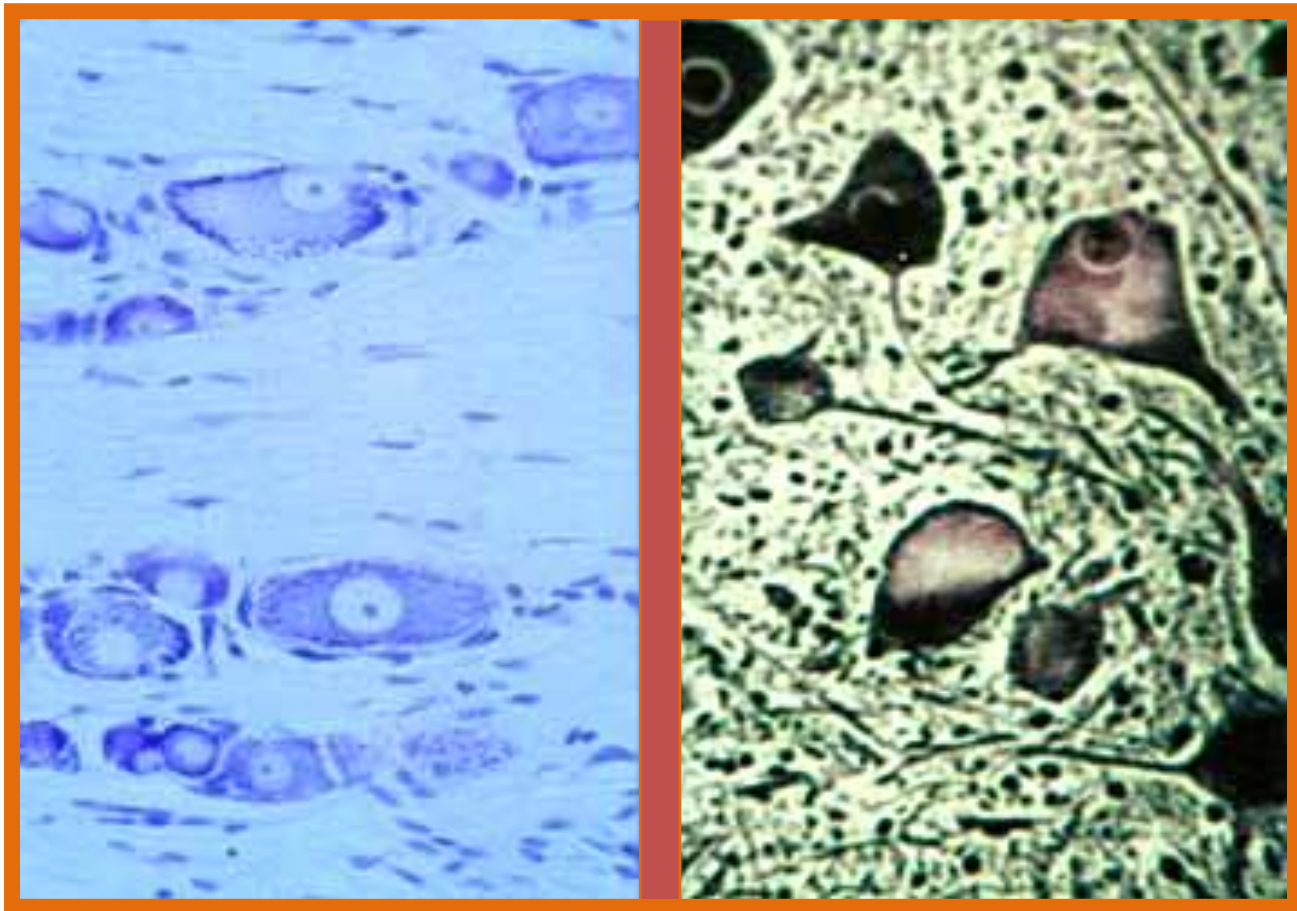
DISTAL AXON STUMP DEATH

BREAKDOWN OF MYELIN

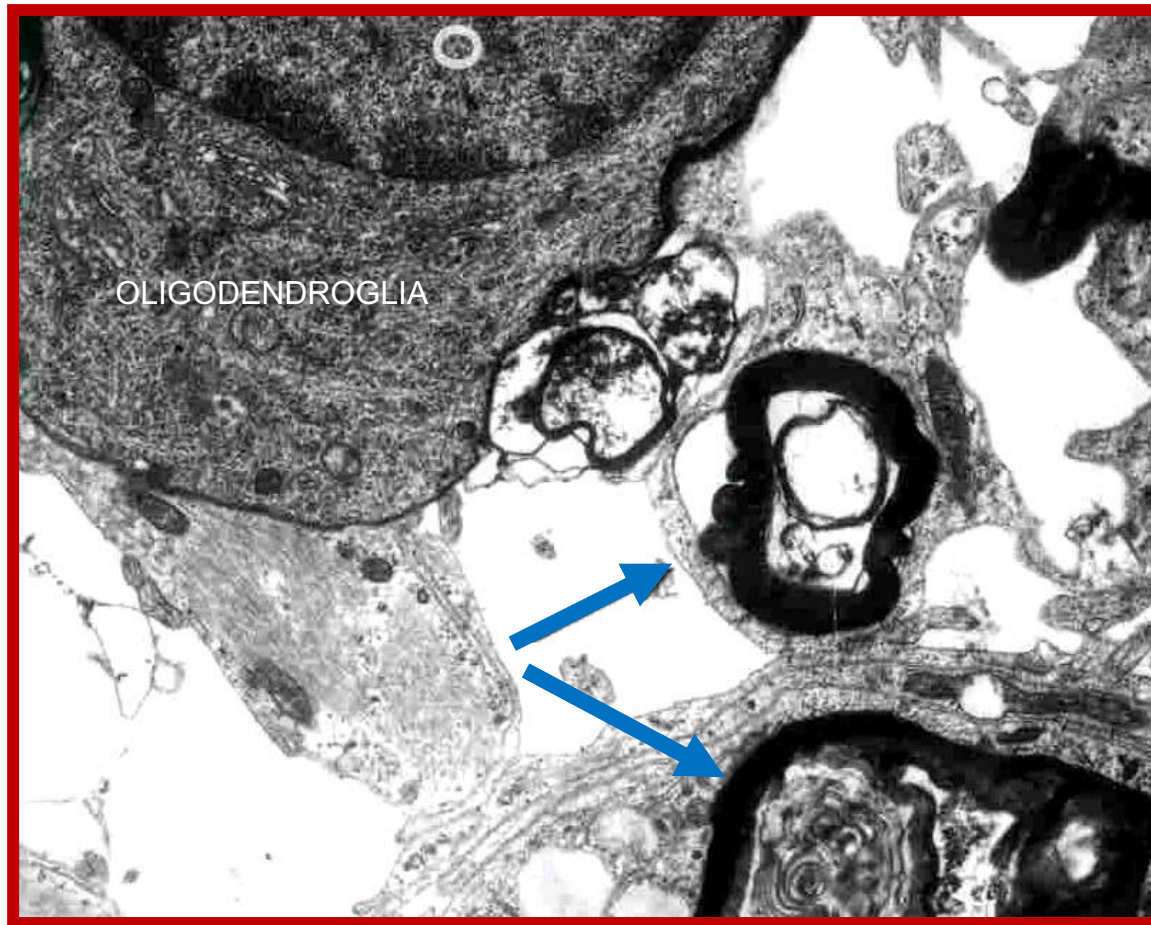
MICROGLIA INFILTRATION

OCCURS IN CNS AND PNS

Chromatolysis

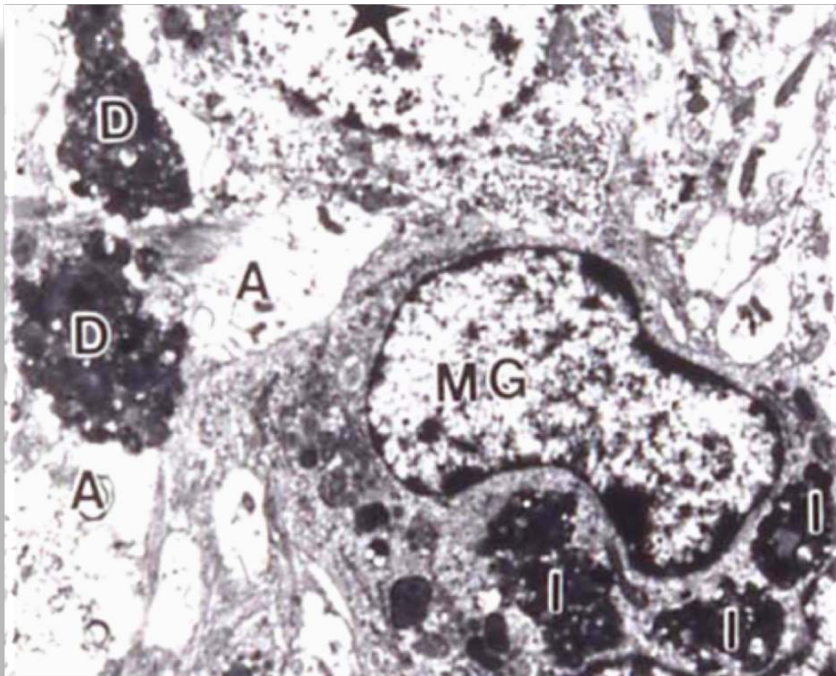


BREAKDOWN OF MYELIN



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DEGENERATING GRANULE CELLS IN THE HIPPOCAMPUS



