Huntington’s Disease & Early Nervous System Development

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The cups fell to the floor with a crash. Was this the alarm signal? Or was it forgetting his sister’s phone number the other day, even though he calls her often? Was the telling event last weekend, when he burst into a string of curse words and tailgated the driver who had just cut him off?

Incidents that to other people may seem like simple clumsiness, forgetfulness or an overreaction brought on by stress could mean disaster for Martin, a 48-year-old shipping agent. For years, he had been observing himself and his siblings with a sharp eye. Any little slip could constitute a somber omen. But after this latest string of mishaps, he could not bear the uncertainty any longer.

He went in for the blood test. Three days later what Martin had feared since childhood was confirmed as the terrible truth: he was suffering from the genetic mutation that had killed his mother, his uncle and his grandfather.
Huntington’s Disease

- An inherited disorder
- Mutation discovered in 1993
- A single mutation that ruins neurons.
- Progressive destruction of the brain.
- No symptoms of disease until middle-aged.
- Progression can be gradual.
- 30,000 Americans diagnosed with HD
- DNA test can identify the mutant gene.
huntingtin gene – chromosome 4

Nancy Wexler and Venezuelan man with Huntington’s disease
Klein/Thorne: Biological Psychology
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Gene:
- A unit of heredity, residing at a specific point on a chromosome;
- A length of DNA that specifies a product

Chromosome:
- Condensed, linear DNA and protein, containing genes and intervening sequences

DNA:
- The genetic material in all living organisms;
- In eukaryotes, located in the nucleus on chromosomes
Aligning pairs of similar chromosomes during meiosis

Replicating genetic material

 Crossing over

Breaking apart and rejoining at the crossover
If the CAG sequence appears 35 to 40 times or more on the gene, the resulting protein will contain glutamine molecules that are too long.
Primitive Organisms

Paramecium caudatum

A Sponge.
Jellyfish – no true nervous system

Jellyfish have a nerve net with individual nerve cells having a sensory or motor function.
Planaria

Ganglia, appear in planarian (flat worms) and the ganglia are connected by nerve cords forming a true nervous system.
Roundworm: more advanced!

Circumpharyngeal nerve ring controls actions throughout the nervous system.
Earthworm: segmented

Each segment can act independently from the others.

*Sensory* neurons convey information from the outside world to the ganglion *in only one segment*, and *motor* neurons control the responses of that segment.
The nervous systems of an insect: Klein/Thorne: Biological Psychology
Insect Nervous Systems: three vesicles
### Table 3.1
Comparison of Vertebrate and Invertebrate Nervous Systems

<table>
<thead>
<tr>
<th>Vertebrate</th>
<th>Invertebrate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protective covering over CNS</td>
<td>No protective covering over CNS</td>
</tr>
<tr>
<td>Cell bodies inside bony coverings; axons outside</td>
<td>Axons in inner core of ganglia; cell bodies in outer ring</td>
</tr>
<tr>
<td>CNS located on dorsal surface</td>
<td>Nerve cord usually on ventral surface</td>
</tr>
<tr>
<td>Motor responses controlled contralaterally</td>
<td>Motor responses controlled ipsilaterally</td>
</tr>
<tr>
<td>Sensory information contralateral and ipsilateral</td>
<td>Sensory information exclusively ipsilateral</td>
</tr>
<tr>
<td>Myelinated axons for rapid transmission of neural messages</td>
<td>Few giant axons for rapid transmission of neural messages</td>
</tr>
<tr>
<td>Larger number of neurons</td>
<td>Smaller number of neurons</td>
</tr>
</tbody>
</table>
Brains of Several Vertebrate Species

- Human
- Monkey
- Cat
- Goose
- Alligator
- Frog
- Codfish

Legend:
- Yellow: Forebrain
- Red: Midbrain
- Purple: Hindbrain
Figure 3.11 A cross section of the human brain
Klein/Thorne: Biological Psychology
Amount of cortex devoted to different body parts in some mammals.
Structural Development: Formation of Nervous System

- When the neural tube fails to close, a Neural tube defect (NTD) is produced.
- One of these is Spina bifida, which may result in paralysis, limb deformities and mental retardation. Many cases of spina bifida can be prevented with supplemental Folic Acid.
Neural Plate cells = stem cells
unlimited capacity for self renewal

Neural plate: the thickened ectodermal layer of the embryo. The ectoderm will become the nervous system.
21 DAYS

Neural fold
Neural groove
Neural tube
Neural crest cells migrate away from the neural tube to form several types of tissue – including the sensory and autonomic neurons of the PNS.
Initial differentiation into three vesicles:

