9.14
Class #18: Midterm Review

NAMES:

Santiago Ramon y Cajal (father of neuroanatomy; Spain)

Walle J. H. Nauta (father of modern experimental neuroanatomy) (M.I.T. Professor)

George Parker (earliest evolution of nervous system, exemplified in simple multicellular organisms)

Ross Harrison (inventor of tissue culture method applied to study of developing nervous system; living growth cones)

Speidel (first looked at growing axons in the living animal).

Hans Spemann (prolific experimental embryologist, evidence for induction in embryonic nervous system, the "organizer")

Hilde Mangold (experiments with Spemann on induction and the organizer were her Ph.D. thesis, but she died before publication)

[Graham Dunn (first to specifically study role of axon retraction in axonal growth)

Pasko Rakic (prolific modern neuroanatomist; evidence for neuronal migration using radial glial guides in cortex) (early work done at Harvard, now at Yale)

D. Kent Morest (Golgi evidence for neuronal migration as nuclear translocation, without glial guidance; specializes in auditory system anatomy and development)

Rita Levi-Montalcini (discoverer of NGF -- nerve growth factor -- with V. Hamburger at Washington University in St. Louis. Still active in Rome.)

Victor Hamburger (co-discover of NGF; inspired much work on motor neuron survival and death, and the neurotrophic theory)

Robert Horvitz (experimental analysis of genetic control of body and nervous system development in the nematode *C. elegans,* which led to the discovery of programmed cell death and some of its controlling molecules) [M.I.T. professor]

Hermann Steller (discoverer of the reaper gene in fruit fly, which responds to signals and triggers cell death by activating the critical protease) [former M.I.T. professor]

Planes of section; Cytoarchitecture; Fibroarchitecture, or fiber architecture; myeloarchitecture

Chemoarchitecture (e.g., the distribution of acetylcholinesterase)

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Nauta stains, silver stains. Neurofilaments are argyrophylic; so are degenerating cell components.

Problems in experiments using neuroanatomical tracers for charting axonal pathways:
---- Discriminating artifacts from the real thing
---- Uptake of label: defining the region of adequate uptake.
---- The fiber-of-passage problem.
---- Sensitivity of the method (this varies widely)
---- Selectivity: many morphological details are missing with any one method.
---- Actual synaptic connections not really seen without electron microscopy.

HRP: three main uses in neuroanatomical studies (retrograde tracer, anterograde tracer, intracellular filling)

Golgi methods

Retrograde vs. anterograde degeneration.

Retrograde and anterograde transneuronal degeneration, occurs mostly in the very young CNS.

In situ hybridization; ^{3}H-proline autoradiography; Immunohistochemistry

Parts of a cell:
---- Soma; Dendrites (receiving), Axon (transmitting), axon hillock;
---- Terminals and synapses (vesicles, mitochondria, presynaptic thickening, postsynaptic thickening)
---- Excitatory synapse (round vesicles, asymmetric thickenings), inhibitory synapse (flattened vesicles, symmetric thickenings); gap junction (very narrow cleft; ionic exchange through special channels)

Types of synapse: Axo-axonal, axodendritic, axosomatic, dendrodendritic, dendro-axonal (very rare).

Subcellular components: nucleus, nucleolus, RER (rough endoplasmic reticulum), ribosomes, Golgi apparatus, cytoskeleton (microtubules, neurofilaments, microfilaments), vesicles, mitochondria.

Afferent, Efferent; anterograde, retrograde

Nissl substance, stains (named for Franz Nissl). Nissl stains shows location of RER stacks.

Types of neurons: unipolar, bipolar, multipolar; examples.

Axoplasmic transport; why? How? What are organelles involved in transport? What are the motors for anterograde and retrograde transport? What is transported by fast, and what by slow transport?

Transneuronal tranport.

Myelin; nodes of Ranvier

Pial-glial membrane

Meninges: the three layers, the Latin terms.

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CSF = cerebrospinal fluid. Production of CSF by choroid plexus cells. Mostly in lateral ventricles and fourth ventricle. Drainage: Flow of CSF – through foramina, through subarachnoid space, finally into venous circulation.

Hydrocephalus caused by blockage of CSF flow, usually at the aquaduct of Sylvius.

Role of foramina of Luschka (lateral apertures) and Magendie (median aperture) (foramen = opening, in this case in the roof plate)

Choroid plexus

Schwann cells vs oligodendrocytes (oligodendroglia)

Astrocytes (fibrous, protoplasmic), Microglia, ependymal cells, radial glia.