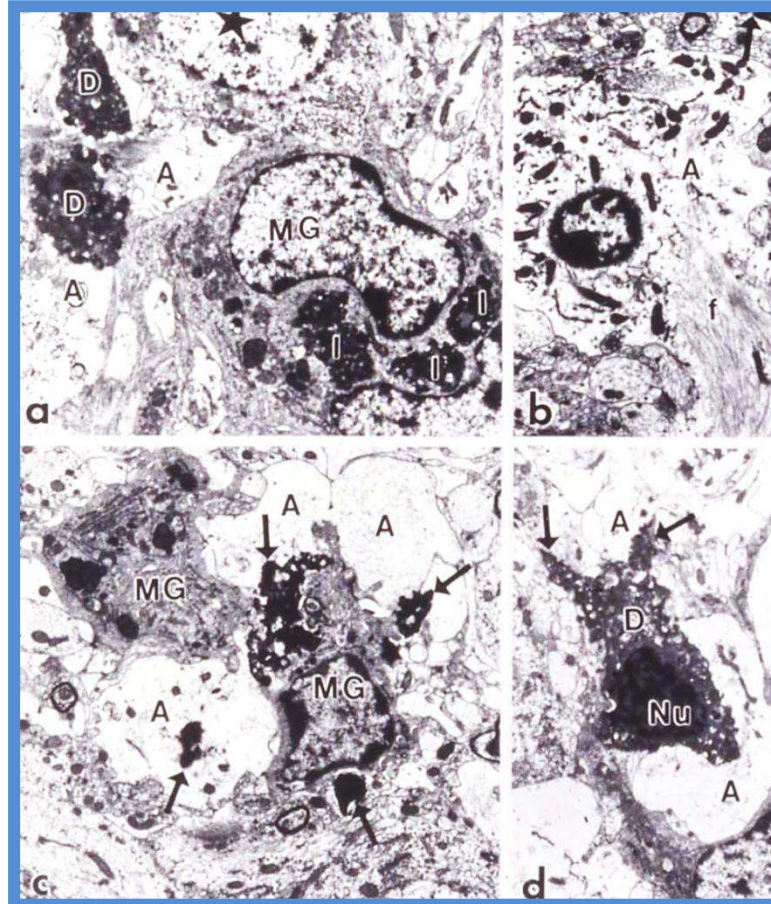
CORTICOSTERONE DEPRIVATION EVOKES GRANULE CELL DEGENERATION IN THE HIPPOCAMPUS

DARK BODIES OF DEGENERATING CELLS ARE VISIBLE (D)

HYPERTROPHIC ASTROCYTE PROCESSES ARE NUMEROUS IN THE FIELD (A)

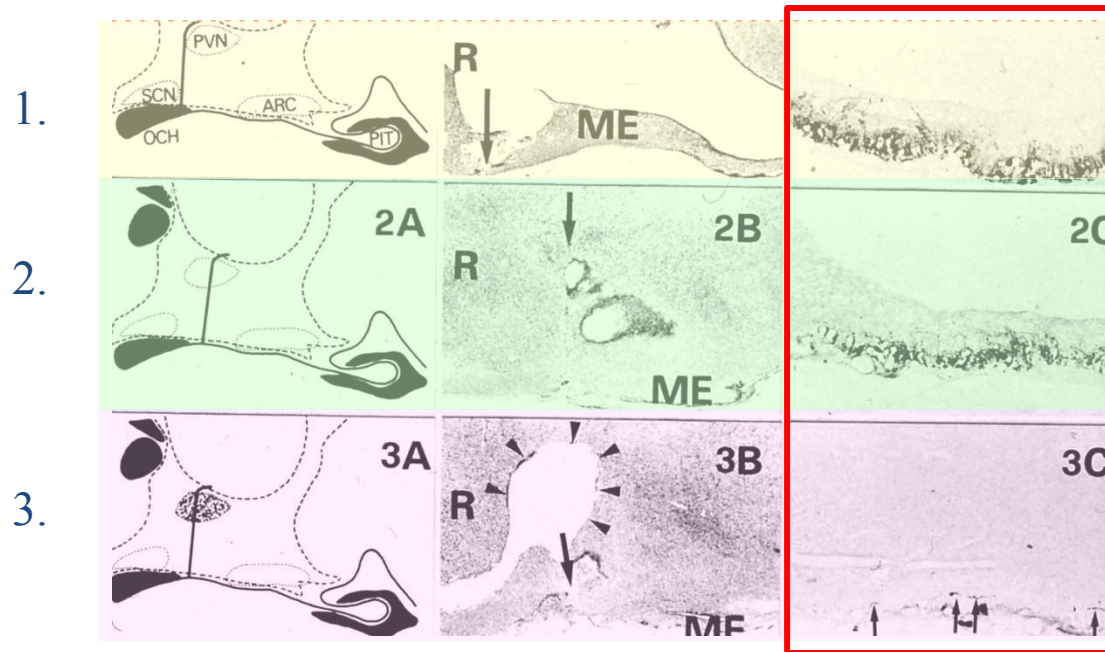
MICROGLIA (MG) IS IN THE VICINITY OF DETERIORATING NEURONS WITH ENGULFED NECROTIC PARTS OF THE CELLS (I)

