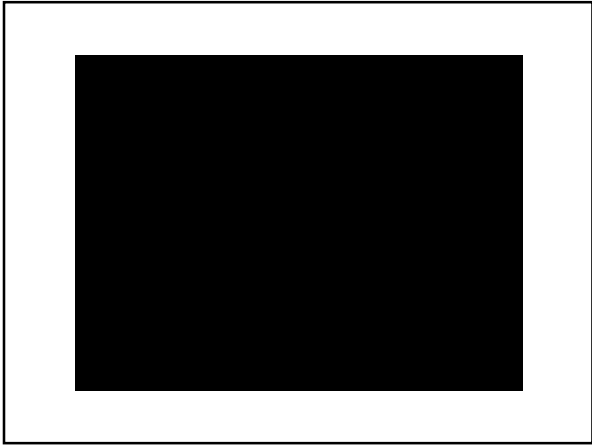
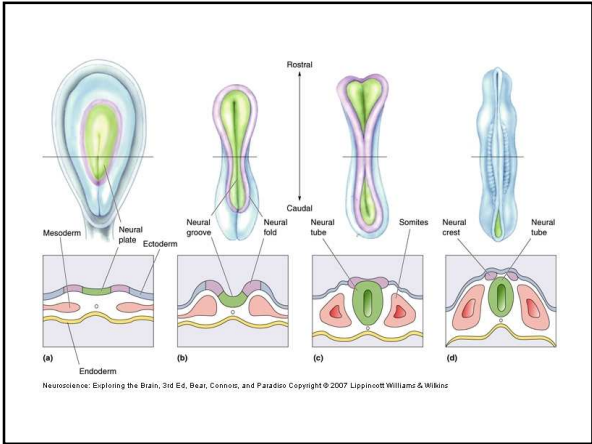
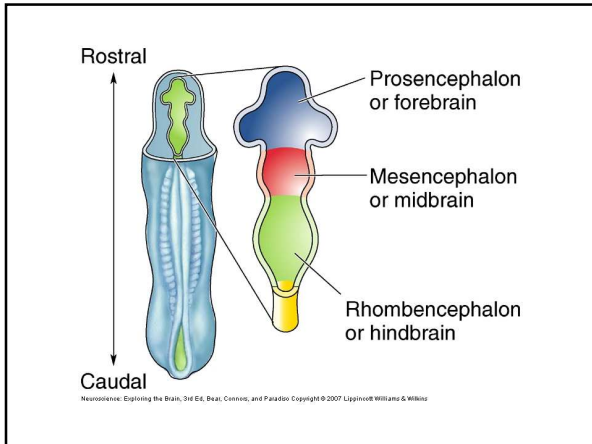


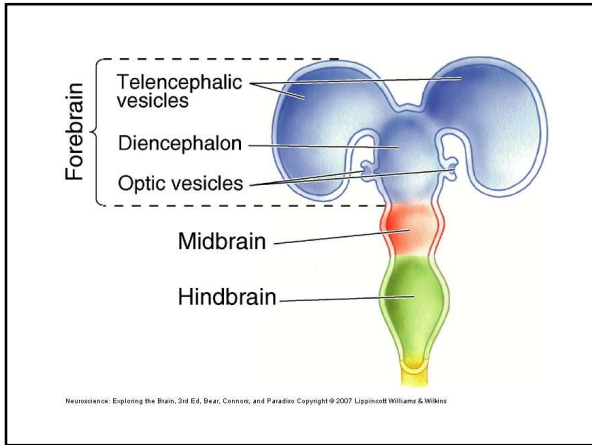
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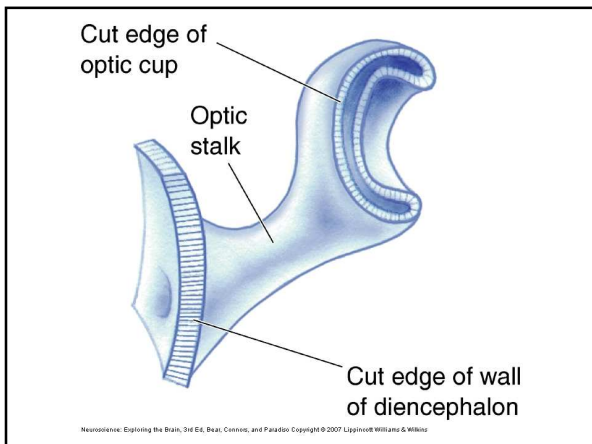
Lecture on Neural Development