- **Prosencephalon** or forebrain
  - **Telencephalon** (cerebral cortex, basal ganglia, and the limbic system)
  - **Diencephalon** (epithalamus, thalamus, and hypothalamus)
- **Mesencephalon** or midbrain (does not divide)
- **Rhomencephalon** or hindbrain
  - **Metencephalon**
  - **Myelencephalon**
Differentiation of the Brain

**Three-Vesicle Stage**
- Forebrain (prosencephalon)
- Midbrain (mesencephalon)
- Hindbrain (rhombencephalon)
- Caudal part of neural tube

**Five-Vesicle Stage**
- Telencephalon
- Diencephalon
- Mesencephalon
- Metencephalon
- Myelencephalon
- Caudal part of neural tube

**Adult Form**
- Cerebral cortex, basal ganglia, hippocampus, amygdala, olfactory bulb
- Epithalamus, thalamus, subthalamus, hypothalamus, retinas, optic nerves and tracts
- Midbrain (tectum, tegmentum)
- Pons and cerebellum
- Medulla
- Spinal cord
Ventricular system develops in the cavity inside the neural tube, contains CSF

Four ventricles:
- Two lateral ventricles
- Third ventricle
- Fourth ventricle
Structural Development: The Developing Spinal Cord

- **Alar plate** (dorsal portion of neural tube)—gives rise to sensory neurons and interneurons of the spinal cord’s dorsal horn.
- **Basal plate**—forms ventral portion of the spinal cord where motor neurons originate and the interneurons of the ventral root form.
- **Sympathetic** and **Parasympathetic** nervous systems also derive from the basal plate.
28 days
**Leading process of migrating neuron**

**Nucleus of migrating neuron**

**Stationary process of a radial glial cell**

**Trailing process of a migrating neuron**

**Ventricle**
Cellular Development: Formation of Neurons and Glial Cells

- **Migrating cells**
  - Also guided by glycoproteins
  - Glycoproteins allow neurons to bind to other neurons or radial glial cells (a handhold).
  - Failures of the adequate production of glycoproteins may lead to behavioral deficits.
  - Cell migration dysfunction is implicated in schizophrenia where abnormal distributions of neurotrophins have been found in the brains of schizophrenic patients.
Proliferation of neurons

23 days

25 days
Cellular Development: Formation of Neurons and Glial Cells

- **Migrating cells**
  - Some daughter cells migrate from the inner to outer areas of the nervous system.
  - Guided by radial glial cells
  - Creep along it like a rope
A layer of ectodermal cells form on the inner surface of neural tube and divide to form:

- **Ventricular layer**
  - Divide into daughter cells
    - Some go to marginal layer (or outer surface of neural tube)
    - Some go to intermediate layer of neural tube
    - Some become neurons or glial cells and some migrate back to the ventricular layer
Figure 3.19 The proliferation of neurons and glial cells on the inner surface of the neural tube
Cellular Development: Formation of Neurons and Glial Cells

- Daughter cells migrate to:
  - layer between the intermediate layer and marginal layer and form the cortical plate which develops into the cortex.
  - subventricular layer is formed between the intermediate and ventricular layer, becoming either glial cells or interneurons.
  - daughter cells remaining in the ventricular layer develop into ependymal cells, which form the lining of the brain’s cavities (ventricles and central canal of the spinal cord).
Figure 3.22  The growth cone
Klein/Thorne: Biological Psychology
Neural Cell Differentiation

- **Cell-autonomous differentiation** is controlled by genetic programming.
  - A Purkinje cell will develop into its distinctive form even if grown in culture out of its environment.
- **Induction**—other cells influence the final form.
  - Spinal motor neuron is influenced by the notochord to become a spinal motor neuron.
    - Vitronectin is the chemical which directs the development of spinal motor neurons.
Cell autonomous differentiation - neurons develop without outside influence by genetic programming that directs them to develop in a particular way.
Cell interactions model
Cells differentiate into their distinctive type, e.g. unipolar, multipolar, etc.

Image shows Purkinje cells at different developmental ages
Neurogenesis is the formation of new neurons.

- Few neurons are formed after birth in humans
- Exceptions are:
  - cerebellar cells, olfactory receptor neurons, hippocampal neurons, and some cortical neurons
  - These exceptions allow for neuroplasticity.
Glial Cell Development

- Glial cells develop from the ventricular layer.
- Glial cells develop more after birth.
- A major function of glial cells:
  - Myelination of neurons by Schwann cells in the peripheral nervous system and by oligodendrocytes in the central nervous system.