ACTIVATION OF MICROGLIA AND ASTROCYTES



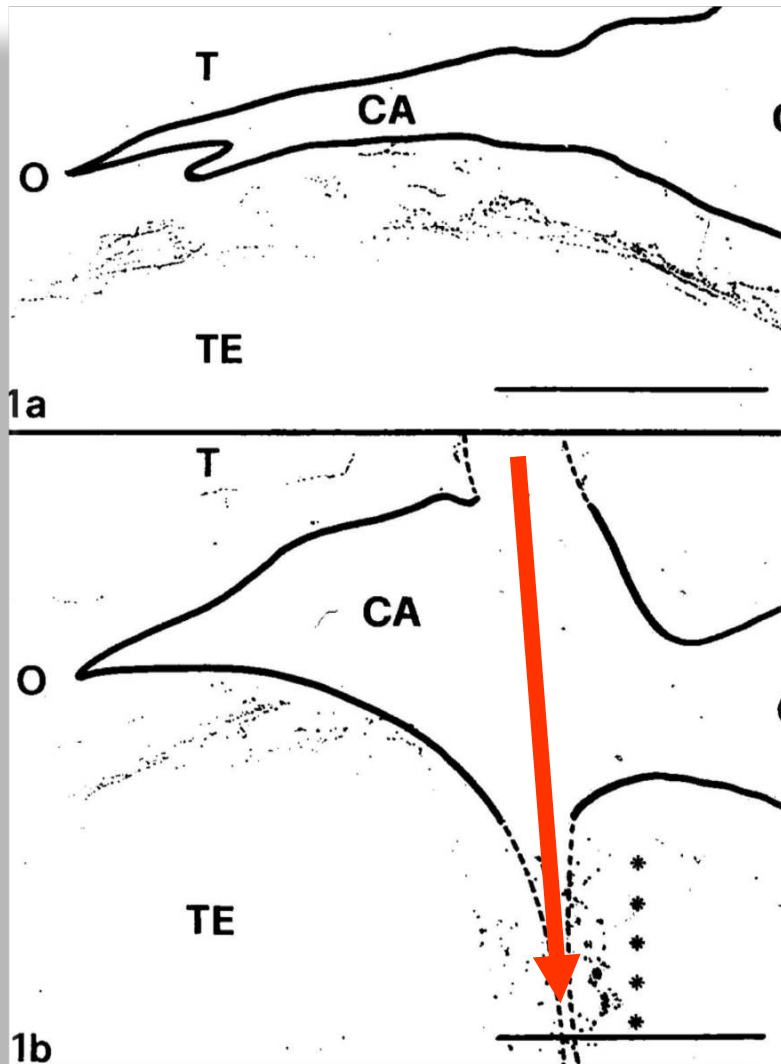
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EXPERIMENTAL USE OF AXOTOMY FOR DETECTION OF NEURONAL PATHS



1. LESION PLACED IN FRONT OF THE PARAVENTRICULAR NUCLEUS (PVN) HAS NO EFFECT ON CRH AXON IMMUNOREACTIVITY IN THE MEDIAN EMINENCE (ME)
2. PARTIAL DESTRUCTION OF THE PVN RESULTS IN THE DECREASE OF CRH AXON IMMUNOREACTIVITY IN THE MEDIAN EMINENCE
