Sensitivity Periods in Brain and Behavioral Development

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Does timing of interventions matter?

- Longstanding controversy in psychology: are experiences in the early years uniquely important?
- Can early adverse experiences be overcome?
  - To what degree?
  - Under what conditions?
  - Is it ever too late?
- Are the first 3-5 years more important or just like any other 3 year period?
- Timing of interventions may yield insights that have clinical, research and policy implications.
- How should we prioritize our investments?

Two Stories:
John and Julie
**Early Experiences**

<table>
<thead>
<tr>
<th>Age</th>
<th>John</th>
<th>Julie</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prenatal</td>
<td>Alcohol, crack, limited prenatal care</td>
<td>Alcohol, crack, limited prenatal care</td>
</tr>
<tr>
<td>Birth</td>
<td>Partner violence, substance abuse, neglect</td>
<td>Partner violence, substance abuse, neglect</td>
</tr>
<tr>
<td>12 months</td>
<td>Father jailed, mother using; placed with grandparents</td>
<td>Removed by CPS; placed with relatives</td>
</tr>
<tr>
<td>24 months</td>
<td></td>
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<tr>
<td>30 months</td>
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**Clinical Picture at 30-36 Months of Age**

- A “wild child;” no language; aggressive and violent tantrums; unable to feed himself; fearful of grandmother; unresponsive socially; headbanging; emotionally dysregulated; in diapers; slept poorly with many nightwakings and bedtime struggle.
- Grunted and pointed only; choked family dog; hits, kicks, shoves, and “bullies” people; tantrums, hyperactive; impulsive; self-injurious; poor social skills, mood swings, rocking back and forth, destructive; indiscriminate with adults; masturbating, hoarding/stuffing food; erratic sleep.

**Clinical Picture at 3-8 years**

- 3 years: Aggressive; explosive outbursts; overreaction to prohibitions; language delays.
- 4 years: Continued aggression and explosive outbursts; school expulsion; firesetting; inability to learn from mistakes; limited peer relations.
- 5 years: Aggressive; uncooperative, defiant behavior at home; hyperactive in school.
- 6 years: Same problems at home; clownish behavior in school; off task; poor peer relations.
- 7 years: Some hyperactivity & impulsivity; no aggression.
- 8 years: Some problems at home; clownish behavior in school; off task; poor peer relations.

**Clinical Picture at 3 years**

- 3 years: Aggressive, explosive outbursts; overreaction to prohibitions; language delays.
- 4 years: Continued aggression and explosive outbursts; school expulsion; firesetting; inability to learn from mistakes; limited peer relations.
- 5 years: Aggressive; uncooperative, defiant behavior at home; hyperactive in school.
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- 8 years: Some problems at home; clownish behavior in school; off task; poor peer relations.
<table>
<thead>
<tr>
<th></th>
<th>Speech and language therapy</th>
<th>Speech and language continued; Special education placement; Individual therapy begun; aripiprazole, lamotrigine, methylphenidate; 2 psychiatric hospitalizations</th>
<th>Status unchanged; all meds continue; school placement threatened</th>
</tr>
</thead>
<tbody>
<tr>
<td>John</td>
<td>3 years</td>
<td>Referred to IMH program; all meds dc’d; speech and language; PCIT begun</td>
<td>Taking methylphenidate; on grade level; adopted and thriving</td>
</tr>
<tr>
<td>Julie</td>
<td>4 years</td>
<td>Transitioned to preadoption placement</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5 years</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>8 years</td>
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**Interventions and Outcomes at 8 Years**

**Different outcomes at age 8 years**

- Early experiences
- Genetic vulnerability/differential susceptibility
- Gender
- Interventions

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**Newsweek**

Your Baby’s Brain

From Jaekely Ta, and Karl Science: Unlocking the Inner Lives of Infants
Point 1
Brain development is a protracted process

"Young man, go to your room and stay there until your cerebral cortex matures."

Point 2:
The child's brain is not a smaller version of the adult's brain

Point 3: Much Development is Prenatal

15 1/2 weeks    22 weeks    23 weeks    24 weeks

15 1/2 weeks

Adolescent brain
(black box)

Ungrateful...talk back...
risk taking...doesn't
see room...moody
Brain Development

• There are general principles of brain development that apply to (nearly) all members of the species.....

