Cognitive network development

Early development produces the macroscopic structure of the neocortex, including corticocortical pathways.

After early development:
1) the neocortex contains a very large number of neurons grouped in columnar assemblies
2) these assemblies fill the entire neocortex of both hemispheres
3) the neocortex is subdivided into areas based on cytoarchitecture
4) within areas, the neurons of the assemblies are interconnected to form local networks
5) small local networks within an area are interconnected to form larger networks within the area
6) assemblies in different areas are interconnected to form large-scale (transcortical) networks
7) life experience (learning) continues to modify the cortical connective structure – experience converts cortical networks into cognitive representations

The same processes that create networks during early ontogeny are thought to continue to shape them by experience throughout life.
The cognitive development of the cortex involves:

a) the competitive *selection* of neural elements: axon branches, dendritic spines, etc that form active connections are selected to the exclusion of those that do not form connections.

b) *construction* of network structure by the formation of active synaptic connections.

Neuronal group selection theory (Edelman, 1987):

1) a *primary repertoire* of columnar neuronal groups (assemblies) forms during development by cell division, migration, selective cell death, & growth of axons and dendrites

2) through experience, a *secondary repertoire* of functional neuronal groups emerges from the primary repertoire; groups that discharge together in response to a stimulus strengthen their synaptic interconnections and become selectively responsive to that stimulus
3) through reentry of activity between different cortical areas, large-scale networks are created.

4) these networks exhibit degeneracy, the capacity to elicit the same response when their different components are stimulated.

Cortical network formation depends on use-dependent synaptic plasticity – the change in synaptic strength with neural activity.
Evidence for use-dependent synaptic plasticity:

1) *sensory deafferentation*: the loss of sensory input to a portion of the somatosensory cortex causes reorganization of the sensory map, with expansion of cortex devoted to the surviving input at the expense of that devoted to the lost input – thought to result from competitive rewiring of input connections

2) *sensory deprivation* causes lower numbers of dendritic spines and synapses in sensory cortex

3) *enriched environments* cause the numbers of dendrites and dendritic spines to be greater than impoverished environments.

Use-dependent plasticity is thought to operate by the *Hebbian principle of synaptic facilitation*: neurons that are repeatedly active at the same time become associated by synaptic strengthening.
Cortical areas

An isomorphic relation exists in the visual system between the cognitive hierarchy of visual perception and the cortical visual hierarchy.

We first review cortical anatomical structure.

What defines a cortical area?

All of the neocortex has the same basic 6-layer structure, but differences in 3 factors distinguish different cortical areas.

Cortical areas differ in:
   a) local cytoarchitecture
   b) sources of their connections
   c) targets of their connections

These structural differences are thought to be the basis for the specialized functions of different cortical areas.
Horizontal laminar organization of cortex:

6 layered sheet with common laminar pattern throughout:
I: plexiform layer
II: small pyramidal cells that project to ipsilateral cortical areas
III: small pyramidal cells that project to contralateral cortical areas
IV: stellate cells that receive thalamic input & input from hierarchically lower
cortical areas (striking appearance in primary visual cortex; absent in primary
motor cortex)
V, VI: large pyramidal cells that project to subcortical structures, including
thalamus, basal ganglia, midbrain, spinal cord
Vertical organization:

1) apical dendrites & primary axons of pyramidal cells are arranged vertically
2) vertical *minicolumns* span cortical width – considered to be smallest processing unit of neocortex
3) connectivity and cell density are dense within columns & sparse between columns
4) columnar width in range of 30-50 microns
5) columns originate in primordial matrix of proliferative layer
6) each column results from upward migration and superposition of ~100 neurons
7) functional macrocolumns in primary sensory and motor areas are 50-500 microns wide; unified by common extrinsic connections

In association cortex, functional modularity is not obvious. Minicolumns are still seen, and interareal connections terminate in vertical patches 200-500 microns wide.
Extracortical influences

Cortical network formation is subject to modulating influences from other brain structures.

