The FASD Learning Series is part of the Alberta government's commitment to programs and services for people affected by FASD and those who support them.

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Date:
January 12, 2011

Session Goals

• Review principles of brain plasticity
• Review principles of brain development
• Consider brain plasticity and FASD
• Consider the implications for interventions

Principles of Brain Plasticity
Background

Once seen as a static organ, the brain is now understood to be a dynamic organ that undergoes both acute and chronic changes.

The challenge is to identify principles that may control these changes.

Principle 1

Plasticity can be seen at many levels of analysis.

Levels of Analysis

1. Behaviour
2. Maps – noninvasive and invasive
3. Physiology
4. Neuronal morphology
5. Genetics and epigenetics
6. Proteins and other molecules
Neurons ‘R Us

Measuring Connections
Connection numbers can be estimated by knowing the length of cell branches.

The number of connections can go up or down with experience – more is not always better.

The same experience can produce opposite changes in different places…

Principle 2
When the brain changes, this is reflected in behavioural change.

This change is known by names such as learning, memory, addiction, maturation, aging, recovery, etc.
Arnold Scheibel's Story

Cell Structure
1. Complexity of computations
2. Education
3. Occupation
4. Sex Effect

Principle 3
The cortex is altered by a surprisingly wide range of events including:

1. Sensory & motor experience
2. Learning
3. Gonadal hormones
4. Psychoactive drugs
5. Natural rewards
6. Diet
7. Stress

Experiential Treatments

Complex Housing  Tactile Stimulation

All ages  Infant  Adult
How can this happen?

Experience alters brain activity, expression of genes, brain chemistry, behaviour, and so on.

Any one of these can alter connectivity and thus function.

Principle 3

The cortex is altered by a surprisingly wide range of events including:

1. Sensory & motor experience
2. Learning
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Learning can only occur if the brain changes

Cognitive Tasks
The cortex is altered by a surprisingly wide range of events including:

1. Sensory & motor experience
2. Learning
3. Gonadal hormones
4. Psychoactive drugs
5. Natural rewards
6. Diet
7. Stress

Relative volume of cortical regions in women and men
This means that females and males should behave differently!
(Goldstein et al., Cerebral Cortex, 2001, 11, 490-497)
All psychoactive drugs leave a footprint

Psychoactive Drugs Alter the Frontal Lobe

Drugs include:
- nicotine
- caffeine
- cocaine
- amphetamine
- methylphenidate
- antidepressants
- valium
- THC
- antipsychotics
- morphine
- and more...

The effects are area specific:
- mPFC VS OFC
- PFC VS other cortical regions
**Principle 3**

The cortex is altered by a surprisingly wide range of events including:

1. Sensory & motor experience
2. Learning
3. Gonadal hormones
4. Psychoactive drugs
5. Natural rewards (e.g. play, sex)
6. Diet
7. Stress

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**All mammals have play behaviour with rules**

![Image of rats playing]

**Little Play:** Adult + Juvenile

**Limited Play:** 2 Juveniles

**Enriched Play:** 4 Juveniles

Bell, Pellis & Kolb, BBR, 2010
Play alters frontal lobe development. The absence of play will lead to an abnormal frontal lobe.

**Principle 3**

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Enhanced vitamin/mineral diet enhances plasticity and behaviour
Principle 3

The cortex is altered by a surprisingly wide range of events including:

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Stress Effects are Area-Specific

Hippocampus: loss of cells in dentate gyrus
Medial PFC: loss of synapses
Orbital PFC: increase in synapses
(e.g. Liston et al. J Neuroscience, 2006, 26, 7870-4)

Stress Effects are Area-Specific

fMRI studies show similar results in humans
(e.g. Liston, McEwan & Casey, PNAS, 2009)
**Principle 4**

Changes are age-specific and can occur in response to both pre and postnatal experiences

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**Prenatal Experiential Treatments**

- **Complex Housing**
  - Dad or Pregnant Mom

- **Tactile Stimulation**
  - Pregnant Mom

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**Other Prenatal Treatments**

- **Prescription Drugs**
  - Antidepressants
  - Anxiolytics

- **Social Interactions**
  - Parent-Infant
  - Stress

- **Other Drugs**
  - Stimulants
  - Alcohol
  - & likely all other ‘recreational drugs’
**Prenatal Alcohol?**

1. Ethanol does disrupt dendritic organization in medial prefrontal cortex – shorter dendrites
2. More importantly, it alters the nature of dendritic spines

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**Principle 5**

Experiences interact – “metaplasticity”
Drug exposure reduces the capacity for further change

Drug treatment + = ?

