Genetics, brain development, and behavior

Jan. 13, 2004

Questions:

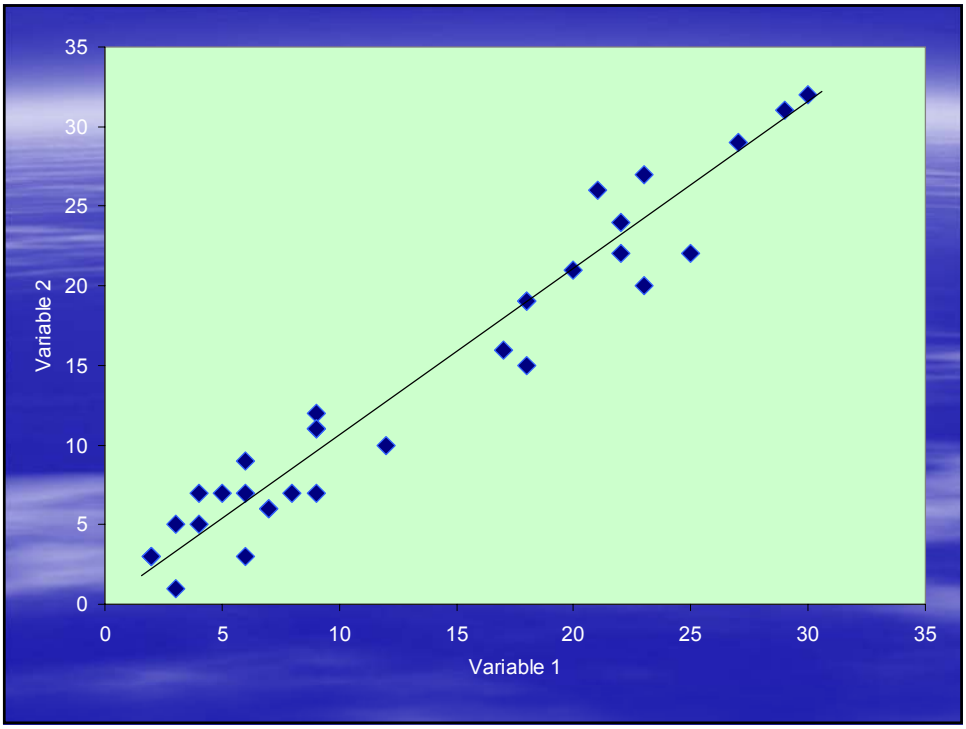
- Does it make sense to talk about genes “for” behavior?
- How do genes “turn into” brains?
- Can environment affect development before birth?
- What happens to turn 1 cell into a baby in 9 months?

Outline

- Behavior genetics
- Biology of genetics
  - How cells divide
  - How genes make proteins
- Brain Development
  - Role of genetics
  - Role of environment
- Where does behavior come from?

