Phylogeny of the cortex

The neocortex of mammals developed out of the primordial neopallium, which, like that of certain present-day amphibians, consisted of one layer of pyramidal cells.

Evolution of the neocortex led to the present-day layered neocortex, which is similar across all mammalian species.

The volume of tissue represented by the neocortex has also grown with evolution in comparison to the rest of the brain. The process by which the neocortex becomes larger and heavier with evolution is called neocorticalization.

Evolutionary development of the neocortex with respect to total brain size is greatest in primates.

Growth took place in both thickness and surface area, but more so in surface area. The expansion in surface area is 1000-fold from mouse to man. It was achieved by an increase in the number of radial columnar units. New areas developed from older ones in this process.
Each mammalian species has cortical representations for the same 5 basic sensory modalities, but the number of specialized areas for each modality varies greatly across species.

The apical dendrites of cortical pyramidal cells lengthen with neocorticalization. The pyramidal cells with soma in the deepest layers (V & VI) have the longest apical dendrites, and are the largest and oldest. Their greater dendritic surface area allows greater numbers of spines and synapses. Consequently, they have greater network-forming capacity.

The volume of subcortical white matter also greatly increased along with neocorticalization. This indicates an increasing number of cortical areas and a greater number of pathways between them.

**Conclusion:** 3 phylogenetic factors have contributed to the capacity of neocortical neurons to form synaptic connections with one another:

1) addition of areas and columns
2) elongation of apical dendrites
3) increase in number of axonal fibers in the white matter

Because this capacity is greatest in the human brain, **the ability to form complex networks that support cognition is greatest in humans.**
Ontogeny of the cortex

In ontogeny, the neocortex develops to a greater degree in size and volume than other parts of the brain. Also, the relative growth of the white matter beneath the cortex is far greater than elsewhere in the CNS.

The neocortex is largest relative to the rest of the brain in humans.

During embryogenesis, neuroblasts (neuronal precursor cells) proliferate in the ventricular zone (ventricular wall of the neural tube). Neurons migrate from the ventricular zone along glial fibers to a region directly below the cortical surface.

Ontogenetic sequence:
1) formation of a primordial plexiform layer under the cortical surface
2) outward migration of neurons from the underlying ventricular zone to the upper layers of cortex
3) descent of cell bodies to deeper cortical layers
4) proliferation of layers II to VI (and subdivisions), as descending cells settle at various distances from the surface

Newer cells migrate past older ones, which are pushed downward to form the deep layers. The thickness of the neocortex reaches more than 2 mm in full development.
Neurons proliferate and migrate within \emph{radial columnar “units”}, with their base in the germinal zone of the ventricular wall.

Migration of the pyramidal cells is primarily radial, but some interneurons also travel tangential to the cortical surface.

After the (prenatal) period of neurogenesis, cortical neurons continue to grow in size and develop their axonal and dendritic processes:
\begin{itemize}
  \item [a)] Dendrites continue to lengthen and thicken postnatally, and develop spines along their shafts.
  \item [b)] Recurrent axonal collaterals develop between neighboring pyramidal cells.
  \item [c)] Synaptogenesis begins in the third trimester of pregnancy, and continues postnatally.
\end{itemize}

Neural development is characterized by cycles of \emph{exuberant growth} followed by \emph{attrition}.

Genetically determined patterns of development are modified by \emph{trophic} (growth-promoting) factors.
For example, \emph{thyroxine}, a hormone released by the thyroid gland, promotes and protects normal cortical development.

Another group of trophic substances are called \emph{neurotrophins (NTs)}, including \emph{nerve growth factor (NGF)}.
NTs are released from dendrites dependent on neuronal activity. Cortical neuronal activity promotes the genes that cause NT expression by dendrites. It is hypothesized that groups of synchronously active neurons release NTs, which enhance synapse formation and the efficacy of transmission within the groups (reminiscent of Hebb’s neuronal assemblies).

The vast majority of synaptic connections that form in the cortex are of cortical origin, either local or distant.

The corticocortical synaptic connections of sensory and motor areas form as functional hierarchies, with primary sensory and motor areas maturing earliest, and higher areas maturing progressively later. Maturational changes in prefrontal cortex continue into puberty.
The role of experience

The development of the structure of the neocortex proceeds according to a genetic plan (*genotype*). However, the expression of the genotype as the structural phenotype is subject to influences both internal and external to the cortex.

Experience in the form of sensory-motor interactions with the environment plays a guiding role in development. Those interactions promote the development of corticocortical axonal fibers that will form the networks of cognition.

This process involves:
1) selective stabilization of neural elements that have been overproduced
2) competition for inputs among neurons and axonal terminals
3) *critical periods* – time windows before or after birth during which a set of enabling factors act to guide normal development
Cognitive network formation

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 (cognits)

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.
Extracortical factors

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 knowledge. 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.
A well-studied phenomenon that may be responsible for use-dependent synaptic plasticity is *long-term potentiation* (LTP) – enhancement of synaptic strength from rapid presynaptic firing.

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.
Basic structure of cognitive networks

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

2. The development of knowledge 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 knowledge representations also may be viewed as a continuation of phylogenetic development.

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

That structure may be considered a form of memory since it contains information about the world and the species that has been stored during evolution. Fuster calls it *phyletic memory* (memory of the species).

Phyletic memory can be retrieved by the individual organism for adaptation to its surroundings. The *critical periods* of early development are critical for tuning the basic sensory and motor apparatus (representing phyletic memory) to the individual’s environment.
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.
Fig. 2.15:
A: the network associates 2 coincident visual stimuli
B: memory of the associated visual stimuli is retained in the pattern of facilitated synapses within visual cortex
C: the network associates visual and tactile stimuli
D: memory of the associated visual-tactile stimuli is retained in the pattern of facilitated synapses within visual and somatosensory cortices and in heteromodal association cortex