• Beginning with the formation of the embryo

Prenatal Development

Development begins with fertilization, in which male gamete (sperm) and female gamete (oocyte) unite to give rise to zygote

≈20,000 genes on 46 chromosomes (23 pairs)
1 pair = sex chromosome (X,Y)
22 pairs = autosomes
1st Prenatal Month

• Two celled zygote becomes 4, then 8, then 16, etc.
• ~1 week after conception cell mass separates into 2 masses:
  • Embryo
  • Umbilical cord, placenta, amniotic sac
• 3 weeks after conception the embryo divides into 3 layers – inner, middle, outer
  • Inner layer gives rise to internal organs; middle gives rise to skeletal system; outer gives rise to the brain

Stages of Brain Development

• Neural tube forms (3rd-4th prenatal week)
  • Error in neural tube formation: spina bifida ("open spine"
• Once tube has closed (end of 4th week), brain cells start to form (neurogenesis). This will continue through 2nd (or so) postnatal year
  • Error in neurogenesis: microcephaly

Stages of Brain Development (cont.)

• Between 4th and 25th week (or so), baby neurons move around to eventually form 6 layers of the cerebral cortex (cell migration)
  • Errors in cell migration: schizophrenia
• Once immature neurons move to their predetermined location, they mature into adult neurons (differentiation). This includes forming appendages referred to as dendrites and axons
  • ...and once this happens, dendrites and axons can form connections (synaptogenesis).
  • Errors in synaptogenesis: autism?
Neurogenesis, Synapses and Circuitry

A Synapse

[Diagram of a synapse with labels for Axon, Bouton (foot), Vesicles, Receptor Sites, Dendrites of next neuron, Mitochondria, Synaptic cleft, Neurotransmitters]
Synapses and Pruning

- Overproduce
  - neurons,
  - synapses –
    - newborn has many more synapses than adult brain.
    - prune synapses to adult numbers over early years

What guides brain development?

- Synapse creation and elimination shaped powerfully by experiences
- After repeated stimulation, synapse stabilizes; otherwise it tends to be eliminated ("use it or lose it" principle)
- Pruning/recruitment of synapses occurs in response to experience.

Axon elaboration and synapse formation

Axon elaboration

Abnormal circuitry remains even after restoration of normal experience
Stages of Brain Development (cont.)

• Final stage of brain development is when axons are coated with a fatty substance called myelin. This insulates the cell and improves how fast one neuron communicates with another.
• Gray matter refers to unmyelinated brain tissue; white matter refers to myelinated brain tissue
• Although much of the brain is myelinated by the end of the preschool period, some regions continue to myelinate until mid life
• Errors in myelination: nutritional deficiencies.

Gray and white matter

Summary of Brain Development

Figure provided by Heckman (2013).
Individuality is the product of both biological inheritance & personal experiences

- Our genes specify the properties of neurons and neural connections to different degrees in different pathways and at different levels of processing.
- Brain circuitry relies on experience to customize connections to serve the needs of the individual.
- Experience shapes these neural connections and interactions but always within the constraints imposed by genetics.

Experience = environment ↔ brain

- Specific experiences vary, depending on the history, maturation, and state of the individual’s brain.
- Brain maturity has impact on experience:
  - Different areas of the nervous system mature at different rates.
  - Lower level processing areas mature earlier than those at a higher level.
  - Initially, more basic environmental factors influential, but as maturity continues, more subtle features impact

Brain Architectural Principles

- Circuits that process basic information are wired earlier than those that process more complex information.
- Higher circuits build on lower circuits, skills beget skills
- Development of higher level capabilities is more difficult if lower level circuits are not wired properly.
Brain Development

I. The impact of experience on the brain is not constant throughout life.
II. Early experience often exerts a particularly strong influence in shaping the functional properties of the immature brain.
III. Many neural connections pass through a period during development when the capacity for experience-driven modification is greater than it is in adulthood.

Interim Summary

I. The impact of experience on the brain is not constant throughout life.
II. Early experience often exerts a particularly strong influence in shaping the functional properties of the immature brain.
III. Many neural connections pass through a period during development when the capacity for experience-driven modification is greater than it is in adulthood.