Behavior Genetics

- Estimate contribution of genes and environment to behavioral characteristics
- Measures how DIFFERENT people who are related to different degrees are
  - If there isn't any variability, there's NO effect of genetics according to this math
  - Behavioral genetics does not measure the amount of behavior caused by genes!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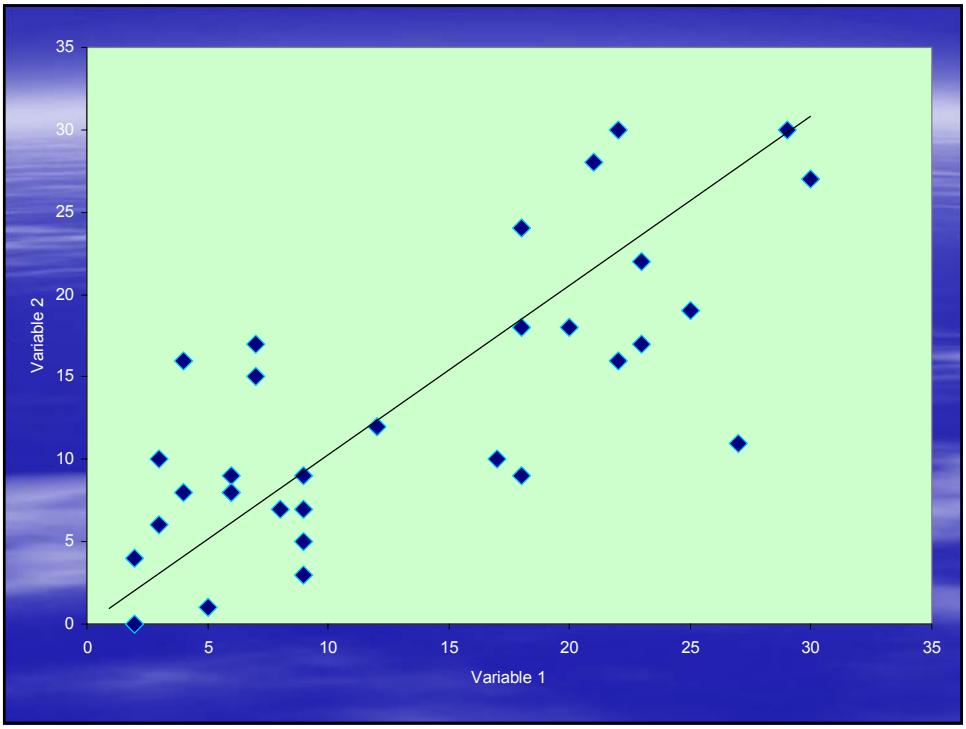
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Behavior Genetics

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- Methods
  - Twin Studies
  - Adoption Studies

Twin Studies

- How similar/different are identical vs. fraternal twins?
  - How do people treat twins who do and do not look alike?
  - Within a stable environment, identical twins may be very similar, but in very different environments, they may be very different
    - Prenatal environment
    - Adoption

Adoption Studies

- How similar are adopted people to their adoptive families (environment) vs. their biological families (genetics)
  - How similar is the environment into which the child is adopted (selective placement)?
  - What can be considered a "different" environment?
  - What is the effect of prenatal environment?

Environmental contributions

- Shared environment
  - Environment that siblings/twins have in common (effects of family, community, etc.)
- Non-Shared environment
  - Effects specific to an individual (school, hobbies, etc.)
- Gene/environment correlation
  - Children may shape their own environment because of their genetics
    - Passive – Parents interests influence children's environments
    - Evocative – Others in the world react to individuals because of their genetic traits
    - Active – Individuals seek or create environments based on their genetic traits

Can fraternal twins appear alike?

Can identical twins appear different?

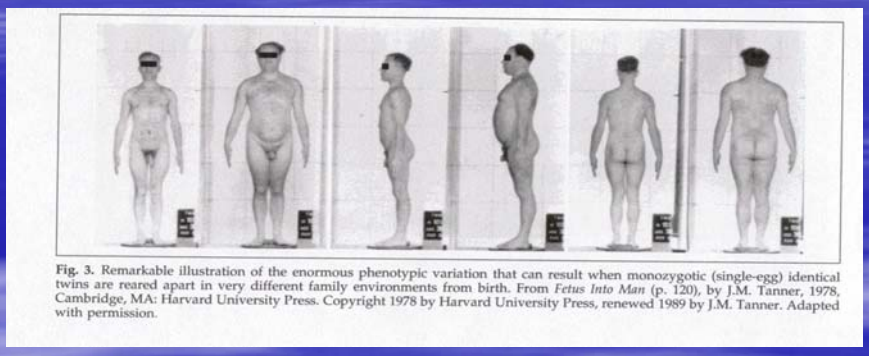


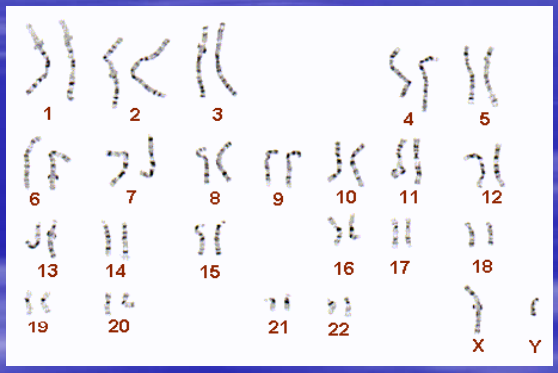
Fig. 3. Remarkable illustration of the enormous phenotypic variation that can result when monozygotic (single-egg) identical twins are reared apart in very different family environments from birth. From *Fetus Into Man* (p. 120), by J.M. Tanner, 1978, Cambridge, MA: Harvard University Press. Copyright 1978 by Harvard University Press, renewed 1989 by J.M. Tanner. Adapted with permission.

