presence of 8M urea.

The γ Subunits. The enzymatic activity of the 7S NGF complex resides in the γ subunits. The three individual subunits, γ^1, γ^2 and γ^3, normally isolated from fresh 7S NGF preparations all have the same specific activity. While the rate of hydrolysis of typical substrates by the γ enzyme is linear from the time of addition to substrate, 7S NGF displays a lag phase before reaching maximal velocity. The extent of the lag phase is diminished by incubating the diluted 7S NGF solution by itself prior to addition of substrate, by high pH or high ionic strength. These are effects which would be anticipated provided that the incubation conditions produced a shift in the 7S NGF equilibria toward more subunits and also provided that the only enzymatically active species are γ subunits which are dissociated from the 7S NGF complex. The lag phase would then reflect the time required to achieve the new dissociation equilibrium and produce the relevant concentration of "free" γ subunits. Support for this idea comes from the fact that the lag phase is restored if incubated dilute solutions are concentrated or the pH and ionic strength brought back into the range of 7S NGF stability. Also, addition of an excess of the enzymatically inactive subunits, α and β, before dilution of 7S NGF into the assay system decreases the observed specific activity of the latter to about 10% of its value in the absence of those subunits. Since these are conditions which suppress dissociation of 7S NGF, they measure more accurately the intrinsic specific activity of the 7S NGF complex. The latter is sufficiently low to suggest that the γ subunit bound in the 7S complex is inactive. Suppression of the γ activity requires interaction with both α and β, either subunit alone having very little effect on the observed activity of the γ subunits. These changes in enzymatic activity of the γ subunit parallel changes in its physical properties on aggregation and suggest that the two are linked. In spite of the significant difference in net charge (or isoelectric points) which exist between the three individual γ subunits, 7S species reformed from them by recombination with one given α subunit and the β subunit all have the same net charge, showing that the segments of the γ subunits which differ are hidden in the recombination process. Whether this involves a conformational change in the γ subunit is not yet known.

The association of an esteropeptidase enzyme with a protein (the β subunit) which stimulates neuroblast differentiation is an intriguing one, especially since enzymes of this type are themselves being implicated increasingly in processes to do with cellular growth and differentiation. Thus esteropeptidase activity is associated with the mesenchymal growth factor while thrombin, itself an enzyme of this type, has an NGF-like activity. Also the thymotropic factor present in extracts of mouse submaxillary gland, and which promotes differentiation of certain lymphocytes, is an esteropeptidase. Grossman, Lele, Sheldon, Schenkein and Levy have recently described the effects of other submaxillary esteropeptidases on the growth of cultured rat hepatoma cells. Of great interest is the recent report that the epidermal growth factor (EGF) can be isolated from mouse submaxillary glands as a 70,000

molecular weight complex containing two subunits. One of these subunits is relatively small and acidic and possesses EGF activity while the other is an esterase with properties very similar to those of the γ subunits. The exact chemical and physiological relationship of these various enzymes to the γ subunit of 7S NGF is unknown but is clearly of interest. It should also be noted that the γ enzyme is a glycoprotein.

The Metabolic Properties of Certain Synaptosomal Membranes. The methods for the extraction and electrophoretic analysis of at least 90% of mouse brain protein have been described by Grossfeld and Shooter. Using these techniques it has been determined that the half-lives of the proteins of various whole mouse brain fractions increase with increasing solubility; the supernatant and hypotonic extractable proteins had half-lives of about 13 days while the membrane proteins solubilized with Triton X-100 and SLS had half-lives of about 18 days. The proteins of the subfractions of synaptosomes had half-lives ranging from 15 to 19 days; those in the cytoplasm had a half-life of 18.3 days; in the membranes, about 17 days and in the synaptic vesicles, 15.6 days. Although the half-life of the synaptic vesicles was not significantly different from other synaptosomal subfractions, the vesicles gave a different protein pattern on acrylamide gels, which implies that the proteins of the vesicles are qualitatively different from those of other synaptic membranes. The data derived from the relative specific activities of synaptosomal fractions compared with their whole brain analogs supports the contention that a sizeable fraction of the synaptosomal cytoplasmic proteins is transported to the synapse by axoplasmic flow. The relative specific activity of synaptosomal membrane and synaptic vesicle protein rises much more quickly than for the cytoplasmic material and the alternate possibility of *in situ* synthesis has to be considered.

The Proteins of the Sarcoplasmic Vesicle Membrane. Because of its relatively simple protein composition this membrane is ideal for the development of solubilization methods and of chemical probes of membrane structure. The proteins of the sarcoplasmic reticulum isolated from rabbit skeletal muscle have been shown by electrophoresis and other physical methods to be still aggregated when solubilized in either Triton X-100 or in water by the method of prior solubilization in 80% phenol. Total solubilization of the proteins is achieved in sodium dodecyl sulfate and electrophoretic analyses in the presence of detergent showed the presence of a major protein component with a molecular weight of 100,000 daltons. Labeling of this protein with ^{32}P indicated that it was the ATPase present in the sarcoplasmic reticulum membranes. This protein was purified on SDS slab gels and its amino acid composition was shown to be identical to that of all the proteins in the reticulum. Electrophoresis of the major protein component on phenol:urea:acetic acid gels indicated that it was in fact composed of two proteins. When the major protein component was chemically modified and analyzed on sodium dodecyl sulfate acrylamide gels two protein components were now observed. The major protein components have either three or four disulphide bonds and cross-linking with dimethylsuberimidate confirmed that the 100,000 units are major constituents of this tissue.

E. M. Shooter - Some Aspects of Molecular Neurobiology

PERSONNEL

Postdoctoral

M. Baker - Nerve growth factor - physical properties and relationship of enzymatic and biological activities

J. Bamburg - Nerve growth factor - molecular composition and mechanism of action

I. Morgan - Synaptosome biochemistry

R. Perez - Nerve growth factor - structural studies

T. Schenker - Nerve growth factor - chemical characterization of differences between subunits and sequence work

Predoctoral

K. Borden - Specific acidic proteins in nerve cells

K. Herrup - Nerve growth factor - biological studies and mechanism of action

S. Reed - Membrane biochemistry - isolation of ATPase enzymes

W. Mobley (Medical student) - Nerve growth factor - structural and chemical studies

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