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enveloped and confined to vesicles inside the neurites. Probably virus was released by fusion of vesicle wall and neuritic plasma membrane.

Abstract 42. Metabolic alterations of HSV-1-infected neurons: studies using the PC12 cell as a model system
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In order to examine alterations in neurotransmitter metabolism associated with HSV-1 infection, we have studied infection of the PC12 cell line, which is derived from a rat pheochromocytoma and responds to nerve growth factor by undergoing morphological and physiological "differentiation". These cells possess both adrenergic and cholinergic properties. We have found that activities of both acetylcholinesterase and choline acetyltransferase were rapidly and progressively depressed during the replication cycle. Studies with metabolic inhibitors and temperature-sensitive (ts) mutants suggested that this decline in enzyme activities was associated with events occurring early in replication, likely related to expression of the immediate-early (α) group of viral polypeptides. In contrast, catecholamine uptake, content, and K⁺-stimulated release were all preserved nearly intact during a 24-hr period of productive infection. Tyrosine hydroxylase (TH) activity underwent a more complex pattern of alteration with an initial depression of activity reaching a nadir at 6 hr post inoculation, but recovered rapidly with a return to baseline by 8-9 hr. Subsequently, TH activity again fell with a second, more variable rise occurring at 24 hr post inoculation. Metabolic inhibitors and ts mutant experiments showed that these alterations were dissociated from morphological cytopathology and likely required expression of late (γ) viral gene products. These observations illustrate the complexity of alterations in cellular metabolism during HSV-1 infection and indicate that the program of viral gene expression can exert selective effects upon individual host cell processes.

Abstract 43. Neural cell cultures as a tool in analyzing neurovirulence and persistence of viruses
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Persistent murine corona virus (JHM strain) infection of rat brain causes a chronic demyelinating disease, possibly involving a functional impairment of destruction of the myelin forming glial cells, the oligodendrocytes. Also, evidence suggests that T cells sensitized to myelin play a pathogenetic role in the demyelinating process. To analyze the complex features of this disease, primary glial cell cultures consisting of oligodendrocytes and astrocytes are being utilized to determine direct virus-cell interactions. Cultures prepared from newborn Lewis rat brain are maintained for at least 2 months. Oligodendrocytes express myelin-specific components and form glial cell junctions as in situ. Cultures are infected with either neurotropic wild type (WT), neurotropic temperature sensitive strain (TS43) or non-neurotropic strain (PL) of JHM. At 24 hours post-infection (PI) all three strains infect astrocytes and oligodendrocytes. Cells infected with WT or TS43 fuse to form syncytia, whereas PL infects only scattered single cells. WT infects all cells by ten days, TS43 by 4 weeks and PL does not spread substantially even after 4 weeks. After cultures are clear of glial cells, fibroblasts repopulate the dish, apparently resistant to viral infection. These results reveal differences in direct virus-glial cell interactions of 3 strains of JHM corona virus and parallel the findings in the infected rats. The persistent nature of neurotropic TS43 in culture may reflect the delayed mechanism of primary demyelination in rat brain. This system will allow a detailed analysis of the effect of viral persistence upon specialized glial functions including myelin maintenance.

Abstract 44. Paramyxovirus induced changes of β-adrenergic receptor response and its immunological modulation
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Persistent virus infections in CNS derived cell lines can specifically impair neuro-receptor mechanisms (1-6). It was shown where such impairments are located in the molecular organization of different receptor/adenylate cyclase systems (E-adren., PGE, and opiate receptors) on neuron-like (NG108-15) and glia-like (C6) cell lines.

An example is the rat glioma C6 cell persistently infected by measles-SSPE virus which show impaired E-receptor mediated cAMP synthesis caused by viral glycoproteins in the cell membrane. The effect of antiviral antibodies on the expression of viral proteins in respect to the impairment was studied (8). Results show that such virus induced dysfunctions of CNS cells may be involved in certain CNS diseases. This work is supported by the DFG (Sonderforschungsbereich 105, C3).

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Abstract 45. In vitro cultivation of nerve cells as models for studies on nerve cell-virus interactions

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During the last decade, nerve tissue culture techniques have been applied to fundamental questions concerning the mechanisms of nervous system development and function. Tissue slices, mixed cell cultures consisting of dissociated or aggregate cells, and "purified" cell cultures of neurons, astrocytes, oligodendrocytes or Schwann cells have been employed. Culture conditions have varied from complex growth media to chemically-defined growth media. Research has focused on 1) the electrophysiological properties, 2) neurotransmitter uptake and release, 3) neuropeptide content, 4) influence of trophic factors, 5) neurochemical receptor binding, 6) receptor mediated-cellular activation i.e. stimulation of cAMP or cGMP synthesis, and 7) synapse formation. This extensive literature forms a basis for future studies of viral effects on neural function. This overview will briefly cite some of the previous applications of nerve tissue culture techniques to various aspects of viral pathogenesis during acute and persistant infection of neurons or cells with neuronal properties.

The main purpose of this presentation, however, will be to stimulate interest in the use of nerve tissue culture techniques in studies of possible relationships between persistent viral infections and behavioral disorders.

Several approaches including studies of cellular receptors for virus, viral neurotrophism, viral-induced alterations in neuronal function, and microinjection of viral genes or gene products into neurons will be discussed.

Abstract 46. Rabies impairment of neural functions by neuropharmacological and electrophysiological criteria

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Rabies virus infection is characterized by mild histopathological lesions and unconstant immunopathological reactions. In order to test the involvement of specific functions of the CNS, neuronal function modifications are investigated.

The binding affinity of antagonists to muscarinic acetyl choline receptors (mACHR) on the