3. TOTAL ABOLISHMENT OF THE PVN EMPTIES THE CRH CONTENT OF THE MEDIAN EMINENCE DUE TO DEGENERATION OF CRH AXONS

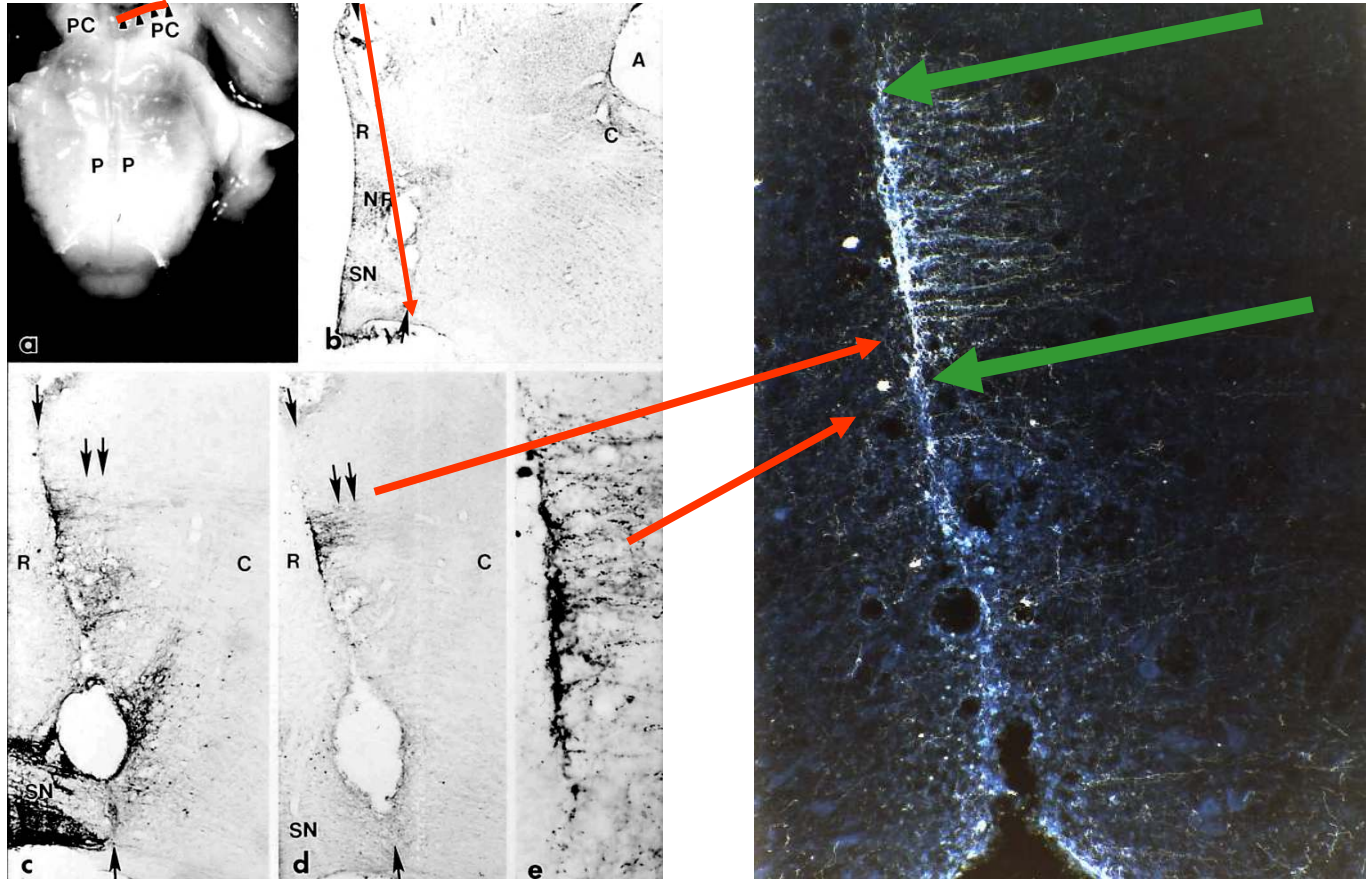
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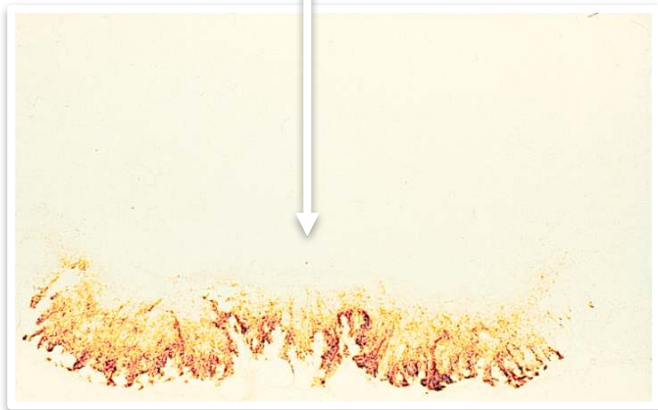
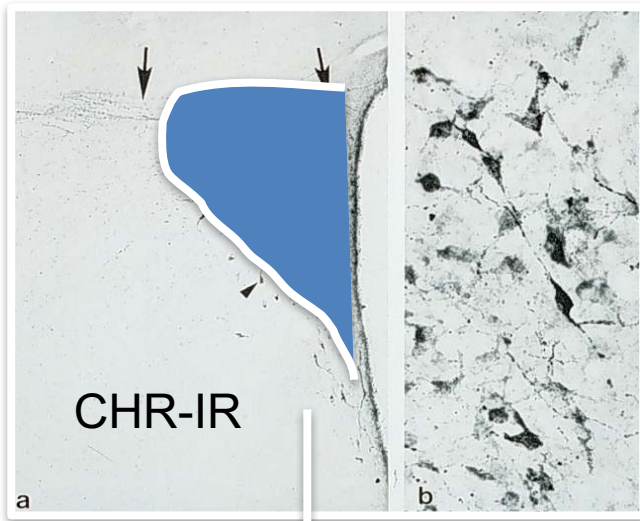
TRANSECTION OF DESCENDING
GnRH-IMMUNOREACTIVE
TRACT IN THE MIDBRAIN

