The Teen Brain: Insights from Neuroimaging and Implications for Public Policy

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Short talk, huh?
Oh, you mean they found one?
Isn’t that a contradiction of terms?
What is your next talk on – the Loch Ness Monster?
Inside the Teen Brain
The reason for your kid’s quirky behavior is in his head

Microsoft Tries to Go Simple

Home Medical Tests
The adolescent brain is not a broken or defective adult brain!

It is exquisitely forged by the forces of our evolutionary history to have different features compared to children or adults.
“The Teenage brain isn’t broken. It has been exquisitely forged by evolution.”

A new scratch play about the teenage brain created and performed by 25 young people aged 13-16.

For years scientists thought that the teenage brain was simply a 'broken' adult brain. But now we know something very different - the teenage brain is unique, perfectly designed and beautiful.

Thursday 21 March 7pm  London  Price: £6 adults, £4 concessions

http://www.islingtoncommunitytheatre.com/brainstorm
Adolescent Behavioral Changes in Social Mammals

- Increased risk taking
- Increased sensation seeking
- Greater peer affiliation

Facilitate separation from natal family?
Less inbreeding = evolutionary advantage?
Hall of Human Origins
Smithsonian Museum, Washington DC
Brain volume increase driven by change in environment
Digital Revolution

- Remarkable advances in technologies that enable the distribution and utilization of information encoded as sequences of 1s and 0s have dramatically changed our way of life.
The Digital Revolution

The way we learn, play, and interact with each other has changed more in the last 15 years than in the previous 570 years since Gutenberg’s popularization of the printing press.
Adolescents

Young enough to embrace change
Old enough to master the technology
GENERATION M²
Media in the Lives of 8- to 18-Year-Olds
A Kaiser Family Foundation Study
Media Exposure, Over Time

Among all 8- to 18-year-olds, total amount of media exposure in a typical day, over time:

- 1999: 7:29
- 2004: 8:33
- 2009: 10:45

Increase of 1:04 from 1999 to 2004
Increase of 2:12 from 2004 to 2009

Among all 8- to 18-year-olds, total amount of media exposure, multitasking and media use in a typical day, over time:

- Total media exposure: 10:45 hours
- Total media use: 7:38 hours

29% Media multitasking

Multitasking
“Millennials will benefit and suffer due to their hyperconnected lives”

Anderson, J., & Rainie, L.
_Pew Internet and American Life Project_ (2012)
Digital Revolution: Learning

**Upside**
- Unprecedented / immediate access to vast amounts of information
- Content from best minds on planet
- Potential for personalization of instruction

**Downside**
- Signal to noise
- Mile wide / inch deep?
- Multitasking?
# Digital Revolution: Play

## Upside

- Really really fun
- Physical component
- Potential for learning through play

## Downside

- Time away from homework / other noble pursuits
- Sex
- Violence
Digital Revolution: Social Interaction

**Upside**
- Enables connection to other people
- Fulfills some basic human desires
- "global" community

**Downside**
- Different type of interaction
- Lots of time
- Cyberbullying
## Digital Revolution: Social Interaction

### Upside
- Enables connection to other people
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- “global” community

### Downside
- Different type of interaction
- Lots of time
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It aint natural!
The Double Edged Sword of Adolescent Brain Plasticity

Opportunity

Vulnerability
Why Adolescence?

- Time of dramatic change in brain, body, and behavior
- Time of peak emergence of:
  - Schizophrenia
  - Depression
  - Anxiety
  - Substance Abuse
  - Eating Disorders

- Not Autism, ADHD, Alzheimer’s

- Moving parts get broken?
Adolescent Brain Changes

sMRI
WM ↑
GM ⊆

fMRI
Diffuse → focal
↑ “frontalization”
↑ integration

EEG
Delta sleep ↓
Cyclic power ↓

PET
↓ glucose utilization

Postmortem
Overproduction/
Selective elimination
Synapses
Neurotransmitters
Risks for psychopathology during adolescence

**Typical behavior changes**
- ↑ Risk taking
- ↑ Novelty seeking
- ↑ Social priorities

**Schizophrenia**
- Exaggeration of typical regressive changes:
  - • Delta sleep
  - • Membrane phospholipids
  - • Synaptophysin expression
  - • Synaptic spine density
  - • Neuropil
  - • Prefrontal metabolism
  - • Frontal gray matter

**Substance Abuse**
- ▼ Sensitivity to hangover, sedation, and motor impairment
- ↑ Hippocampal vulnerability

**Depression**
- Hormonally mediated limbic effects preceeding maturation of cognitive-regulatory system
Why Adolescence: Schizophrenia

• Is schizophrenia related to an exaggeration of typical regressive changes of adolescence?