ABSENCE OF THE EXPECTABLE ENVIRONMENT

Inadequate input (neglect)
Excessive/unwanted input (abuse, exposure to violence)
Infant room at St. Catherine’s

Extreme Neglect Reduces Brain Power

Positive Relationships

Extreme Neglect
**Total Cortical White Matter**

- **CAUG**: $B = -24.1, t = -2.17, p = .03$
- **FCG**: $B = -18.1, t = -1.5, p = .12$

Regression controlling for age and gender

- Sheridan et al. 2012

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Institutional rearing and EEG power are mediated by changes in white matter development

- **White Matter**
- **History of Institutionalization** (length of time and age removed from the institution)
- **EEG Alpha and Theta Power**

- Sheridan et al. (2012)

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**Bayley Scales of Infant Development**

- Institutionalized vs. Family

- $p = .000$

- Foster Care
- Community
Completely formed attachments at 22 months
Institutionalized vs. Family

Smyke et al., 2007

30,000,000 word gap

Cumulative Vocabulary (Words)

Child’s Age (Months)

Hart & Risley (1995)

Hart & Risley (1995)

Number of Words Heard by Children Differs Across Income Groups
PTSD

- Exposure to trauma
- Re-experiencing
- Avoidance
- Alterations in mood or cognition
- Hyperarousal
- Impairment
- One month duration

Functional neuroanatomy of chronic anxiety, fear and PTSD

Chronic Severe Stress Changes Brain Architecture
**Cortisol Studies**

- Diurnal cortisol metabolism
- Stress response

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**Lack of Daily Patterning in Cortisol Production for Children in Romanian Orphanage**

Carlson & Earls, 1997
Salivary Cortisol Levels in 7-12 year olds
6+ years post adoption

Romanian Adoptees

- PI Children, 8+ mos
- 0-2 mos at adoption
- Birth Children

Gunnar, Morison, Chisholm, & Schuder, (2001)

Cortisol Reactivity

- CAUG
- FCG
- NIG

Processes of Brain Development

- Genetic unfolding of blueprint
- Experience incorporated into the structure of the brain in two ways.
  - Experience expectant development
  - Experience dependent development
Experience expectant development

- Expected experiences
  - Patterned light information facilitates the development of
    - low-level visual abilities (e.g., depth perception)
    - high-level visual abilities (e.g., face perception).
  - Complex auditory information facilitates the development of speech and language processing.
  - Availability of a caregiver facilitates the development of attachments.

Experience dependent development

- Unique is to each person
- Active formation of new synaptic connections throughout the life span, based on individual's interaction with the environment.
  - Learning math
  - Remembering events
  - Acquiring vocabulary

Survival of the Species...
Finally, the ability to change the brain decreases over time

Sensitive periods in brain and behavioral development

Sensitive periods in brain development

- Brain is primed for input from the *expected environment* at certain times.
- Should the timing be off development is derailed.
- Children with congenital bilateral cataracts
  - Later surgery occurs, the greater the problems with vision
  - Past a certain point in time, a life-long visual impairment
Definitions

Sensitive period:
• When the effect of experience on the brain is particularly strong during a limited period in development.

Critical period:
• A special class of sensitive periods that result in “irreversible” changes in brain function.

Konrad Lorenz
Imprinting in geese

Hubel and Weisel:
Classic studies on sensitive periods

Monocular deprivation in early infancy led to deficits in brain organization in visual cortex
**Influence of Experience**

**Speech and Language Development**

- 6 months -- infants discriminate phonemic contrasts from most languages
- 9-12 months, they begin to lose this ability
- If 9 month olds given ~5 hours of exposure to non-native language (by live “tutor”), can recapture this ability
  - If via audio or videotape, no effect

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**Face Processing**

- Evidence that experience plays essential role in development of face processing:
  - Infants who have congenital cataracts removed a few months after birth show remarkable recovery of general visual function but show persistent, subtle deficits in face processing
  - “Other race effect” in which adults are better at recognizing faces from familiar races (generally their own) vs. less familiar races
  - “Other species effect”

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**Other Species Effect**

*Pascalis, de Haan, & Nelson, 2002*
Experiment 1: Training Infants

- Visit 1: 6-months
  - VPC
  - Sent home with monkey face book
- Visit 2: 9-months
  - Visual Preference (trained faces)
  - VPC (novel faces)

Summary

- The “other species” perceptual window closes ~9 months, unless additional experience is provided.
- This experience must occur during a sensitive period; even adults who have extensive experience with monkey faces are not as good as infants if that experience was acquired as an adult.

Pascalis, Scott, Kelly, et al., 2005
Sensitive Periods for Integration of Auditory and Visual Information

- Barn Owls
- manipulated their early visual experience
- identified sensitive periods for these inputs

Summary of Experience and Brain Development

- Some circuits develop largely impervious to experience.
- For other circuits, the impact of experience on the brain is not constant throughout life—instead experience exerts an especially strong influence at certain times—sensitive periods.
- Early experience often exerts a particularly strong influence in shaping the immature brain.
- Finally, other circuits remain open to the effects of experience throughout the life cycle.