From Gottlieb, 2000

- Twin, adoption, and family studies can provide important estimates for the role of genes in development and behavior
- However, these estimates do not tell us about how genes turn into the structures that will become a brain
- What are genes, how do they work, and how can they affect behavior?

Basics of genetics

- DNA
  - DNA is a collection of chemicals within the nucleus of each cell that forms the building blocks for proteins, from which the organisms (including the brain) is built
  - 2 functions of DNA
    - DNA replicates itself to form new cells from progenitor cells
    - DNA also produces proteins which can be used to allow different functions for different types of cells



Cellular Reproduction

- Meiosis
  - One cell → one cell
  - Basis for reproduction
  - How are we all different from each other?
- Mitosis
  - Basic cell division
  - One becomes 2 cells
  - If all cells are the same, how do we have different body parts

Meiosis

- Humans have 23 pairs of chromosomes, 22 of which "match". The 23rd pair, the sex chromosomes match in females (both x) but do not match in males (one x, one y)
- One member of each pair comes from each parent.
  - The DNA from each parent is transmitted in the gametes (sperm and egg)
  - Gametes are formed through meiosis
  - Each parent contributes half the DNA that the offspring will have
  - Gametes combine to form a new organism with 2 pairs of each chromosome (1 from each parent)

Cross – over events

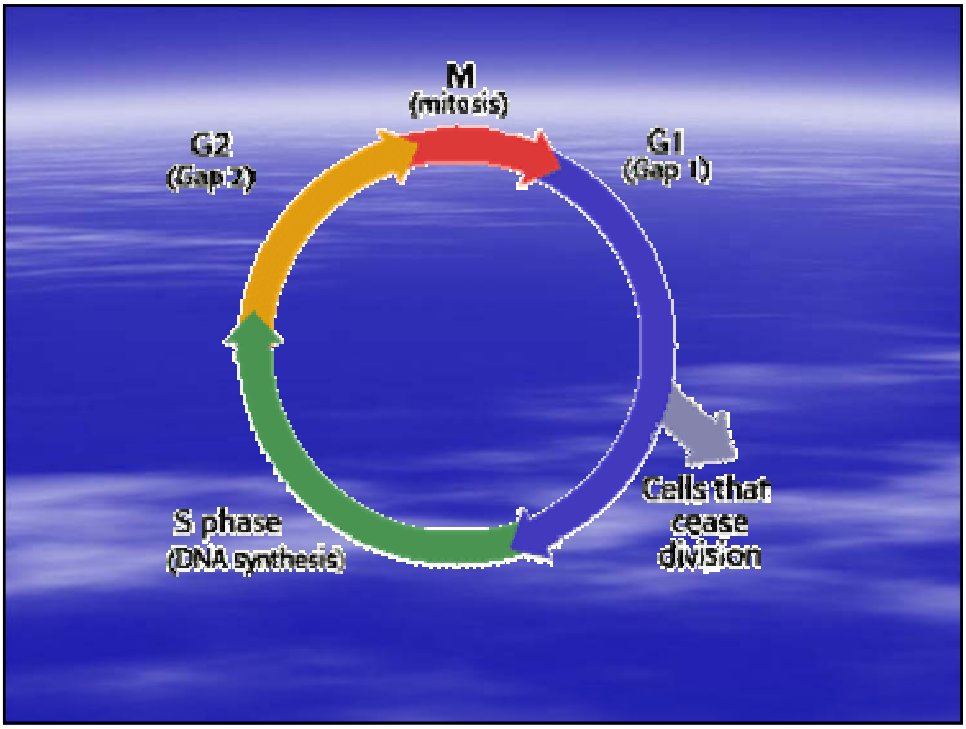
(Or "Why you don't look exactly like your sister")