• Delta sleep (synaptic pruning?) – (Feinberg 1982)
• Membrane phospholipids (Pettegrew et al. 1991)
• Prefrontal metabolism (Andreasen et al. 1992)
• Density of synaptic spines (Garey et al. 1998)
• Neuropil (Selemon et al. 1995)
• Expression of synaptic marker synaptophysin (Eastwood et al. 1995)
• Frontal cortical gray matter (Sporn et al. 2003)
Gray Matter thickness changes in Childhood Onset Schizophrenia
Percentage Change in Regional Cortical Gray Matter Volumes Between Healthy Volunteers (N=34) and Childhood-Onset Schizophrenics (N=15) Ages 13-18

Gray Matter Lobe by Diagnosis MANOVA F=3.68, p=.004
Regional percentage change differs by post-hoc test: *p<.05; **p<.01
Consideration, not explanation

- Increase in pre and perinatal adverse events
- Subtle cognitive, motor, and behavioral anomalies during childhood years before illness onset

Support for earlier developmental disturbances underlying the abnormal maturational events during adolescence.
Twins

- 130 Monozygotic ("identical") pairs
- 105 Dizygotic ("fraternal") pairs

- Structural Equation Modeling
  - A Additive Genetic Factors
  - C Common Environment
  - E Error/ Unique Environment
Heritability varies by age and region

Heritability (a2) at ages 5, 12, and 18 years. Colorbar shows heritability values from 0.0 to 1.0

Red arrows - heritability higher at younger ages
Green arrows - heritability higher at older ages

Lenroot et al, 2008
What are the implications of substantial age x heritability interactions for the design and interpretation of imaging/genetic studies?
THE LASTING ECHO OF EARLY ENVIRONMENTS

SUBTLE DIFFERENCES IN BIRTH WEIGHT AMONGST HEALTHY CHILDREN

LASTING DIFFERENCES IN BRAIN DEVELOPMENT INTO THE THIRD DECADE OF LIFE
We paid $500,000 for the egg of a supermodel and the sperm of a Nobel laureate...

...She didn't quite turn out like we planned...
ApoE effects on brain morphometry during pediatric development

T statistical map of thinning in e4 carriers compared to non-carriers

Thickness of the entorhinal cortex by ApoE genotype during childhood

Philip Shaw, 2008
Y genes matter

Scientists have identified a gene that results in:

- 4x increase violent crime
- 8x increase arrested for murder
- 50x risk of being on death row
- 100x fondness for The Three Stooges movies
Nearly all neuropsychiatric disorder of childhood onset have different prevalences, ages of onset, and symptomatology between boys and girls.
Summary of Sexual Dimorphism

- Overwhelming more alike than different
- Developmental *trajectories* more different than final destination
- Male brain morphometry more variable
- Differences are between groups – does NOT imply constraints for individual boys or girls
- Effects of environment, sex chromosomes, hormones being elucidated
Men are from North Dakota, women are from South Dakota
Male / Female differences as clues to mechanisms of illness

Autism 4-8:1

Early – Male

Post puberty - Female
Sex Difference Investigations Involving Clinical Populations

- Anomalous numbers of X and Y chromosome
  - XXY (Klinefelter’s Syndrome)

- Anomalous hormone profiles
  - Congenital Adrenal Hyperplasia
  - Androgen Insensitivity Syndrome
  - Familial Precocious Puberty
  - Kallmann Syndrome
Not exactly “illness” (i.e. hardware problem), but …

- Unplanned pregnancy
- Sexually Transmitted Disease
- Motor Vehicle Accidents
- Criminality (law enforcement)
- Life Decisions
The Double Edged Sword of Adolescent Brain Plasticity

Opportunity

Vulnerability
Goal

To explore the path, mechanisms, and influences on brain development in health and illness through longitudinal studies combining brain imaging, genetics, and psychological / behavioral assessments.
NIMH Child Psychiatry Data Base

- Longitudinal Assessment (~ 2 year intervals)
  - Imaging (sMRI, fMRI, DTI, MTI)
  - Genetics (blood, saliva)
  - Neuropsychological / Clinical

- 7000+ Scans from 3000+ Subjects
  - ~ ¼ Typically-Developing Singletons
  - ~ ¼ Typically-Developing Twins
  - 25 Clinical Populations
    - ADHD, Autism, Childhood Onset Schizophrenia, Sex Chromosome Variations (XXY, XXX, XXY, XYY, XXXXY), ...
3 Key Points of Brain Maturation

• The brain matures by becoming more “connected” (white matter) and more specialized (gray matter)

• A changing prefrontal/limbic balance affects reward circuitry, hot vs cold cognition, temporal discounting, and decision making

• Enormous plasticity confers both vulnerability and opportunity
How the Brain Looks to MRI
The Neuron

- Cell body (the cell’s life support center)
- Dendrites
- Axon
- Myelin sheath
- Terminal branches of axon

Neuronal Impulse

Donald Bliss, MAPB, Medical Illustration
How the Brain Looks to MRI

- 3 km of axons
- 90,000 neurons
- 400 m of dendrites
- 4,500,000 synapses
How do we bridge gaps across disciplines?