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SURGICAL TRANSECTION OF THE ASCENDING ADRENERGIC BUNDLE



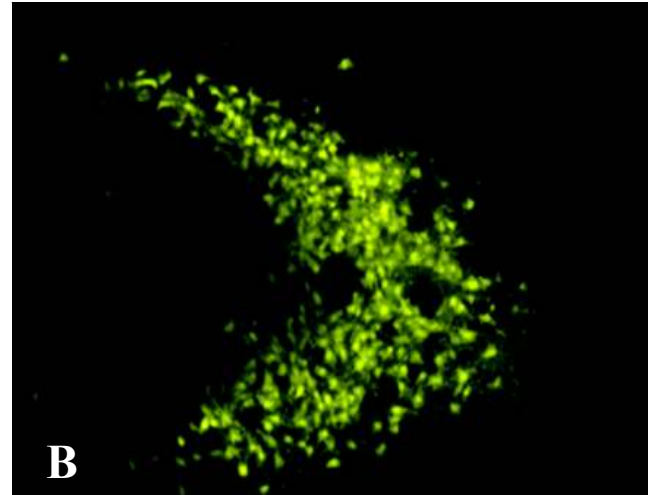
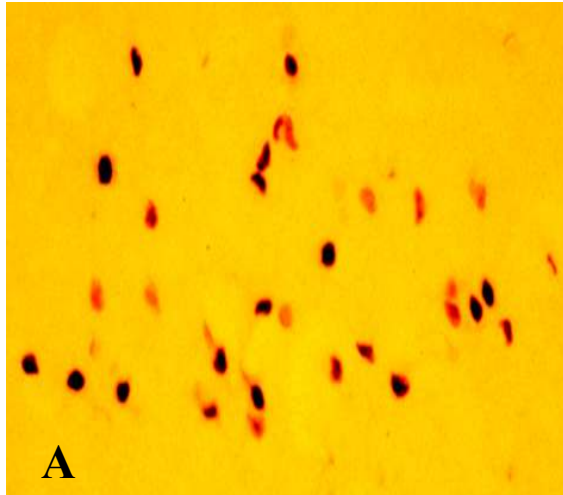
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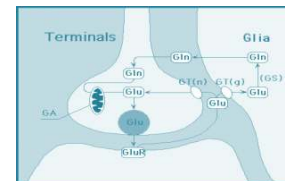
LESION OF THE PVN

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CHEMICAL LESIONING OF THE BRAIN