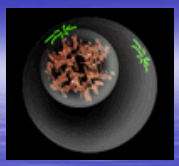
Cross – over events

(Or "Why you don't look exactly like your sister")

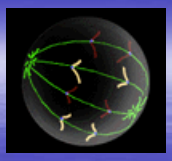
Mitosis: The cell cycle

- The cell cycle includes 4 phases
  - G1 is the period before DNA replicates
  - During the S phase, DNA replicates itself
  - G2 is the period after DNA replicates and before the cell divides
  - During Mitosis, the cell divides into 2 daughter cells, which are genetically identical to the original cell

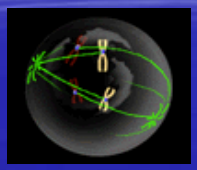




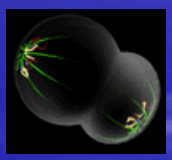
Prophase: Chromosomes and spindles begin to form



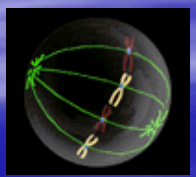
Anaphase: Paired chromosomes separate and move to opposite sides of the cell



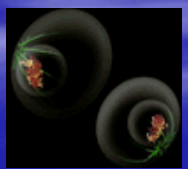
Prometaphase: Chromosomes begin moving into alignment



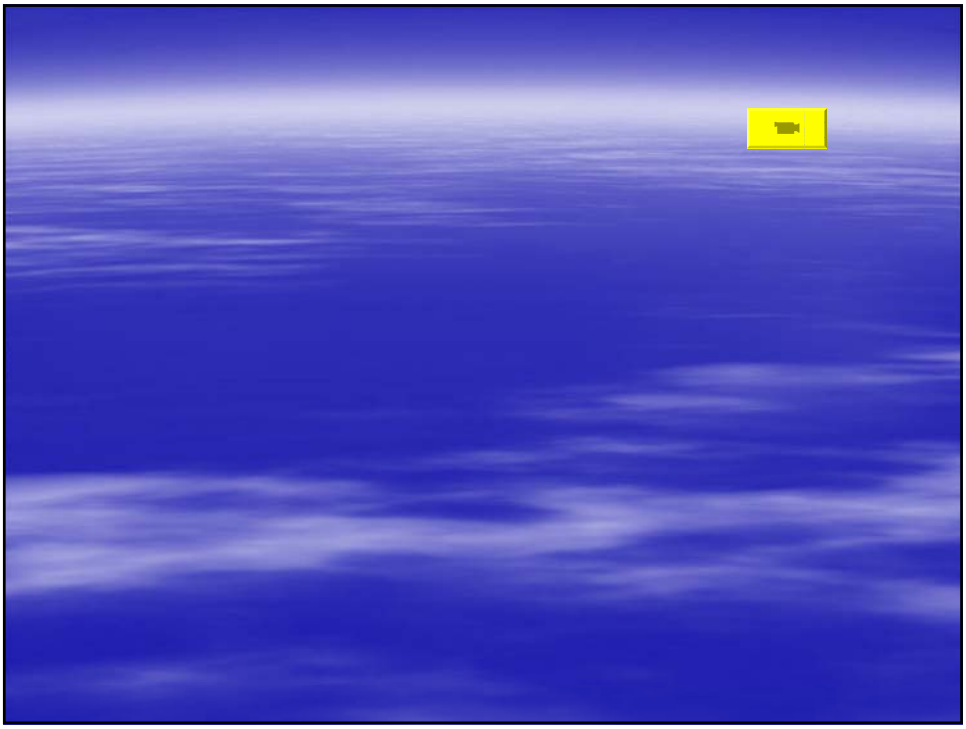
Telophase: Chromosomes disperse and spindles Begin to separate cells

