VISITING SCHOLAR PROGRAM

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Public Lecture Offerings

Brain Waves and Brain Wiring

The brain is the most incredible computational machine imaginable. There are over one trillion nerve cells in the brain, and each cell can make 10,000 synaptic connections with other nerve cells. How are connections wired up during development? Let's focus on the Visual System as an example. The wiring problem is solved sequentially, first by forming a basic scaffold of connectivity according to genetic blueprints: strict molecular cues guide growing nerve connections along appropriate pathways to reach correct target regions. But once this basic scaffold is in place, the story is not over. These initial connections are diffuse, and adult precision only emerges gradually over an extended period of development, during which the exact details of each circuit are fine-tuned by pruning and sculpting synapses from immature connections. The decision-making process that determines which connections remain and which are pruned is also genetically specified, but in this case, brain function is required. Surprisingly, even before birth and before vision, the brain generates its own internal neural activity patterns-"brain waves"- which jump-start the sculpting process. Then, during postnatal developmental critical periods, as sensory systems such as the eyes and ears mature, experience of the external world takes over to influence brain wiring. This circuit-tuning process is thought to occur throughout the brain during development, endowing it with a vast capacity to adapt to the environment and laying the foundation for the brain's ability to learn throughout life.

Rejuvenating the Brain: Can Lessons from Brain Development Teach Us about Alzheimer's Disease?

Memories are stored in synapses and neural circuits, which are progressively lost in Alzheimer's disease (AD). Genetic mutations, inflammation, and other factors increase soluble beta-amyloid oligomers, which later aggregate into plaques, long treated as the primary disease cause. Yet repeated failures of plaque-targeting therapies suggest this model is incomplete. Insights from brain development offer an alternative perspective. During development, neural circuits are first assembled and then refined through activity-dependent synapse pruning, a process regulated by genes including some traditionally associated with the immune system. One such gene, PirB, is required for synapse pruning and is aberrantly activated in AD. In mouse models, loss of PirB protects against cognitive decline. PirB and its human homolog LilrB2 bind soluble beta-amyloid oligomers before plaque formation and are expressed at excitatory synapses—the synapses most affected in AD. Dysregulation of these receptors may therefore drive pathological synapse loss. These findings suggest that AD therapies focused solely on plaques may act too late and miss critical mechanisms of synapse degeneration. Targeting synapse-pruning pathways informed by neural development may open new avenues for treatment.

Classroom Discussion Topics

Any of the above lecture topics may be adapted for classroom discussion.