Predictions

1. Makes no difference
2. Blocks the effect of experience in the regions altered by the drug
3. Alters the effect of experience
4. Blocks the effect of experience all over

The drugs either block or alter the later experience-dependent changes throughout the cerebrum – NOT just in drug-affected regions.
Principle 6

By understanding the normal brain changes in response to experience, it is possible to stimulate functional “recovery” after cortical injury or dysfunction.

But first, we will consider brain development.

Principles of Brain Development

Why Do We Care About Brain Development?

You are your brain.

BUT
Your brain is not just produced by your genes.

Your brain is sculpted by a lifetime of experiences. The most important time in brain development is the first few years of life – including prenatal life.
What Is Experience?

*Everything* that you encounter both pre- and postnatally as well as in adulthood...

Examples: sounds, touch, light, food, thoughts, drugs, injury, disease...

Developing the Cerebral Hemispheres

80 billion neurons
10\(^{14}\) connections

= An engineering marvel...

Your brain is sculpted by a lifetime of experiences, especially in the first few years of life.

Gross Development of the CNS
Cells must migrate to the right region AND the right layer.
Cell Maturation

Axons must find their targets

Myelination

Abnormal competition leads to abnormal organization.
Brain Plasticity:
1. Pruning during development.
2. Changing the wiring diagram...

Brain cells develop connections over the first 2 years

Then they are sculpted actively for 20+ yrs

Cell Death and Synaptic Pruning
Development does not end at birth

It continues for at least 20-25 more years

Brain development is prolonged. Blue = boys, Red = girls

Hot colours are thick cortex; cold colours are thinner cortex
**A Caudal-Rostral Gradient**

There is an obvious back to front gradient in maturation of the cerebral cortex.

Temporal lobe peaks around 16 years whereas although motor cortex peaks around 12 years, the PFC is much later, well into the 20s. The dorsolateral PFC precedes the OFC.

BUT, the trajectory is set very early on...

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**Inferring Neural Development from Behaviour**

As behaviors emerge we can make inferences about what changes must be happening in the nervous system.

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**Behaviours emerge as the brain develops**

- **2 months**: Orient hand toward an object and gropes to hold it.
- **4 months**: Grasps appropriately shaped object with entire hand.
- **10 months**: Uses pincer grasp with thumb and index finger opposed.

Behaviours cannot emerge before necessary brain is mature enough...
The results reflect differential brain maturation

Both infant humans and monkeys can learn the concurrent discrimination sooner than the seemingly easier matching task.

The former task (a habit task) is dependent on the basal ganglia whereas the later task is cortical.

Thus, abnormal brain development can produce counterintuitive symptoms.
Some behaviours take a long time

Solving difficult problems takes until about 16 years of age…

Correlations in brain and behaviour can be counter intuitive:
This shows the correlation between decreasing cortical thickness and improving motor skills. Red dots show regions of cortical thinning.

Similarly, this shows the correlation between decreasing cortical thickness and improving vocabulary skills. Red dots show thinning.
Abnormalities in brain development are related to behavioural disorders.

**FASD and Brain Plasticity**

1. The FASD brain has reduced plasticity. Recall the lack of immature spines:

   A:
   
   ![Diagram showing immature and mature spines]

   B:
   
   ![Bar graph showing number of spines]

   Spine Phenotypes of Basal Dendrites
   - Mature
   - Immature

   Graphs showing the number of spines in mature and immature conditions.
FASD and Brain Plasticity

1. The FASD brain has reduced plasticity. Recall the lack of immature spines

2. Reduced neurogenesis in adult hippocampus

The generation of new cells is necessary for memory. This is reduced in FASD. In addition, the survival of those cells that are made is not as good as normal.

3. Absence of NMDA receptors
The NMDA receptor is a key to plasticity. FASD brains have a reduction in these receptors, resulting in poor plasticity.

FASD and Brain Plasticity

1. The FASD brain has reduced plasticity. Recall the lack of immature spines.
2. Reduced neurogenesis in adult hippocampus.
3. Absence of NMDA receptors.
4. Absence of ocular dominance plasticity.
Implications for Interventions

What are the major obstacles in FASD brains?
1. Abnormal brain development, especially frontal and temporal regions
2. Impaired plasticity
3. Poor nutrition
4. High stress (including prenatally)

What can be done?
The experimental literature has suggested several things:
1. Early intervention with tactile stimulation
2. Exercise to increase hippocampal neurogenesis. Still a problem with cell survival…
3. Some form of environmental enrichment
4. Enhanced diet
The Challenge

To develop rehabilitation strategies that will enhance plasticity.

To develop novel treatments that can work around the problems with plasticity.

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For information on upcoming sessions in the FASD Learning Series:
www.fasd-cmc.alberta.ca

Please take the time to fill out the on-line evaluation

Thank You!