Neural Development 1

• Genes “versus” environment
• Nature “versus” nurture
• Instinct “versus” learning
• Interactive theory of development…

• Hair color
• What language you speak
• Intelligence? Creativity?

How Genes Affect Behavior

- Genes do not directly produce behaviors

- Genes produce proteins that increase the probability that a behavior will develop under certain environments

- Genes can also have an indirect effect
Genes on chromosome in cell nucleus

CCACCATGCAGATGGATA
GACAGAATCTTTTCTCTGA
CTAGTCATTAGGATCAGGG
GCCTCTGTGGAGTTTGT
GTTTTCTTGAAAGAATAGCTG
GCAGAGTTGGTATAAAA
GACACGAATATCTCTCTGGT
CTATAAGGATACTCTCTGATA
DNA → mRNA → protein
Basic Concepts of Heritability

• **Genotype** is the suite of genes possessed by an individual, whereas **phenotype** is a trait that an individual exhibits because of gene-environment interactions.

• **Coefficient of relatedness** \((r)\): represents the average % of genes that two individuals will share based upon their relationship. A parent will contribute half of its **alleles** (forms of each gene) to an offspring \((r=0.5)\). The coefficient is 0.5 for full siblings etc.
Assessing Heritability: Human Twin Studies

- **Monozygotic (MZ)** twins are derived from the same egg and sperm ($r = 1.0$) ("identical twins")
- **Dizygotic (DZ)** twins are from different gametes and share half of their alleles ($r = 0.5$) ("fraternal twins")
- MZ twins raised apart offer insight into genetic influences, as they share all of their genes – what about shared environment? "Control" groups?

Oskar Stohr was raised Catholic in Nazi Germany; Jack Yufe as Jewish in the Caribbean. They both like sweet liqueurs, store rubber bands on their wrists, etc
Assessing Heritability

• Such studies suggest an influence of genes on personality, temperament, social attitudes

• The amount of the phenotypic variability between individuals that can be accounted for by genes is called the heritability for that phenotype, which ranges from 0 to 1.

• Heritability is ~0.5 for personality scores and ~0.7 for IQ (averages from multiple studies).
Epigenetics

• Examines changes in gene expression without modification of the DNA sequence

• Experiences alter gene expression, sometimes for a long period of time
Epigenetics

DNA

Nucleosome: DNA wound around core of histone molecules

Histone tail

Histone
Dutch Hunger Winter

• Dutch men born or conceived in winter (1944-45)
• Nazi embargo
  – starvation in cities
  – but not rural areas (more self-sufficient)
• Cities: 500-750 kilocalories per day during winter
• What happens to human brain development?
- Men examined when 19 years old
- Grouped by occupation of father (manual or nonmanual)
- Similar to results from an intelligence test
Potential weakness/ limitation?

1) the comparability of the city and rural areas (other differences than just famine)

2) Only men were examined

3) Relatively short stress on mothers - they were well nourished for most of their lives before/after the famine

4) Selective survival

5) Other?
Decades later, the investigation was extended to neurodevelopmental disorders that are diagnosed in adulthood. The guiding hypothesis was that prenatal famine could have latent effects which manifest in middle or even late stages of the life cycle. This work was carried out by us (10–13), and was initiated by the son (E. S.) of two of the original authors.

As hypothesized, the risk of schizophrenia was significantly increased in the birth cohort conceived at the height of the famine. (The finding was seen mainly in women in an early, limited study (10) but in both men and women in a later, more complete study (11).) The increased risk was specific to schizophrenia; the incidence of other psychiatric disorders was not increased in this cohort (13). In a twist of fate, the originator of
Prenatal exposure to the Dutch famine and disease in later life:
An overview

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Low birth weight is associated with cardiovascular disease in adulthood. Poor maternal nutrition during gestation contributes to low birth weight.

In this paper, we review the findings from a cohort of 2414 people, aged 50 years, born as term singletons around the time of the 1944–1945 Dutch famine, of which 912 people participated in an interview and 741 subjects were also available for hospital examination. We found more coronary heart disease, raised lipids, altered clotting and more obesity after exposure to famine in early gestation compared to those not exposed to the famine. Exposure in mid gestation was associated with obstructive airways disease and microalbuminuria. We found decreased glucose tolerance in people exposed to famine in late gestation.

These findings show that maternal undernutrition during gestation has important effects on health in later life, but that the timing of the nutritional insult determines which organ system is affected. Future research should shed more light upon the underlying pathophysiology of the far-reaching effects of prenatal exposure to famine.

Transgenerational effects of prenatal exposure to the Dutch famine on neonatal adiposity and health in later life

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At about 23-24 days, the anterior neural folds close to form the brain.

At about 28 days, the forebrain, midbrain, hindbrain, and neural tube are visible.
~350 grams
Development of Neurons

• Proliferation
• Migration
• Differentiation
• Myelination
• Synaptogenesis
Proliferation

• The production of new cells (neurons and glia), primarily early in life
  – cells lining the ventricles divide
  – some cells remain there…“stem cells”
  – other cells become “primitive” neurons or glia that migrate to other locations
At peak of prenatal neural development in humans, ~250,000 neurons are born per minute.
Migration

• movement of the newly formed neurons and glia to their eventual locations
  – distances and speeds

• occurs in a variety of directions throughout the brain
  – immunoglobulins and chemokines
Differentiation

- formation of the axon and dendrites
- axon grows first, either during migration or once neuron has reached its target
- followed by development of the dendrites
Myelination

- The process by which glia produce the myelin sheath that covers the axons of some neurons
  - speeds up transmission of neural impulses
  - first occurs in the spinal cord, and then in the hindbrain, midbrain and forebrain
  - occurs gradually for decades!
Synaptogenesis

- formation of the synapses between neurons
  - occurs throughout life!
  - slows with age
Axons “seek” targets for synaptogenesis:
1. Led by premature axon tip, the growth cone
2. On the growth cone, filopodia sample the environment
3. Molecules are produced by target cells and guide the filopodia
4. Connections are helped by cell-adhesion molecules (CAMs), secreted by targets, and growth cones will adhere to this surface.
Animals produce many more neurons than needed.

Neuron survival requires two conditions:
- Must form synapse with target cell and receive a growth factor (neurotrophin) from that cell
- Must also be stimulated to release neurotransmitters into synapse

Apoptosis (programmed cell death) occurs when a neuron receives too little growth factor.

Competition among neurons for survival is a selection process…neural Darwinism (“use it or lose it”).
Synaptic pruning in human visual cortex
Autism Spectrum Disorder (ASD)

- ASD and autism: general terms for group of complex disorders of brain development
- Difficulties in social interaction, verbal and nonverbal communication, and repetitive behaviors
- Symptoms tend to emerge between 2 and 3 years of age
- 1 in 68 American children is on the autism spectrum
- 4 × more common among boys than girls
- Multiple genes implicated
- Non genetic factors, e.g. advanced parental age at time of conception (both mom and dad); air pollution; maternal illness/stress during pregnancy; difficulties during birth, particularly those involving periods of oxygen deprivation to the baby’s brain.
Autism and vaccines

• First symptoms of autism emerge around the time children receive some vaccinations (between 2 and 3 years of age)

• No conclusive, scientific evidence that any part of a vaccine causes autism