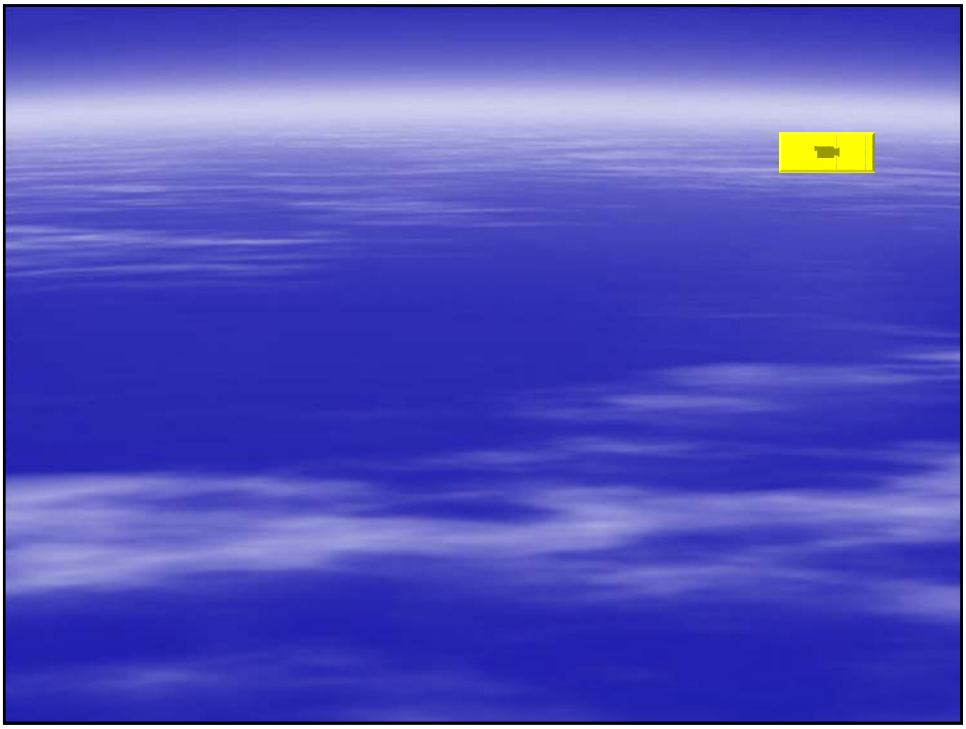


Metaphase: Paired chromosomes line up in the middle of the nucleus

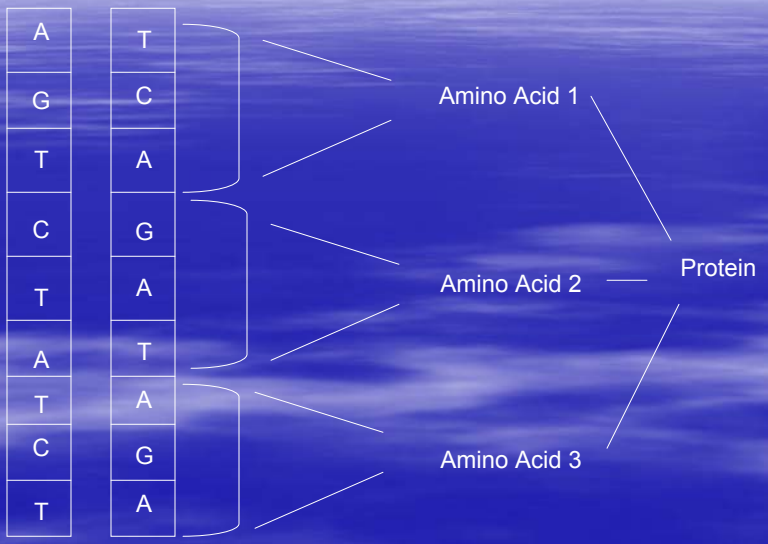


Cytokenesis: Cell is pinched in middle, two daughyer cells form





What do genes do?



- How do genes know to make proteins?
- Genes are regulated
  - By other genes
  - By signals from the environment