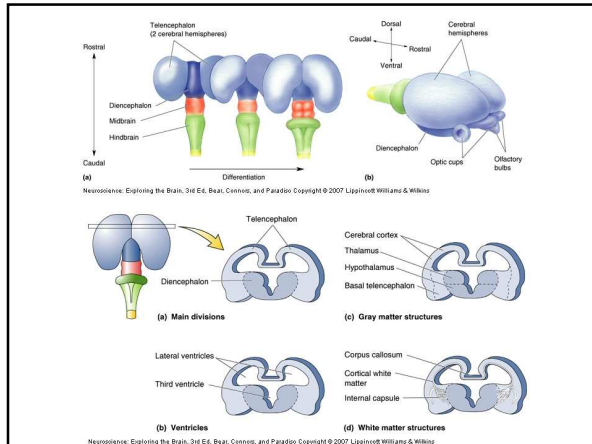


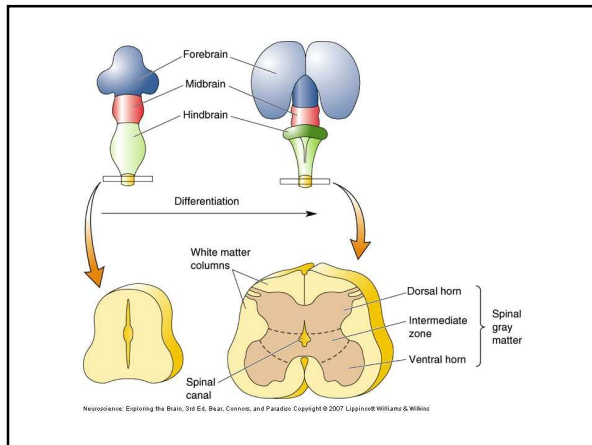


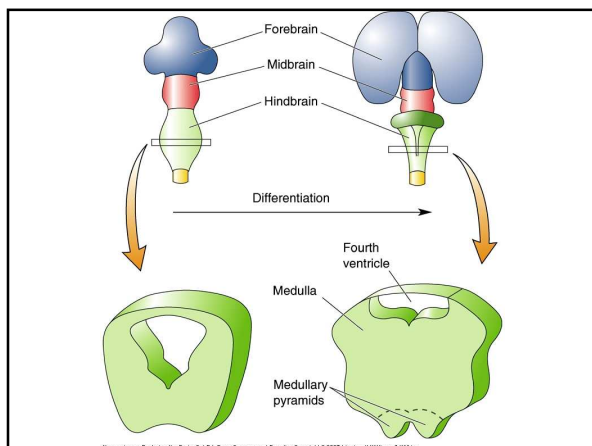


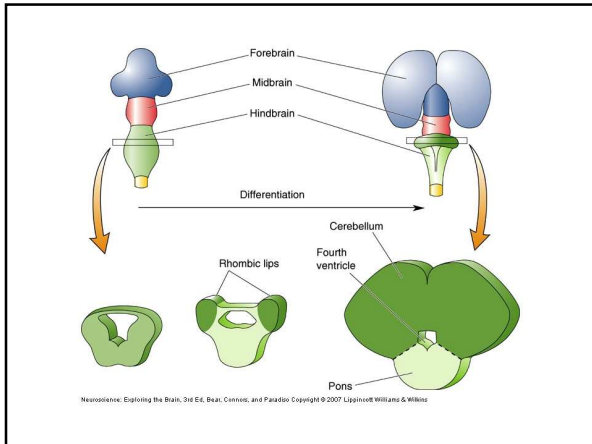


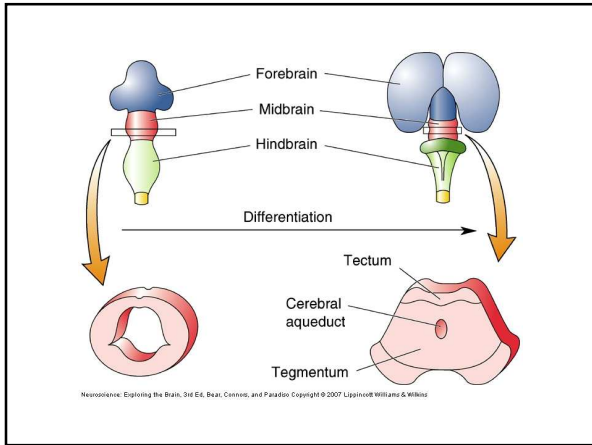


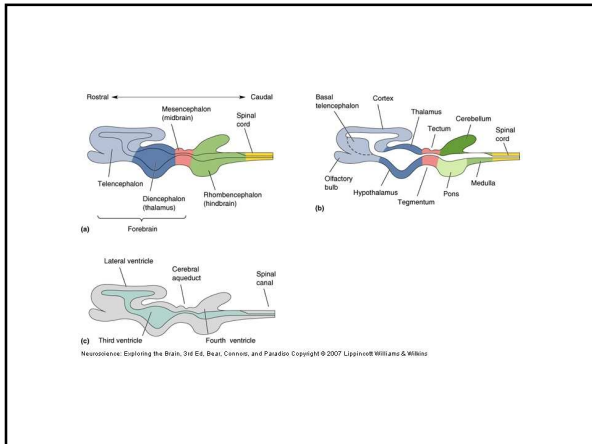


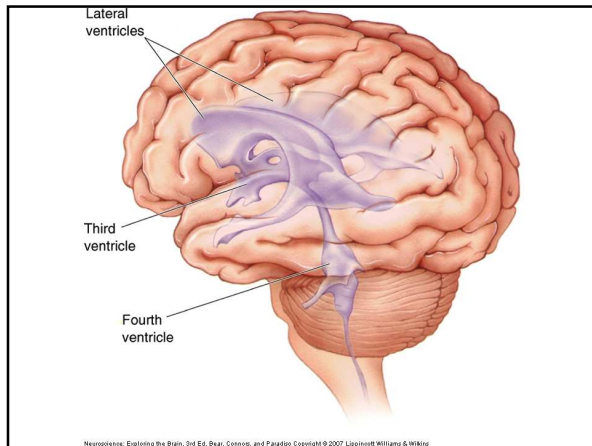


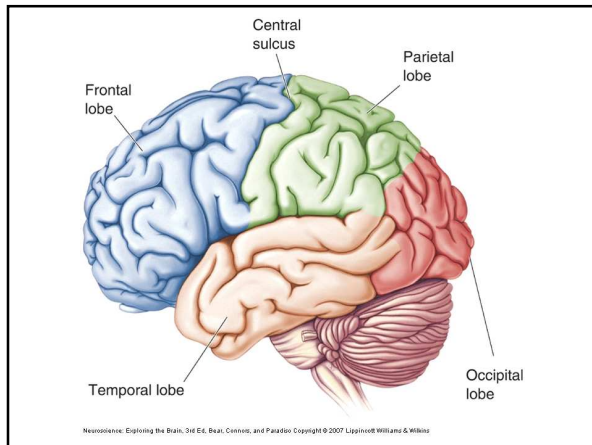


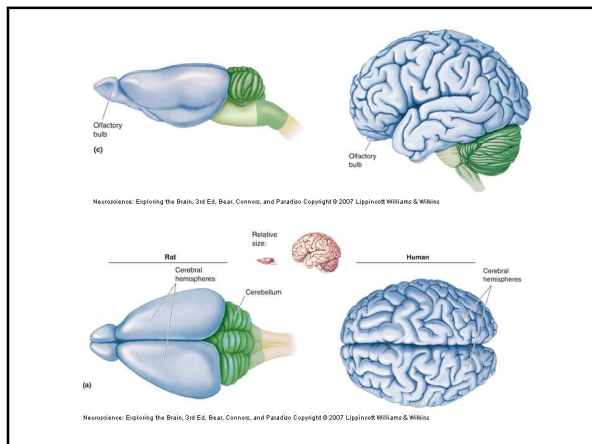


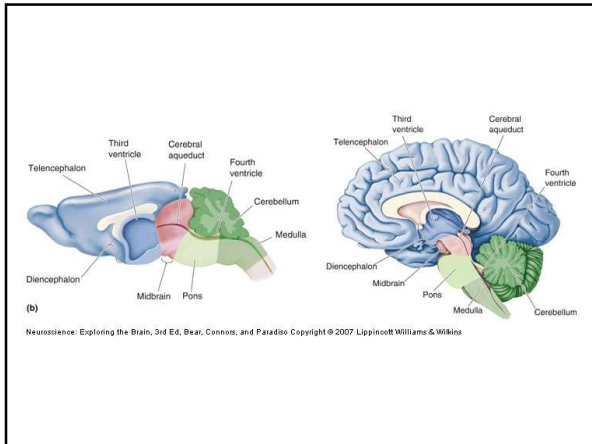


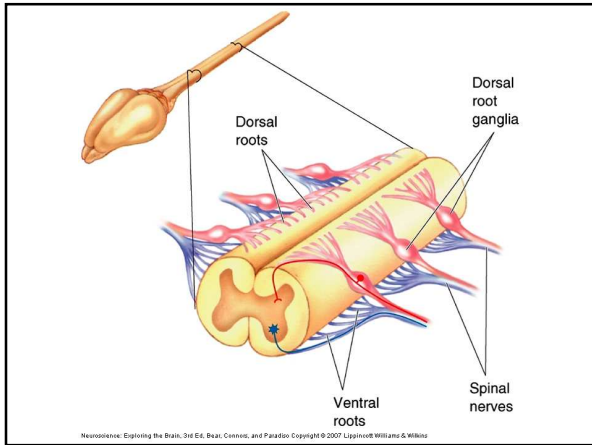


