SCHIZOPHRENIA. ELECTRON MICROSCOPE STUDIES

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PART 1  ELECTRON MICROSCOPY STUDIES IN ADULTS

PART 2  ELECTRON MICROSCOPY STUDIES IN ABORTED FETUSES AND CHICKEN EMBRYOS

PART 3  BLOOD AND CEREBROSPINAL FLUID

PART 4  BIOLOGICAL TEST
SCHIZOPHRENIA ELECTRON MICROSCOPE STUDIES.

SUMMARY:
Introduction. The ultrastructural analysis of tissue morphological alterations through electron microscopy techniques constitutes an instrument of undoubted value to deepen in the pathogenic studies of diseases. Especially in the field of neuropsychiatry pathology it has been an important element to figure out the complex mechanisms in the genesis of the different pathological, inflammatory, immunologic and neoplastic processes, and in the definition of particular entities.

In spite of schizophrenia is an organic brain disease where limbic structures are involved there are few studies of these brain regions in dead schizophrenic patients using electron microscope techniques. This has been due partly to the difficulties in obtaining fresh brain material with this purpose. Patients and methods. In 1977 we started an electron microscope project studying two limbic structures (amygdaline nucleus and hippocampus) and auditory cortex of the left cerebral hemisphere of young dead schizophrenic patients n=16 and controls n=10 observing three main alterations: nuclear bodies, membrane cell proliferation and particles with viral morphology which react to herpes simplex hominis type I antibody (REV NEUROL 2001; 33: 619-23). These findings were considered the first direct evidence of virus in the central nervous system in schizophrenia (Yolken RH, Torrey EF. Viruses, Schizophrenia and Bipolar Disorder. Clin Microb Review 1995; 1: 13145). In the last eleven years we have carried out studies of samples of blood of young patients observing platelets alterations. Some of these alterations are similar to those observed in the central nervous system those that are compatible with: a) the viral hypothesis and b) the virus herpes simplex hominis type I when immunoelectron microscopy techniques were done. Results and conclusion. The results obtained can constitute a biological marker for schizophrenia and an element favouring the possible viral etiology of the illness. The alterations in the morphology of platelets could be the origin of functional alterations that act on the central nervous system. The present work highlights the possible role of the morphological alterations found in the fisiopathology and etiology of this disease.
virus

Schizophrenia

Electron Microscope Studies

*Ultrastructural Study of the Temporal Lobe and Peripheral Blood in Schizophrenic Patients*

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Summary. Introduction. In spite of the human, social and economic impact of schizophrenia and to be considered a disease of organic origin by several evidences, there are relatively few studies about this disease using electron microscope techniques. Patients and methods. For more than 25 years we have made studies of schizophrenia by means of this technique. We have studied limbic structure samples from young adult’s dead schizophrenic patients, from foetuses of schizophrenic mothers and from chicken embryos experimentally inoculated with cerebrospinal fluid from schizophrenic patients. In the last ten years we have performed studies of blood and cerebrospinal fluid samples from young schizophrenic patients. We have found some alterations with the same characteristic to those observed in the central nervous system, which are compatible with:

a) the viral hypothesis and b) with herpes simplex hominis type I virus, when immunoelectronmicroscopic techniques were made. Results and conclusion. The results obtained in this work can constitute a new element favoring the possible viral aetiology of schizophrenia and a biological test for the disease.
Organic character of the disease

The organic character of schizophrenia is based among different studies by the structural alterations in schizophrenic brains in an important proportion of patients that has been shown by imagenologic and morphometric studies which point out to deeper structural atrophies in the limbic system (amygdaline nucleus and hippocampus) specially in the left cerebral hemisphere. However there is practically a lack of electron microscopic post-mortem studies of these brain regions in this disease.
Such approaches give us a broad sense of how the brain looks anatomically and how it functions physiologically. To understand how genes affect the brain in a way that puts it at risk, we need to examine in a much more finely detailed way the actual cells of the brain. We can do this with living brain tissue to some degree, and we can do this with postmortem brain tissue to a much greater degree.

Daniel R. Weinberger

Schizophrenia, image and research

There is a progressive involvement of the vertex and the temporal lobe in schizophrenic patients.

Since 1977 we started an electron microscope study of postmortem tissue of schizophrenic patients. In that study we took brain samples from the left temporal lobe. A similar study was made in controls.

Compatible alterations with the viral hypothesis: particles with herpes simplex hominis type I viral antigen, intranuclear bodies, membrane alterations.
Results: platelet morphological alterations in patients that could be use as a biological marker of the disease.

We are developing a biological test at present of possible diagnostic value.
Ultrastructural analysis of tissue morphological alterations through electron microscopic techniques, constitutes an instrument of undoubted value in the pathogenic study of illnesses at present time. Especially in the field of neuropsychiatry pathology it has been an important element to figure out the complex mechanisms in the genesis of the different pathological, inflammatory, immunologic and neoclassic processes, and in the definition of particular entities.

Schizophrenia: electron microscopy

Young adults
Fetuses from schizophrenic mothers
Chicken embryos inoculated with CSF
Blood and cerebrospinal fluid
There are very few electron microscope studies of schizophrenia from post mortem brain tissue due among other difficulties to obtain autopsy fresh material for this purpose.

*S. Mesa-Castillo: AN ULTRASTRUCTURAL STUDY OF THE TEMPORAL LOBE AND PERIPHERAL BLOOD IN SCHIZOPHRENIC PATIENTS*  
*REV NEUROL 2001; 33: 619-23*
IN OUR WORKS: Samples were taken from three structures which are involved in the pathophysiology of schizophrenia: amygdaline nucleus, hippocampus and auditory cortex.
Patients and controls

- Patients: 16
- Controls: 10
Study cases related to sex

- M: 12
- F: 4
Neuron degenerative changes were observed specially in the amygdaline nucleus. A microglial reaction was present around the degenerated neurons. Arrow.
Schizophrenia: electron microscopy.

Central nervous system findings:
Nuclear bodies
Membrane alterations
Particles with viral morphology

Blood and cerebrospinal fluid findings:
Membrane alterations
Vacuoles
Spherical and hexagonal particles
Glycogen increase
Morphological alterations
Nuclear bodies have been described in several pathologies and can be seen also in normal persons but they have been described specially in central nervous system diseases of viral etiology.
Particles with viral morphology

Budding particle

Nuclear envelope widened

In schizophrenic patients viral like particles were observed within the widened nuclear envelope
Intranuclear particles

Particles with a central core and an envelope related to membrane structures
Most of the viral like particles observed in schizophrenic brain samples have the characteristic that is showed in this figure: a central core (circle) surrounded by filamentous structures. This is a form that herpes virus can be observed in electron microscopy studies.
Immuno-electronmicroscopy

Particles with viral morphology

Particle labeled with peroxidase anti-herpes simplex hominis type I antisera
Particles with viral morphology: below, herpes simplex virus. Above (arrow) particle observed in schizophrenia.

The image below is from Dennis Kunkel's excellent Microscopy Science and Photography Through a Microscope.
Results

- Viral antigen
- Viral like particles
- Membrane alterations
- Nuclear bodies