Specialized glia cells: Bergman glia of cerebellum, Mueller cells of retina, midline radial glia..

Transmitters: Acetylcholine, monoamines (noradrenalin, [adrenalin], dopamine, serotonin), glutamate, GABA, glycine.

Neurotransmitters/neuromodulators: endorphins, enkephalins, substance P, VIP, nitric oxide, etc.

The 2 major pathways from body surface to neocortex, with names

Dermatome: how mapped? What is the clinical relevance?

Three types of cutaneous receptors in skin, and two types of axonal endings (actually the dendritic portion of the primary sensory neurons).

Nociceptors; what do they respond to? (note different types)

Central control of pain input: How does this occur? (Descending pathway from CGA of midbrain to nucleus raphe magnus, and from there via serotonin-containing axons to substantia gelatinosa of spinal cord). Note also the role of central release of endorphins in reduction of pain sensitivity.

Cutaneous receptive field; two-point discrimination; topographic organization.

Primary sensory fiber size and sensory receptor types, and pattern of innervation in spinal cord. (Brodal 209-211.)

Motor neurons: definition, location in spinal cord, locations in brainstem

Locations of peripheral ganglia, and of preganglionic motor neurons, of the sympathetic and the parasympathetic nervous systems. Neurotransmitters used by these neurons.

Enteric nervous system

Eye movement control: Cranial nerves III, IV, VI.

The standard 12 cranial nerves in humans; where does each nerve attach to the brain? Is the nerve sensory, motor, or mixed?

Name 3 cranial nerves not included in the standard list of 12 (terminal, vomeronasal, epiphyseal, lateral line nerve).

Embryonic spinal cord, adult spinal cord drawings (mid-thoracic level). Show motor neurons, secondary sensory neurons, sympathetic nervous system preganglionic neurons.

Spinal cord at an enlargement: motor neurons of axial *vs.* distal muscles.

Clark's column in spinal cord – precerebellar. Ipsilateral pathway to cerebellum (dorsal spinocerebellar tract) .

Propriospinal axons: How could these be traced in a neuroanatomical experiment? What would be an expected result?

Taste fibers in three "mixed nerves" (carrying both sensory and motor components). (7^{th} : anterior tongue; 9^{th} & 10^{th} : throat and posterior tongue)

Three types of output channels from hypothalamus

Ectoderm, mesoderm, endoderm.

Morula, Blastula (with blastocoel), gastrula and gastrulation, neurula and neurulation.

Major cellular activities in forming the embryo: contractions, selective adhesion and changes in adhesion, cell movement, growth (Wolpert)

Dorsal lip of blastopore. [Primitive Streak, Hensen's node;] Organizer; Organizer as an inhibitor.

Induction; Chordamesoderm; prechordamesoderm; Epidermalization of ectoderm vs neuralization of ectoderm.

TGF-β-like polypeptide growth factors: BMPs.

Neural plate, neural folds, neural tube; sulcus limitans, alar plate, basal plate; pseudostratified epithelium.

Closure of neural tube. Incomplete closure results in spina bifida or anencephaly.

Notochord, induction of floor plate and spinal motor neurons. Sonic hedgehog (SHH protein); BMP4 signaling (Bone Morphogenetic Protein).

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Primary brain vesicles, and basic expansions of 1st and 3rd to give secondary vesicles.

Evagination, invagination; formation of retina: optic vesicle, optic stalk, double-walled cup, neural retina vs pigment epithelium

Cell adhesion – homotypic binding via CAMs.

Cell proliferation, neuronal birthdays.

Mitotic cycle for neurons, zone for DNA synthesis, zone where mitoses occur. ^{3}H-thymidine labeling: What does short-term *vs* long-term post-injection survival tell us?

Subventricular zone.

Asymmetric vs symmetric divisions; (Notch and Numb signalling).

Cell migration in CNS. Two modes of migration from ventricular layer: along radial glia; nuclear translocation.
Cell migration in PNS: Neural crest cells; role of cell adhesion molecules, permissive and repulsive cues.
Cell migration in cortex: Formation of cortical plate, intermediate zone; inside-out order of cell proliferation; subventricular layer.
[Cell migration in cerebellum: tangential migration of cells from rhombic lip, formation of external granule layer (transient, only in development), inward migration, formation of internal granule layer; role of astrotactin.]