- Non human primate / other species studies
- Higher resolution imaging
- Nano-Neuro technology
Part 1 – Mapping Trajectories of Anatomic Brain Development

- White Matter
- Gray Matter
White Matter

Male (152 scans from 90 subjects)
Female (91 scans from 55 subjects)
95% Confidence Intervals

White Matter

Volume in cubic cm

Age in years
Myelin → Increased Bandwidth
Speed 100x, Refractory Period 1/30x

Signal “hops” between nodes of Ranvier
More than just maximizing speed ...

- Synchrony
- Plasticity
- Sensitive Periods
- Integration
Facets of “Connectivity”

- Long Term Potentiation (LTP)
- White Matter
- EEG coherence
- fMRI coactivation
- Temporally coupled developmental trajectories
  - fire together $\rightarrow$ wire together $\rightarrow$ grow together?
- Similarly affected by same genetic/environmental factors
- Graph Theory (nodes and edges)
Maturational Coupling Echoes White Matter and FMRI Connectivity

GRAY MATTER CHANGE

WHITE MATTER

rsFMRI

Raznahan, 2011, Neuron

Honey, 2009, PNAS
Facets of “Connectivity”

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Graph Theory: Is it a small world after all? (strangers linked by mutual acquaintance)

- Small world networks
  - Many beneficial properties
  - Surprisingly often seen in natural systems
  - A whole field of mathematics developing to quantify aspects of “connectivity”
Disrupted modularity and local connectivity in childhood onset schizophrenia

Alexander-Bloch (2010)
anatomical coupling correlates with vocabulary scores in linguistically relevant regions

Lee (unpublished)
Part 1 – Mapping Trajectories of Anatomic Brain Development

• White Matter
• Gray Matter
Doctor, what's the matter?

Grey, from the looks of it.

BRITISH NEUROSURGERY HUMOR
<table>
<thead>
<tr>
<th>White Matter</th>
<th>Gray Matter</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Linear increase</td>
<td>- Inverted “U”</td>
</tr>
<tr>
<td>- Not different by region</td>
<td>- Regionally specific</td>
</tr>
</tbody>
</table>
Gray Matter Development in Healthy Children & Adolescents
(1412 Scans from 540 Subjects)

Frontal Lobe Gray Matter

Age in years
Volume in ml
Similar Pattern for Synaptic Density

*Development Differences in Synaptic Density of Layer 3 Human Frontal Cortex* (Huttenlocker 1979)
And for D1 Receptor Density in Striatum
Movie for adolescent students

Zits cartoons © Zits Partnership
Prefrontal Cortex

- “Executive” functions
  - Long term strategy
  - Planning
  - Organization
  - Impulse control
- Integrates input from rest of the brain
- “social” brain circuitry
- “Time Travel”
- Multi tasking bottle neck?
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• Frontal lobe allows integration of past, present, future
  – “counterfactuals”
  – ability to play scenarios out in our minds instead of the physical world
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Limbic circuitry – ignites at puberty
Braking and Accelerating of the Adolescent Brain

B. J. Casey, Rebecca M. Jones, and Leah H. Somerville
“Hot” vs “Cold” cognition

- Lab
  - Alone
  - Hypothetical situations
  - Low arousal

- Life
  - In groups
  - In real situations
  - High arousal
Rate these on a scale from 1 to 7
(I would be at very much risk → I would not be at risk)

• Having sex without protection
• Driving drunk
• Vandalizing property
• Riding in a car with a drunk driver
• Smoking cigarettes
• Stealing from a store
Adolescent Decision Making

• So, not risk perception
• Reward sensitivity
  – Seek high levels of novelty and stimulation to achieve same subjective feeling of pleasure
  – Related to puberty
  – Limbic system
• Self regulation
  – peer influence
  – Future orientation
  – Emotional arousal
How does the brain keep score? Dopamine
movement

motivation

Dopamine

addiction

Reward & well-being
Addiction = hijacking of this reward system
Nothing that is highly addicting has ever been found that does not jack up dopamine in the nucleus accumbens. Nothing.
Summary

• The adolescent brain is developing not defective
• **Journey not just destination**
• Differences in prefrontal/limbic balance affect temporal discounting, reward circuitry, hot vs cold cognition, and decision making that may be relevant to the issues of substance abuse
• Enormous plasticity confers both vulnerability and opportunity
1. Cognitive/Behavioral

2. Male/Female Differences

3. Genetic/Environmental

4. Health/Illness
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• The adolescent brain is developing not defective
• Journey not just destination
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To explore the path, mechanisms, and influences on brain development in health and illness through longitudinal studies combining brain imaging, genetics, and psychological/behavioral assessments.
Implications for Public Policy

• Educational
• Judicial
  – Age of Consent
  – Death penalty (Simmons v Roper, 2008)
  – Life without parole
  – Lie Detection
  – Recidivism prediction
  – Driving laws
• Social
  – Prolonged maturation
They need their parents
They need their parents just as much as they do.
The Infant From Hell