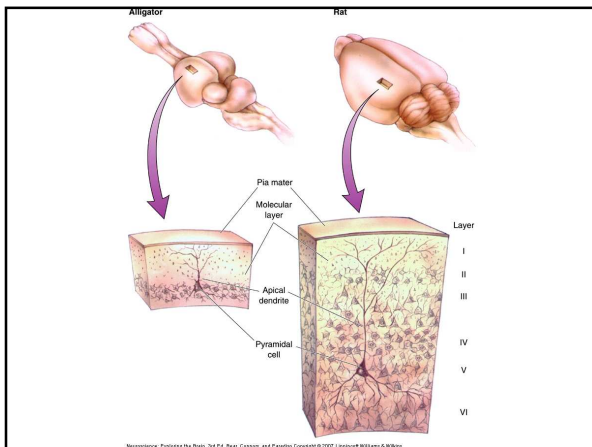












Neural cell categories

- After the ectodermal tissue has folded into the neural tube, another series of signaling interactions determine the type of neural cell to which it gives rise.
- Many of these neural signals have been characterized as GROWTH FACTORS.
- The mature nervous system contains a vast array of cell types, which can be divided into two main categories:
 - the **neurons**, primarily responsible for signaling,
 - and supporting cells called **glial cells**.

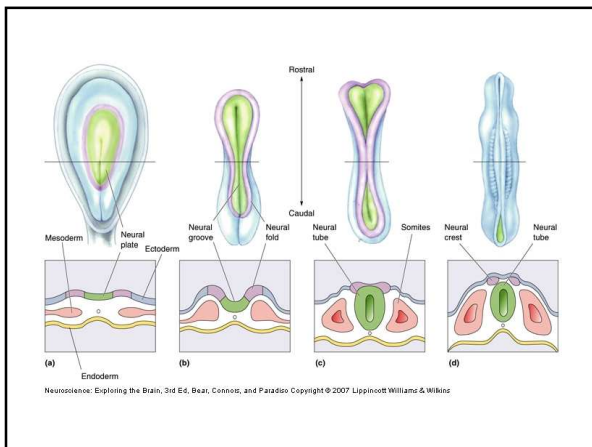
Growth factors are proteins that bind to receptors on the cell surface, with the primary result of activating cellular proliferation and/or differentiation. Many growth factors are quite versatile, stimulating cellular division in numerous different cell types; while others are specific to a particular cell-type.