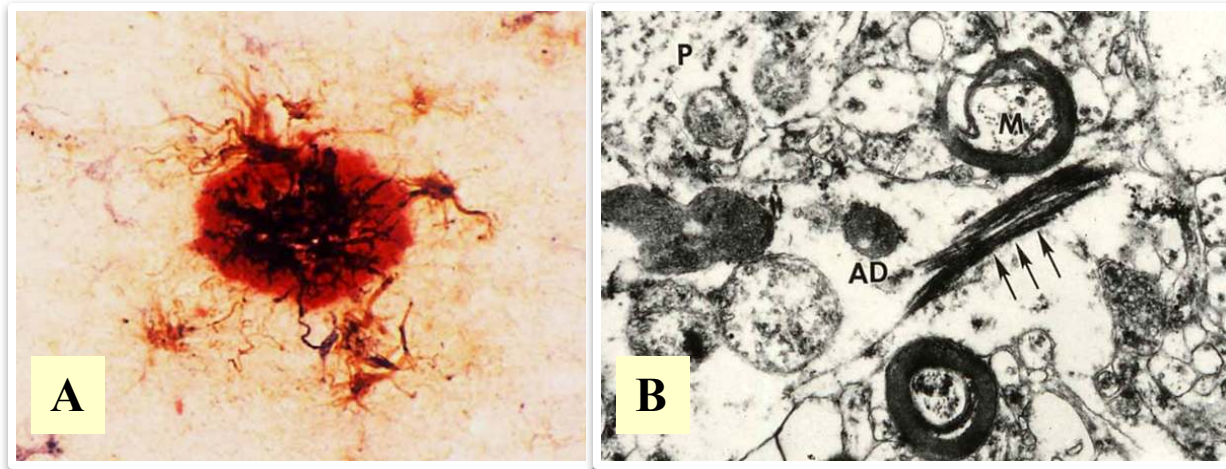


1. ADMINISTRATION OF THE EXCITATORY KAINIC ACID TO MICE AT A 40 mg/kg DOSE EVOKES c-FOS ACTIVATION (A) IN NEURONS OF THE CA3 SECTOR OF THE HIPPOCAMPUS
2. USING THE FLUORO-JADE STAINING FOR VISUALIZATION OF DEGENERATING PROFILES REVEALS AN INTENSE CELL DEATH OF PYRAMIDAL NEURONS IN THE CA3 REGION OF THE HIPPOCAMPUS
3. THE DEGENERATION IS DUE TO THE KAINIC ACID EVOKED EPILEPTIC SEIZURES THAT BADLY DAMAGE HIPPOCAMPAL PYRAMIDAL CELLS



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NEUROPATHOLOGY OF ALZHEIMER DISEASE



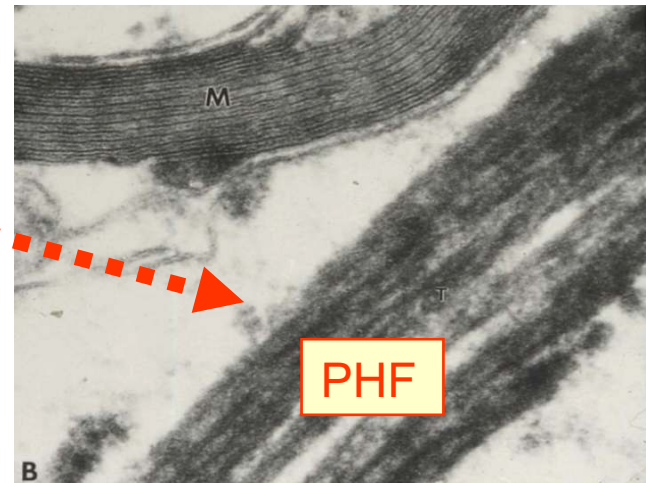
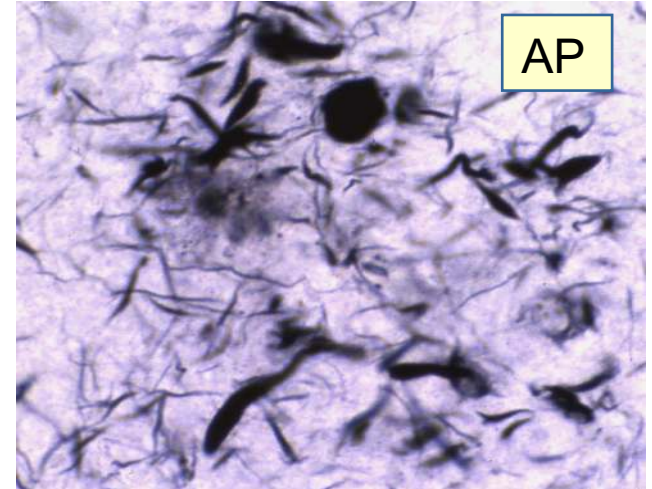
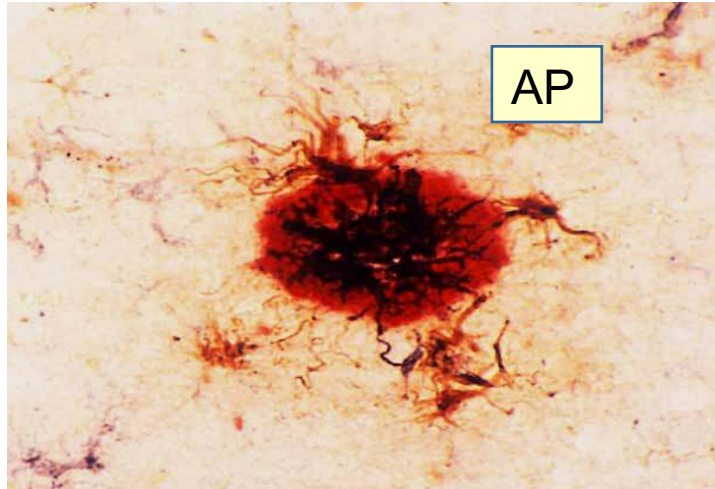
ALZHEIMER DISEASE IS A SEVERE ILLNESS CHARACTERIZED BY NEURONAL DEGENERATION AND GRADUAL DECLINE OF COGNITIVE FUNCTIONS. IT MAY LEAD TO DEMENTIA