Gene Regulation

Gene 1

Gene 2

Gene 3

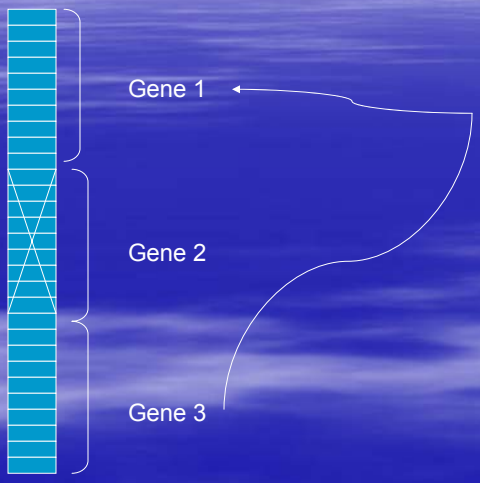
Gene Regulation

Gene 1

Gene 2

Gene 3

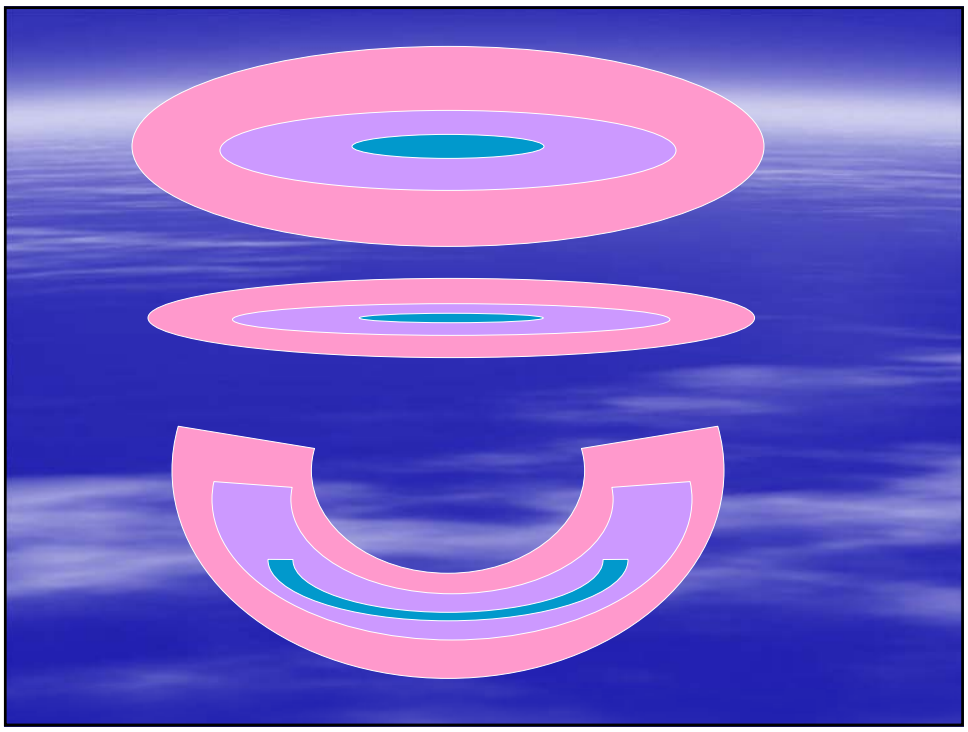
Gene Regulation



- What do proteins do?
  - Protiens form the materials for
    - cells
    - neurotransmitters (the chemicals the brain uses to communicate
    - Receptors (structures on the “receiving end” of communication from another cell

Early embryogenesis

- The early embryo forms 3 layers
  - Ectoderm
  - Mesoderm
  - Endoderm
- Skin and CNS are both made of Ectoderm
  - How can THAT be?



Role of genetics and environment in neural tube formation

- Cells in different parts of forming neural tube respond differentially to neuralizing signals
- These responses represent an interaction between the genes being expressed in the cells and the environment around them

PRENATAL NEURONAL DEVELOPMENT

Phases in life of neurons:

1) **Proliferation - generation of neurons**

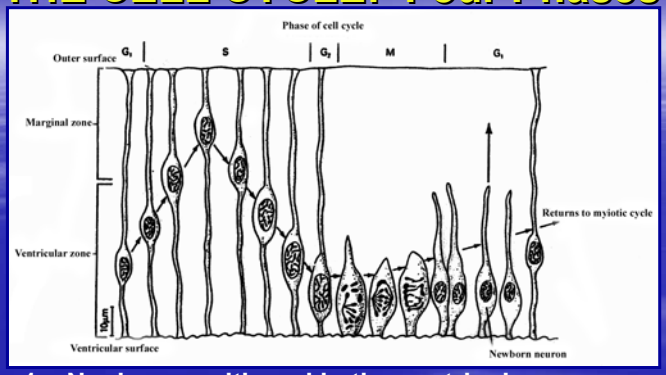
2) **Migration – movement of neurons to target brain region**