Neural crest: define; what happens to it? What are some fates of crest cells? What is a chimera, and what can chimeras tell us about neural crest migration and fates? (Purves & Lichtman 42-44)

"Ontogeny recapitulates phylogeny"? What may phylogenetic comparisons of embryonic development indicate about the human brain? (E.g., which areas are the most "advanced"/ recently evolved.)

Fate mapping (see Purves & Lichtman p. 31 figure for Jacobson experiments). Cf. cell fate "determination".

Morphogenetic field, and phenomenon of regulation.

Membrane addition to a growing axon: origin, movement, sites of incorporation.

Growth cone (named by Cajal): appearance, dynamics, major organelles, examples of molecular constituents.

Extrinsic factors affecting growth cones:

Chemical guidance of growing axons: four types, plus two non-directional influences (increased vigor of growth, decreased vigor of growth) .

Axon guidance in growth of primary sensory axons in grasshopper leg. Experimental evidence?

Two non-chemical guidance factors in axonal growth (from Purves).

Semaphorin III (collapsin): apparent role in innervation of sp. cord by dorsal root axons.

Netrins: Where found? What axons affected, and how?

Intrinsic factors affecting growth cones – e.g., GAP-43.

Growth cone motility: Actin filaments, myosin, GAP-43 possible influence on filopodial formation

Growth cone responsiveness to substrate and chem. environment: adhesion molecules like NCAM, L1; receptors for growth factors, like trkA, trkB, trkC; receptors for collapsing/repelling factors.

Axon extension: Tubulin. Factors in membrane synthesis and transport.

Molecules needed in synaptogenesis (after elongation is complete) – e.g., agrin

Synapses: how detected? (electron microscopy, electrophysiology, transneuronal transport of labeled molecules).

Synapse elimination and multiple innervation

Curare (Indian arrow poison, from South American plants; blocks nicotinic ACh receptors; active agent is the alkaloid d-tubocurarine)

Alpha bungarotoxin (from venom of the poisonous snake, the banded krait *Bungarus multicinctus;* irreversibly binds to nicotinic ACh receptors)

Basal lamina "ghosts" and regeneration of motor neuron axons. Cf. initial development.

Fas II (fasciclin II): What is it? Role in plasticity of fruit fly neuromuscular junction? (Class 10)

Schwann cells: role in collateral sprouting in muscle? (Class 10)

Bioassay for NGF

Multiple effects of NGF on certain neurons, especially on dorsal root ganglia and paravertebral ganglia neurons: promotion of cell survival, influence on direction of axon growth; increased quantity of axon growth and branching.

Immunosympathectomy

Campenot chamber. Describe an experiment and its result using this apparatus.

Trk receptors and the neurotrophin family. Define “trk” and note the selective binding of growth factors to specific receptors.

Autophosphorylation of intracellular domain sites on the trk receptor, a consequence of binding of NGF to the extracellular domain of the trk protein: initiates binding to target molecules, which can initiate a

signaling cascade, which can activate transcription factors, which result in proteins which can affect, e.g., neuronal differentiation or neuritogenesis (axon or dendrite growth).

NGF knockout mouse, or trkA knockout mouse: What sensory and anatomical defects are found in this engineered mutant?

NT-3 knockout mouse – deficits?

Thyroxin and neuronal survival or death. (see P & L, p. 143)

Limb bud extirpation vs. grafting experiments: Explain effects on motor neurons in terms of neurotrophic theory.

Naturally occurring neuronal death: two major purposes.

Transneuronal degeneration / atrophy: example; indicator of trophic influence of innervation.

Excitotoxicity: What is it? Evidence that it may explain vulnerability of developing motor neurons to target loss?

GDNF = Glial Derived Neurotrophic Factor; special role in survival of dopamine neurons.

Apoptosis vs necrosis

Ced-9 and bcl-2: In what species were they discovered? What major role in cell?

Ced-3 and ICE-like protease: similar questions.

Homeotic mutation

Homeobox and homeodomain

Homeobox gene expression patterns

Neuromere; rhombomere, mesomere, prosomere.

Somite *vs.* somitomere. (Branchiomere is a subcategory of somitomeres.)

Spinal segmentation as epigenetic.

Placodal origin of cranial nerve components, vs. neural crest origin. (What is an epidermal or sensory placode?)

Barrel field; Where are barrels, barreloids and barrelettes?

NMDAR1 knockout mouse: What is it? How is development of trigeminal system affected?

Topography of trigeminal nerve afferents to hindbrain: How studied in embryonic rats?

Critical period for influence of periphery on barrel formation: How are the experiments done, and what happens?