(1) The *thalamus* is the most important subcortical structure for the neocortex. The cortex is dependent on the thalamus for sensory information from the environment and for acting into the environment. In fact, the cortex may be viewed as a supplementary device used by the thalamus for processing information.
(2) The hippocampus is a subcortical structure that is critical for the acquisition and consolidation of certain kinds of memory. It influences the construction of neocortical networks in doing so.

Bilateral hippocampal lesion in humans causes severe anterograde amnesia:
   a) loss of ability to form new declarative memories (i.e. for events and facts).
   b) impaired ability to consolidate memories less than 4 weeks old.

The hippocampus is bidirectionally connected to the neocortex through the parahippocampal gyrus.

The neocortical connectivity of the hippocampus:
   1) is limited to association areas
   2) includes both frontal and posterior association areas

Apparently, the primary sensory and motor areas do not need hippocampal input for the formation of new representations. This may be due to the elementary sensory and motor representations being genetically determined to a large degree. That is, they are unique to the species, not the individual.

Since the prefrontal cortex is involved in the generation and control of actions, the hippocampal-prefrontal connection implies that the hippocampus is also involved in consolidation of procedural memory.
(3) Lesions of the *amygdala* also cause memory deficits. Since the amygdala is known to be involved in the assignment of emotional significance to external events, it may provide the neocortex with affective and motivational inputs necessary for the registration of neocortical representations.

(4) The *brainstem neurotransmitter systems* also appear to play a role in the formation of neocortical networks. The *cholinergic* system in particular is important for memory consolidation in neocortex. With cell bodies in the *basal forebrain nuclei* (e.g. nuclear complex of Meynert), ACh is released widely in neocortex. The degeneration of these cells is linked to the severe memory impairments in dementias such as Alzheimer's Disease.
Neurotransmitters in the neocortex

The 2 most prevalent neurotransmitters in the neocortex are gamma-aminobutyric acid (GABA) and glutamate.

GABA is the most abundant inhibitory neurotransmitter. It is the main neurotransmitter of inhibitory interneurons.

Glutamate is the primary excitatory neurotransmitter of the neocortex. It is released in abundance in the transmission between pyramidal cells within and between cortical areas.

One type of glutamate synaptic receptor is the NMDA receptor. This receptor has activity-dependent properties that make it a likely substrate for LTP and other forms of synaptic modification.

Thus the NMDA receptor may play a critical role in the formation of neocortical network representations. It is interesting in this regard that NMDA receptors in the neocortex are most common in layers II and III, which are the preferred layers of termination of some corticocortical axons.
Cognitive networks in the cerebral cortex

1. The representation of memory is central to the processes of perception, learning, memory retrieval, attention, and language.

2. The development of memory representations through learning is a continuation of early ontogenetic development.

The processes of network formation that are focused on primary sensory and motor areas in early life continue into association areas throughout life.

3. The development of memory representations also may be viewed as a continuation of phylogenetic development.

The phylogenetically oldest representations are of the simplest features of the world & motor adaptations to it. They are present at birth in the structure of the primary sensory and motor cortices.

4. The neocortical networks for cognitive representation develop in the same direction as cortical connectivity: they start in lower areas and fan out into higher areas, where they intersect other networks.

A series of corticocortical pathways extend from primary sensory and motor areas to higher associative areas. These pathways are reciprocal, i.e. both
ascending and descending. Every step in both ascending and descending paths contains both *diverging* and *converging* fibers.

5. Intersection of networks in association cortex allows the creation of higher level representations such as cross-modal object representations.