| Growth Factors | | | |
|--|--|--|---|
| Factor | Principal Source | Primary Activity | Comments |
| Platelet-Derived Growth Factor PDGF | platelets, endothelial cells, placenta | promotes proliferation of connective tissue, glial and smooth muscle cells | two different protein chains form 3 distinct dimer forms; AA, AB and BB |
| Epidermal Growth Factor EGF | submaxillary gland, Brunners gland | promotes proliferation of mesenchymal, glial and epithelial cells | |
| TGF- α | common in transformed cells | may be important for normal wound healing | related to EGF |
| Fibroblast Growth Factor FGF | wide range of cells; protein is associated with the ECM | promotes proliferation of many cells; inhibits some stem cells; induces mesoderm to form in early embryos | at least 19 family members, 4 distinct receptors |
| Nerve Growth Factor NGF | | promotes neurite outgrowth and neural cell survival | several related proteins first identified as proto-oncogenes; trkA ("trackA"), trkB, trkC |
| Erythropoietin | kidney | promotes proliferation and differentiation of erythrocytes | |
| Transforming Growth Factor TGF- β | activated Th ₁ cells (T-helper) and natural killer (NK) cells | anti-inflammatory (suppresses cytokine production and class II MHC expression), promotes wound healing, inhibits macrophage and lymphocyte proliferation | at least 100 different family members |
| Insulin-like Growth Factor IGF-I | primarily liver | promotes proliferation of many cell types | related to IGF-II and proinsulin, also called Somatomedin C |
| IGF-II | variety of cells | promotes proliferation of many cell types primarily of fetal origin | related to IGF-I and proinsulin |



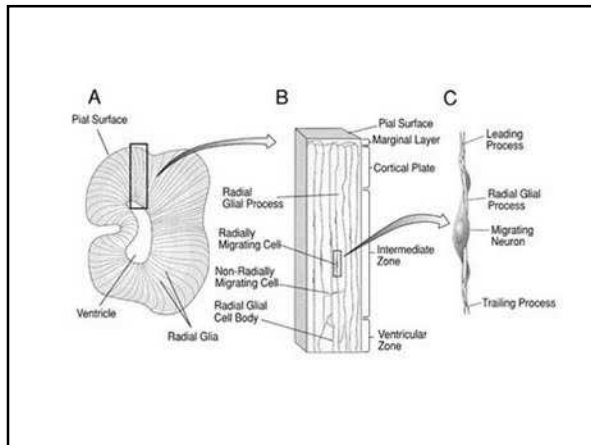
Factors in cell formation

- Researchers are finding that the destiny of neural tissue depends on a number of factors, including growth factors and where the position of the pluri-potent or multi-potent cells are located when they receive the signal.
 - For example, a key factor in spinal cord development is a secreted protein called **sonic hedgehog** that is similar to a signaling protein found in flies.
 - The protein, initially secreted from mesodermal tissue lying beneath the developing spinal cord, marks young neural cells that are directly adjacent to become a specialized class of **glial cells**.
 - Cells further away are exposed to **lower concentrations of sonic hedgehog protein**, and they become the motor neurons that control muscles.
 - An even **lower concentration** promotes the **formation of interneurons** that relay messages to other neurons, not muscles.



Cell Cycle and neuron generation

- Neurons of the cerebral cortex are generated in the ventricular zone of the neural tube, an epithelial layer of **stem cells** that lines the lateral ventricles.
- Once they have left the cell cycle, the neurons migrate (on **glial** cells) out of the VZ to form the cortical plate (gray matter for the cortex).
- On the cortical plate, neurons become organized into well defined layers.



As the brain develops, neurons migrate from the inner surface to form the outer layers. Left: Immature neurons use fibers from cells called glia as highways to carry them to their destinations. Right: A single neuron, shown about 2,500 times its actual size, moves on a glial fiber. (10^{-6} m/hr)

Illustration by Lydia Kibiuk, Copyright © 1995 Lydia Kibiuk.

Improper migration leads to diseases including childhood epilepsy, mental retardation, lack of sense of smell and possibly many others.