SEVERAL CAUSES HAVE BEEN IMPLICATED IN THE PATHOGENESIS OF THE DISEASE: ACETYLCHOLINE, BETA-AMYLOD, TAU AND PRION HYPOTHESES

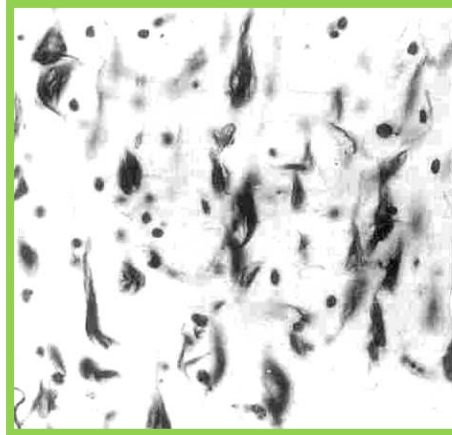
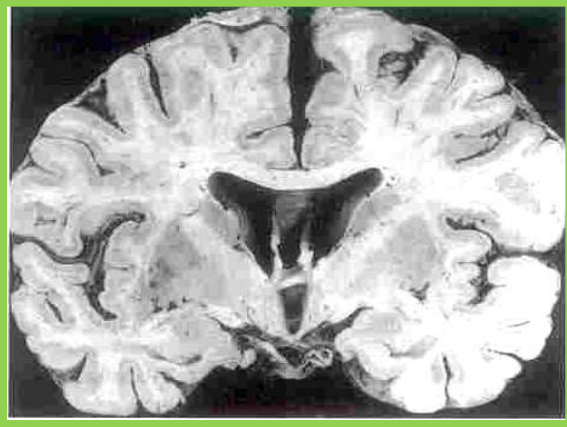
THE FORMATION OF AMYLOD PLAQUES IN THE NERVOUS TISSUE (A) AND THE PRESENCE OF NEUROFIBRILLARY TANGLES (B) IN DEGENERATING NEURONS ARE CHARACTERISTIC NEUROPATHOLOGICAL FEATURES

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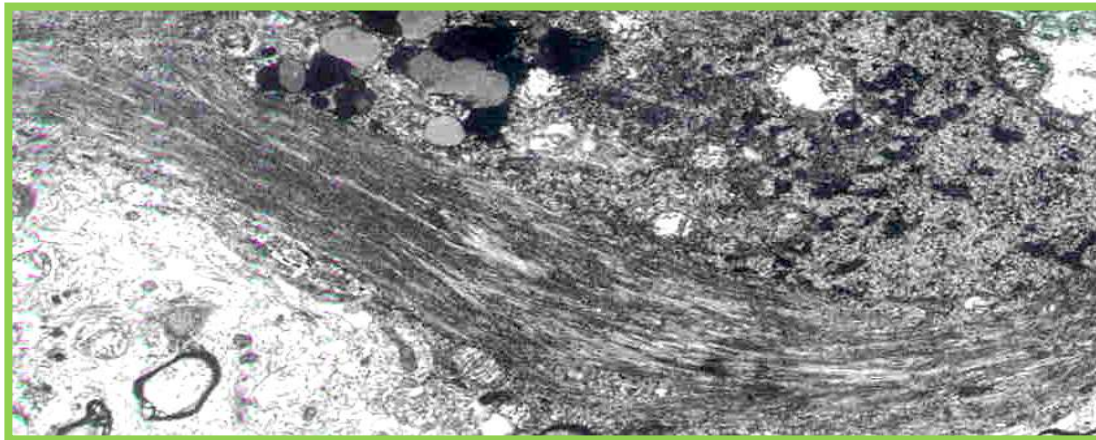
ALZHEIMER DISEASE



