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Rick Gilmore 2017-02-06 11:33:12

Visualizing the microanatomy of the brain (4:29)

Today's Topics

- Cells of the nervous system
 - Glia
 - Neurons
- How do these cells communicate?

How many neurons and glia?

- Old "lore": ~100 billion neurons
- New estimate (Azevedo et al. 2009)
 - $\sim 86 + / 8$ billion neurons
 - -85 +/-9 billion glia
- 100-500 trillion synapses, 1 billion/mm³

Glia (neuroglia)

- "Glia" means glue
- Functions
 - Structural support
 - Metabolic support
 - Brain development
 - Neural plasticity?

Astrocytes

- "Star-shaped"
- Physical and metabolic support
 - Blood/brain barrier
 - Ion (Ca++/K+) buffering
 - Neurotransmitter (e.g., glutamate) buffering

Astrocytes

- Shape brain development, synaptic plasticity
- Regulate local blood flow
- Regulate/influence communication between neurons, (Bazargani and Attwell 2016)
- Disruption linked to cognitive impairment, disease (Chung et al. 2015)

Astrocytes

Myelinating cells

- Produce myelin or myelin sheath
- White, fatty substance
- Surrounds many neurons
- The "white" in white matter
- Provide electrical/chemical insulation
- Make neuronal messages faster, less susceptible to noise

Types of myelin-producing cells

- Oligodendrocytes
 - In brain and spinal cord (CNS)
 - 1:many neurons
- Schwann cells
 - In PNS
 - 1:1 neuron
 - Facilitate neuro-regeneration

Oligodendrocytes

Schwann Cells

Microglia

- Phagocytosis
- Clean-up damaged, dead tissue
- Prune synapses in normal development and disease
- Disruptions in microglia pruning -> impaired functional brain connectivity and social behavior, (Zhan et al. 2014)

Microglia

Microglia in red invading dentate gyrus.

Neurons

Fun facts about neurons

- Specialized for electrical & chemical communication
- Post-mitotic don't divide
- Most born early in life, (Bhardwaj et al. 2006)
- Among longest-lived cells in body, may scale with organism lifespan (Magrassi, Leto, and Rossi 2013)
- Can extend over long distances

Macrostructure of neurons

- Dendrites
- Soma (cell body)
- Axons
- Terminal buttons (boutons)

Structure of neurons

Dendrites

- Branch-like "extrusions" from cell body
- Majority of input to neuron
- Cluster close to cell body/soma
- Usually receive info
- Passive (do not regenerate electrical signal) vs. active (regenerate signal)
- Spines

Dendrites

Dendritic Spines

Soma (cell body)

- Varied shapes
- Nucleus
 - Chromosomes
- Organelles
 - Mitochonrdria
 - Smooth and Rough Endoplasmic reticulum (ER)

Soma

Axons

- Another branch-like "extrusion" from soma
- Extend farther than dendrites
- Usually transmit info
- Parts
 - Initial segment (closest to soma, unmyelinated)
 - Nodes of Ranvier (unmyelinated segments along axon)
 - Terminals, axon terminals, terminal buttons, synaptic terminals, synaptic boutons

Axons

Synaptic bouton (terminal button)

- Synapse (~5-10K per neuron)
- Presynaptic membrane (sending cell) and postsynaptic (receiving cell) membrane
- Synaptic cleft space between cells
- Synaptic vesicles

- Pouches of neurotransmitters
- Autoreceptors (detect NTs); transporters (transport NTs across membrane)

Synaptic bouton (terminal button)

Classifying neurons

- Functional role
 - Input (sensory), output (motor/secretory), interneurons
- Anatomy
 - Unipolar
 - Bipolar
 - Multipolar

Classifying neurons

- By specific anatomy
 - Pyramidal cells
 - Stellate cells
 - Purkinje cells
 - Granule cells

Neurons by type

Neural communication

- Electrical
 - Fast(er)
 - Within neurons
- Chemical
 - Slow(er)
 - Between neurons

How are messages generated?

- Electrical potential (== voltage)
 - Think of potential energy
 - Voltage \sim pressure
 - Energy that will be released if something changes

Potential energy

Types of neural electrical potentials

- Resting potential
- Action potential

Resting potential

- Measurement
 - Electrode on inside
 - Electrode on outside
 - Inside Outside = potential

Resting potential

Resting potential

- Neuron (and other cells) have potential energy
 - Inside neuron is -60-70 mV, with respect to outside
 - About 1/20th typical AAA battery
- Like charges repel, opposites attract, so
 - Positively charged particles pulled in
 - Negatively charged particles pushed out

Where does the resting potential come from?

- Ions
- Ion channels
- Separation between charges
- A balance of forces

We are the champIONs, my friend

- Potassium, K+
- Sodium, Na+
- Chloride, Cl-
- Organic anions, A-

Party On

- Annie (A-) was having a party.
 - Used to date Nate (Na+), but now sees Karl (K+)
- Hired bouncers called
 - "The Channels"
 - Let Karl and friends in or out, keep Nate out
- Annie's friends (A-) and Karl's (K+) mostly inside
- Nate and friends (Na+) mostly outside
- Claudia (Cl-) tagging along

Party On

Next time

• Neural communication

Azevedo, Frederico AC, Ludmila RB Carvalho, Lea T Grinberg, José Marcelo Farfel, Renata EL Ferretti, Renata EP Leite, Roberto Lent, Suzana Herculano-Houzel, and others. 2009. "Equal Numbers of Neuronal and Nonneuronal Cells Make the Human Brain an Isometrically Scaled-up Primate Brain." *Journal of Comparative Neurology* 513 (5). Wiley Online Library: 532–41.

Bazargani, Narges, and David Attwell. 2016. "Astrocyte Calcium Signaling: The Third Wave." Nature Neuroscience 19 (2): 182–89. doi:10.1038/nn.4201.

Bhardwaj, Ratan D., Maurice A. Curtis, Kirsty L. Spalding, Bruce A. Buchholz, David Fink, Thomas Björk-Eriksson, Claes Nordborg, et al. 2006. "Neocortical Neurogenesis in Humans Is Restricted to Development." *Proceedings of the National Academy of Sciences* 103 (33): 12564–8. doi:10.1073/pnas.0605177103.

Chung, Won-Suk, Christina A. Welsh, Ben A. Barres, and Beth Stevens. 2015. "Do Glia Drive Synaptic and Cognitive Impairment in Disease?" *Nature Neuroscience* 18 (11): 1539–45. doi:10.1038/nn.4142.

Magrassi, L., K. Leto, and F. Rossi. 2013. "Lifespan of Neurons Is Uncoupled from Organismal Lifespan." *Proceedings of the National Academy of Sciences* 110 (11): 4374–9. doi:10.1073/pnas.1217505110.

Zhan, Yang, Rosa C. Paolicelli, Francesco Sforazzini, Laetitia Weinhard, Giulia Bolasco, Francesca Pagani, Alexei L. Vyssotski, et al. 2014. "Deficient Neuron-Microglia Signaling Results in Impaired Functional Brain Connectivity and Social Behavior." *Nature Neuroscience* 17 (3): 400–406. doi:10.1038/nn.3641.