7. As networks expand into association cortex, progressively more of the network-forming inputs are internal, i.e. from other high-level networks rather than directly from sensory inputs.
The following methods are used to study cognitive neuroscience:

1. Behavioral Analysis

a. Types
   Verbal (e.g. naming an object)
   Nonverbal (e.g., pressing a button)

b. Measurement
   Behavioral analysis often involves measuring the response time (delay after a stimulus) and/or accuracy (fraction of correct responses)

c. Applications
   Task analysis examines the behavior of subjects engaged in experimental tasks
   Lesion analysis examines the behavioral consequences of accidental or therapeutic brain lesions in humans and experimental brain lesions in animals

d. Tests
   Delayed matching tasks
   Stroop Test
   Wisconsin Card Sorting Task (WCST)
   Sternberg Paradigm
2. Neurophysiology

a. Neuron (unit) activity
   *Single-unit*: spike trains from single isolated neurons in the brain
   *Multi-unit*: spike trains from multiple neurons in the brain

b. Population (field potential or field) activity
   *Electroencephalogram (EEG)*: recording of cortical electrical activity from extracranial sensors
   *Magnetoencephalogram (MEG)*: recording of cortical magnetic activity from extracranial sensors
   *Local Field Potential (LFP)*: recording of cortical electrical activity from microelectrodes in cortex
   *Intracranial EEG (iEEG)*: recording of cortical electrical activity from macroelectrodes in cortex
   *Electrocorticogram (ECoG)*: recording of cortical electrical activity from macroelectrodes on surface of cortex

The Event-Related Potential (ERP) is derived from the EEG, LFP, iEEG, or ECoG by a 2-step process: (1) alignment of multiple time traces to a common sensory, cognitive, or motor event; (2) averaging the traces at each time point. The ERF is produced from the MEG by the same process.
c. Functional brain imaging

*Positron Emission Tomography (PET):* tomographic imaging of brain activity from emitted gamma rays from radioactive tracers

*Functional Magnetic Resonance Imaging (fMRI):* tomographic imaging of brain activity from the Blood Oxygen Level Dependent (BOLD) signal
The use of PET and fMRI in cognitive neuroscience is based on the concept that the neurons in brain regions which are involved in a cognitive function increase their metabolic activity during that function.

Ex 1: in FDG PET imaging, a radioactively labeled glucose analog is injected into the bloodstream, is taken up into the brain, and then in higher amounts in metabolically active cortical neurons.

Ex 2: in fMRI BOLD imaging, the ratio of oxygenated to un-oxygenated hemoglobin in the red blood cells of the local microcirculation is lower in metabolically active cortical regions.
3. Neuroanatomy

a. X-ray Computed Tomography (CT): 2D and 3D images of the brain are constructed by tomography from differences in x-ray absorption

![CT Images of the Brain](image-url)
b. *Structural Magnetic Resonance Imaging (sMRI)*: 2D and 3D images of the brain are constructed by tomography from differences in the radio frequency signal of excited hydrogen atoms as they return to their equilibrium states.
c. **Tractography**: 3D modeling techniques that image brain pathways (tracts) using *diffusion tensor imaging (DTI)* or *diffusion spectrum imaging (DSI)*, two variants of magnetic resonance imaging. Diffusion imaging maps the diffusion of water molecules in the brain.
4. Computational Analysis

a. Logical analysis

Determination of the computational (information processing) steps necessary to perform a cognitive process

b. Simulations

Artificial generation of imitations (or reproductions) of cognitive processes, usually in a digital computer but also in other hardware such as robots
5. Computational Modeling

a. Artificial Neural Network Models (PDP approach)

Models of cognitive processes constructed from ANNs having simple non-algorithmic function

b. Symbolic Models (SSP approach)

Models of cognitive processes constructed from symbolic elements having algorithmic function
6. Perturbation Methods

a. Pharmacology

Pharmacological perturbation is a technique that involves administration of chemical agents that affect brain function.

b. Electrical Brain Stimulation

Electrical stimulation of brain regions or pathways with indwelling electrodes.

c. Transcranial Magnetic Stimulation (TMS)

A noninvasive technique for stimulating focal brain regions in healthy humans. It can be used either to activate a region or to produce a “virtual lesion” by disrupting ongoing activity.

d. Transcranial Direct Current Stimulation (tDCS)

A noninvasive technique similar to TMS that uses electrical rather than magnetic stimulation.

Both TMS and tDCS are used in conjunction with sMRI to localize the target region.