Hiroshima/Nagasaki Effects

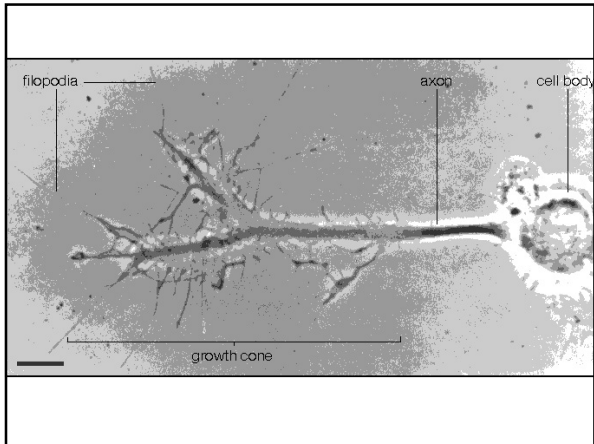


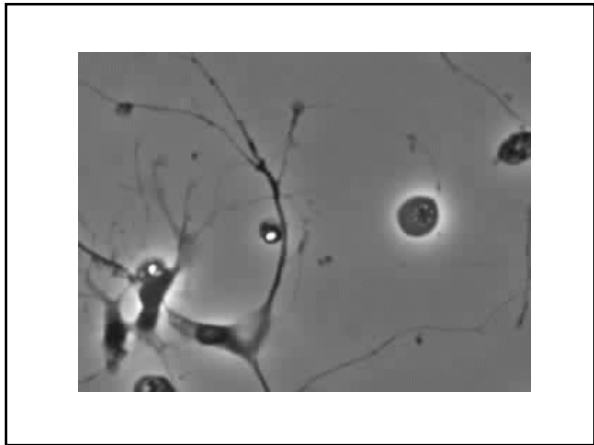
Timing of Cell Differentiation

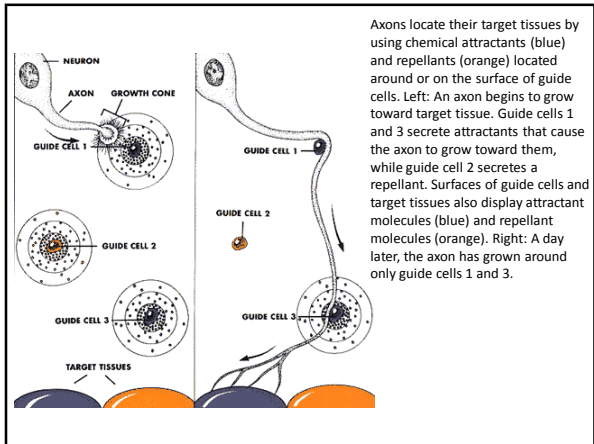
- Remarkably, the final position of the neuron is correlated exactly to its **birthdate**
- Cells leaving later migrate past the older neurons (in deeper cortical layers) to the outermost cortex.
- The layering of the cortex is thus an inside-first outside-last layering.

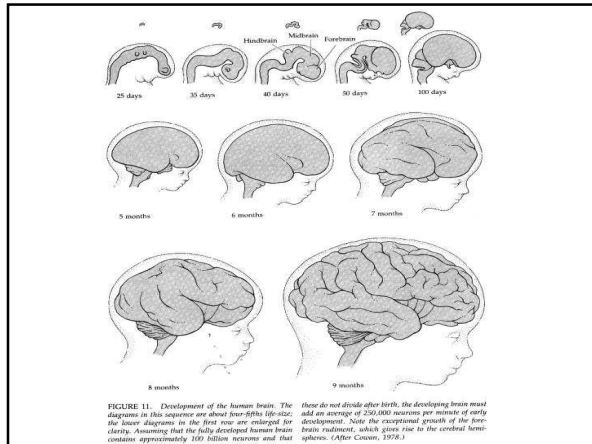
Axon guidance mechanisms


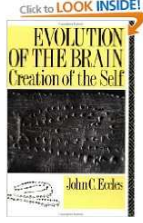
- Axonal growth is led by growth cones
 - Filopodia (growing from axons) are able to sense the environment ahead for chemical markers and cues.
 - Mechanisms are fairly old in evolutionary terms.
- Intermediate chemical markers
 - Guideposts studied in invertebrates
- Short and long range cues
 - Short range chemo-attraction and chemo-repulsion
 - Long range chemo-attraction and chemo-repulsion
- Gradient effects











Sir John Carew Eccles (January 27, 1903 – May 2, 1997) was an [Australian](#) neurophysiologist who won the 1963 [Nobel Prize in Physiology or Medicine](#) for his work on the synapse. He shared the prize with Andrew Fielding Huxley and Alan Lloyd Hodgkin. Eccles was the recipient of many honors, including a knighthood in 1958. In 1963, he was named "Australian of the Year." His research contributed significantly to knowledge of the neurophysiological processes by which thought is processed, and to unraveling the complexities of the human brain.