Feral children and language development

- Shamdeo, the wolf boy
- Found in forest in 1972 playing with wolf cubs
- Walked on all fours, craved blood, ate dirt, hunted chickens, loved the dark, and preferred company of dogs and jackals to people.
Research Design Matters

Ideal study to assess timing

- Comprehensive assessments of infants who have experienced uniform early adversity.
- Randomly assigned to interventions that vary systematically in the age at which individuals receive enhanced caregiving.
- Followed up longitudinally into adulthood.

Research With Rhesus Macques

* Judy Cameron and colleagues
Heritability estimates
(with 126 Rhesus monkey infants)

- Play room test (exploration vs. inhibition)
  - Latency to leave mom, $h^2=1.0$
  - Time away from mom, $h^2=1.0$
- Remote-Controlled Car test (approach to novel object)
  - Vocalizations, $h^2=1.0$
- Human Intruder test (approach to stranger)
  - Movement (profile), $h^2=0.54$
  - Movement (stare), $h^2=0.75$
  - Teethgrinding (stare), $h^2=0.89$
- Novel Fruit test (approach to novel rewarding stimulus)
  - Latency to inspect, $h^2=1.0$
  - Latency to touch, $h^2=0.74$

Separation from Mother

- 6 months
- 3 months
- 1 month
- 1 week

Summary of results

- 3 month separated
  - minimal effects
- 1 month separated
  - depressed initially
  - followed by clinging behavior, persists into adolescence
- 1 week separated
  - aloof
  - asocial
Super Mom Results

- Pairing with an experienced mother is more effective when initiated earlier.
- Critical period of 7 days after which remediation no longer possible.
**Bucharest Early Intervention Project**

Community Group

- 136 Institutionalized Children (6-30 months)
- Community n=72
- Care As Usual n=68
- Foster Care n=68

Assessments at 30, 42, 54 months

Follow-ups at 8 and 12 years

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**Persistence to age 15 years of deprivation specific patterns of impairment**

- Quasi-autism
- Cognitive impairment
- Inattention
- Overactivity
- Disinhibited attachment

Rutter et al., 2010

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**IQ and age of placement in foster care**

- DQ/IQ

**Age of placement subgroups**

- Expressive
- Receptive

**Attachment security and age at entry**

Smyke et al., 2010

**Distribution of alpha power across the scalp by timing and group**

CAUG - FCG > 24

FCG < 24 - NIG
Cortisol Reactivity

Placed before and after 24 months of age

Timing of placement effects

<table>
<thead>
<tr>
<th>Variable assessed</th>
<th>Sensitive period “closes”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stereotypies</td>
<td>12 months</td>
</tr>
<tr>
<td>Expressive language</td>
<td>15 months</td>
</tr>
<tr>
<td>Receptive language</td>
<td>15 months</td>
</tr>
<tr>
<td>Reading</td>
<td>24 months</td>
</tr>
<tr>
<td>Security of attachment</td>
<td>24 months</td>
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<tr>
<td>Organization of attachment</td>
<td>24 months</td>
</tr>
<tr>
<td>IQ at 54 months</td>
<td>24 months</td>
</tr>
<tr>
<td>ERN during flanker 8 years</td>
<td>20 months</td>
</tr>
<tr>
<td>Alpha and theta 8 years</td>
<td>24 months</td>
</tr>
<tr>
<td>Teacher rated social skills 8 years</td>
<td>20 months</td>
</tr>
<tr>
<td>Cortisol response 12 years</td>
<td>24 months</td>
</tr>
<tr>
<td>RSA response 12 years</td>
<td>18 months</td>
</tr>
<tr>
<td>Competence 12 years</td>
<td>20 months</td>
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Importance of the Infant Caregiver Relationship

Importance of child caregiver relationships

- Human infants require caregivers’ protection and support to ensure survival for years after birth.
- Relationships with caregivers essential in helping children regulate responses to stressors and adversity.
- The most important context for child development is child's relationship(s) with caregiver(s).

Protection within risk

[Graph depicting Aggressive Behavior over time with measures of parenting stress and childrearing-related parenting stress.]

Tharner et al 2012
Children with histories of severe deprivation

- Security of attachment at 42 mos.
- Psychiatric symptoms, disorders and impairment at 54 mos.
- Caregiving quality at 30 months

McGoron et al., 2012

What builds healthy brains?

Thankyou!
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