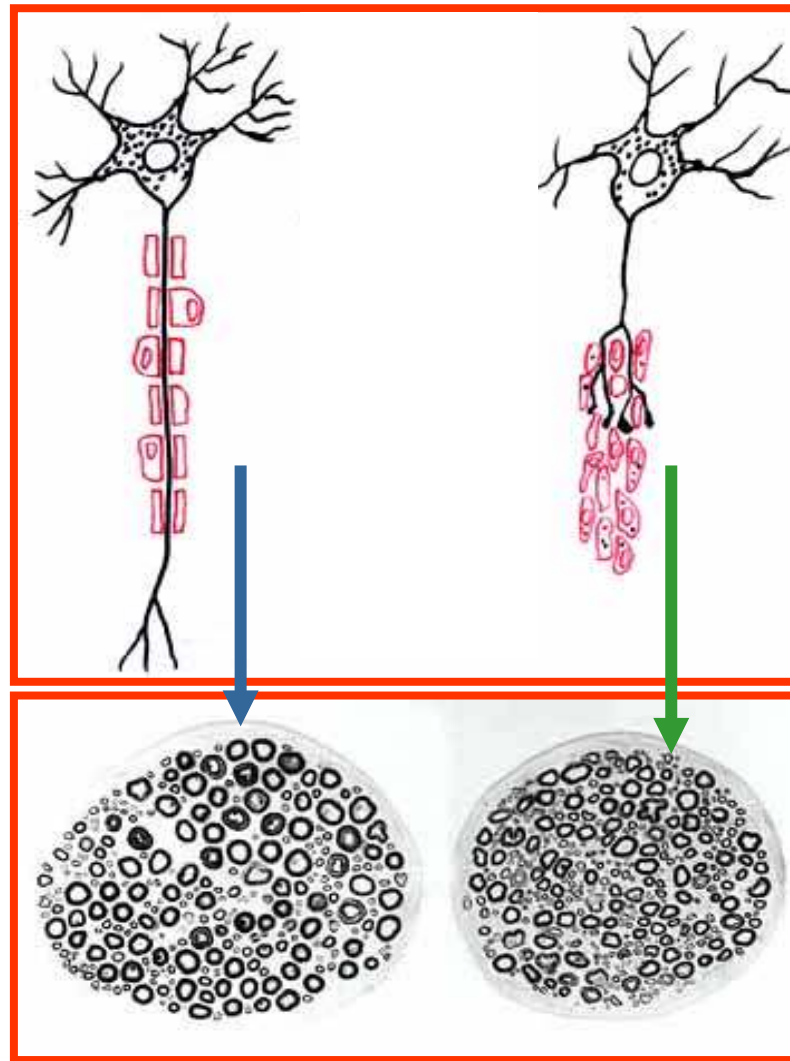
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BOXING

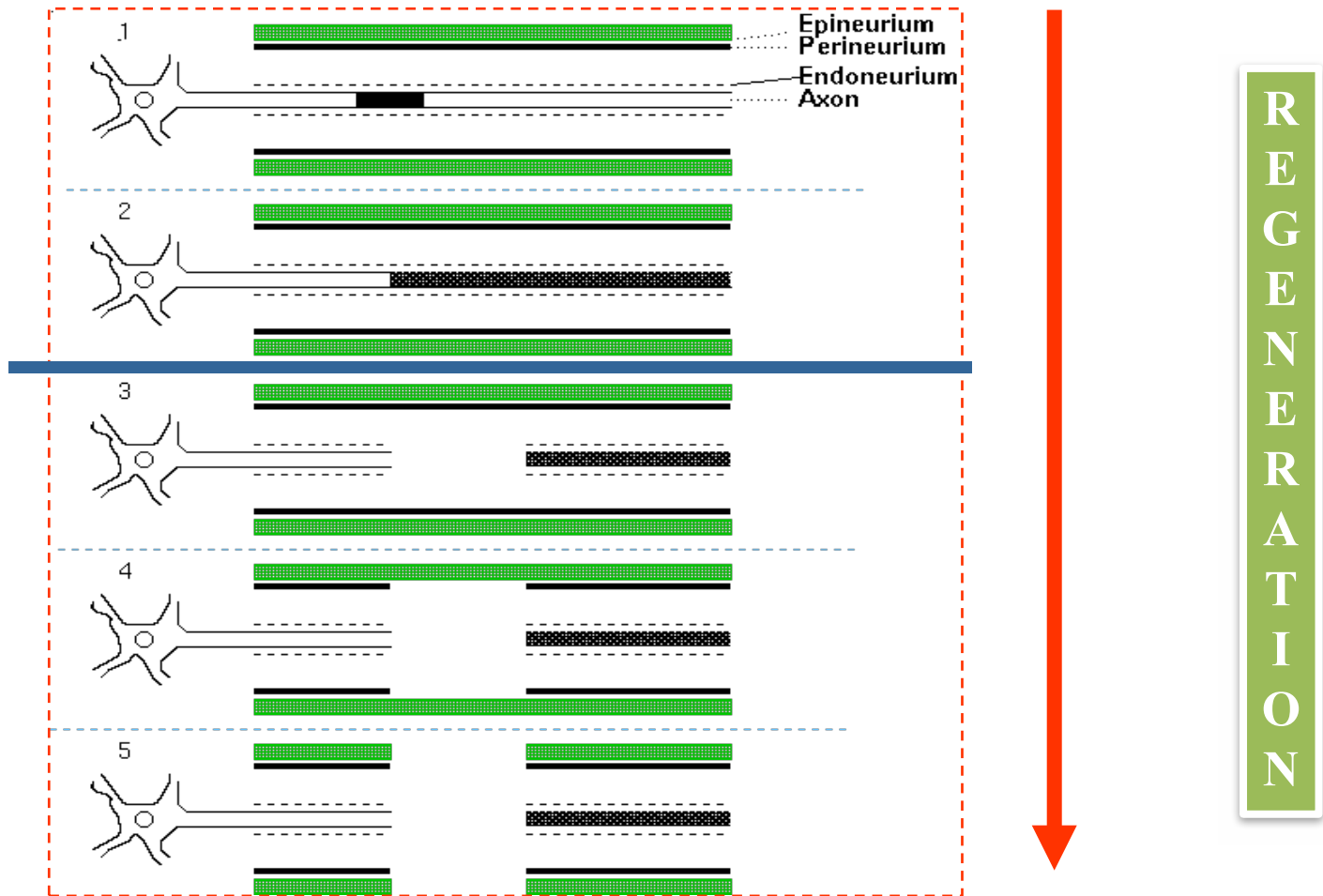


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REGENERATION

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