3) **Differentiation - connection with other cells, functional specification**

Proliferation

- Neurons in the cortex multiply
- A large number of neurons are made in the area surrounding the ventricles (the marginal zone).
- How are genes involved?
  - Cells multiply through mitosis, the phase of the cell cycle influences when cells will stop dividing
  - These events are probably influenced by external signals – gene expression through signals from outside the cell

THE CELL CYCLE: Four Phases



Gap1: Nucleus positioned in the ventricular zone.

Synthesis: Nucleus migrates toward marginal zone, where DNA synthesis occurs.

Gap 2: Nucleus migrates back to ventricular zone, it retracts the cytoplasmic process that attached it to the ELM.

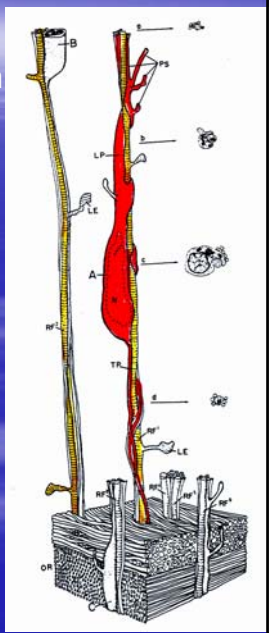
Mitosis: The cell divides (undergoes mitosis), and each of the two cells send out cytoplasmic processes that attach to the ELM.

Migration along radial glial cells

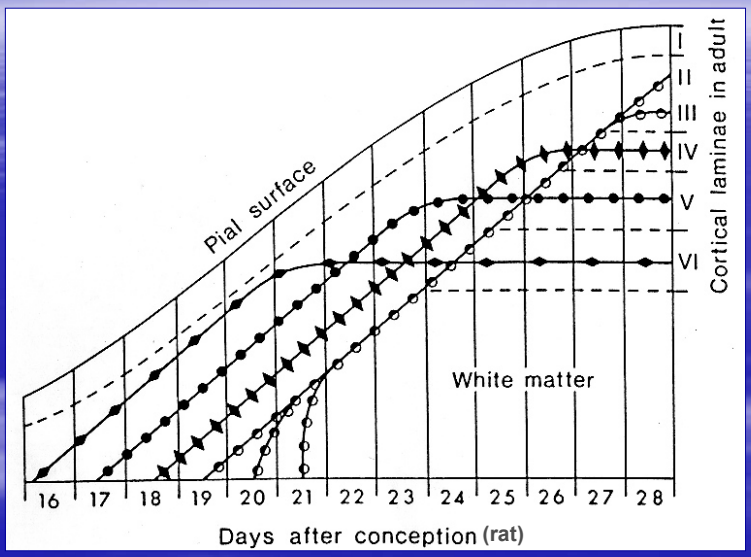
Radial glial cells form a kind of scaffold run from the margin of the Proliferative Zone to outer edge of the brain.

After the new neuron has it's birthday:

- locates a nearby radial glial cell
- attaches and propels along radial glial
- "recognizes" final destination and detaches
- neurons that are produced early in development form the deep layers of cortex, cells that are produced form the surface layers



INSIDE-OUT SPATIOTEMPORAL ORDER



Gives rise to the layered organization of the cortex.

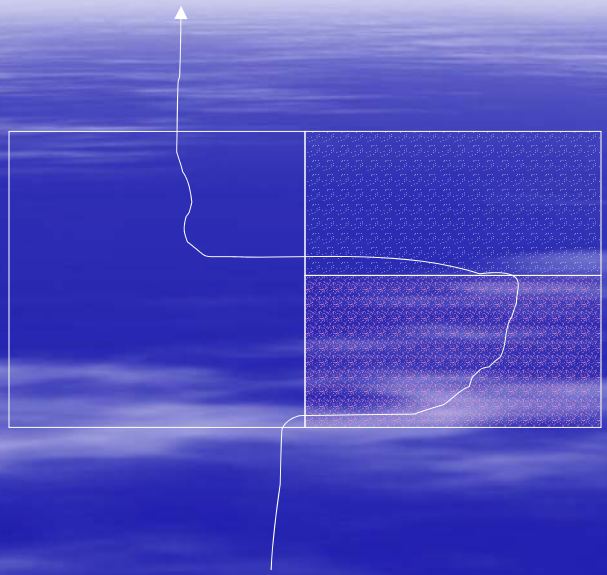
Role of genetics in migration

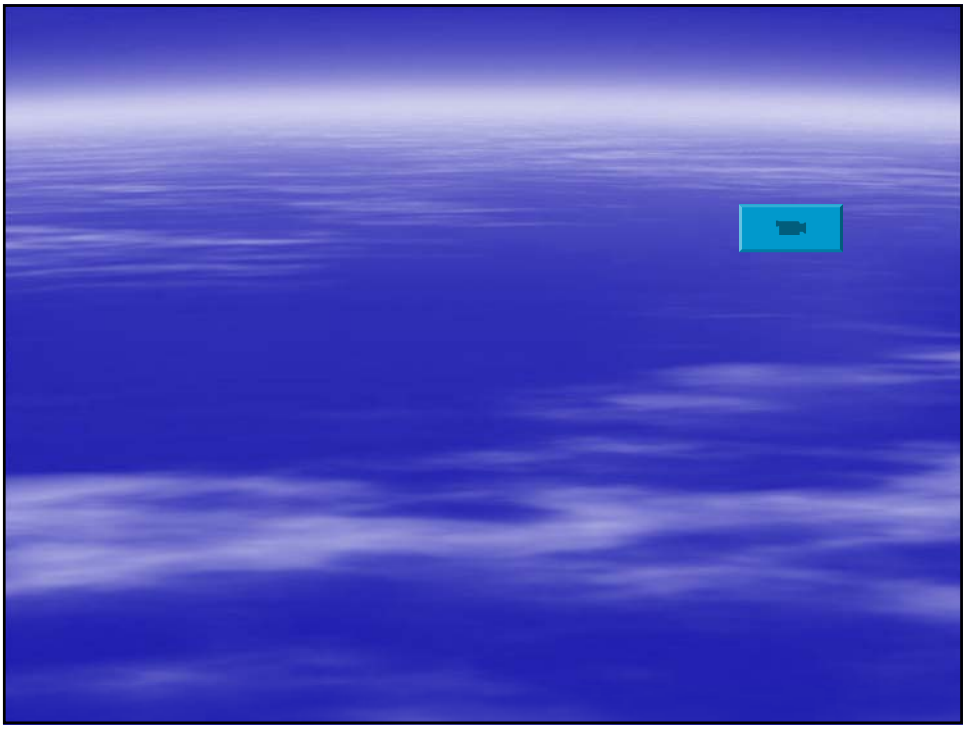
- There is a signal that affects mitosis and commences migration
  - Not clear how this signal works or what it is, but it is probably in response to timing and/or characteristics of the material around the proliferating cells

CELL DIFFERENTIATION

- Once in place neurons begin to generate axons and dendrites.
- They acquire enzymes necessary to produce neurotransmitters.
- They acquire receptors to receive synaptic transmissions.

- Movement of growth cones is affected by the substrate (the chemistry surrounding the area through which the axon is migrating
- Formation of connections may be related to activity – either spontaneous or in response to experience





Conclusions

- Behavior genetics can give us information about the relative roles of genes and environment in development
- However, the interaction between genes and environment is probably more important than either individually
  - Genes do not ever act in isolation – they are always expressed, usually in response to some environmental signal

- Meiosis is important in development because it adds variability to the population
- Mitosis is involved in cell division, and it is probably during this process that the environment can signal cells to develop into particular types of cells

- Throughout brain development, the environment within the developing brain, in utero, and postnatally influences gene expression, leading to the adult-like brain
- How does this lead to behavior?
  - Most behaviors can be traced to brain
    - Some are obvious: memory is the result of changes in brain connections
    - Others are less direct: Social behavior probably involves brain systems set up early in development for understanding social information (e.g., other people's expressions.
      - Later social behaviors may be only very indirectly related to brain function