Neuroplasticity in the Infant Brain: Structure and Function Part I

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Objectives

- Describe age-dependent stages of nervous system development in childhood
- Recognize the link between activity and neuronal development
- Explain the concept of critical periods and implication for treatment
Outline

* Fetal development/movement
* Infancy
  * Synaptic competition
  * Environmental influence on plasticity
  * Early motor experience
Definition

* Neuroplasticity: ability of the nervous system to respond to intrinsic or extrinsic stimuli by reorganizing its structure, function, and connections  Cramer, Steven C., et al. "Harnessing neuroplasticity for clinical applications." *Brain* 134.6 (2011): 1591-1609.
Synaptic pruning

- Every circuit (sensory, motor, emotional, cognitive) shapes the way circuit gets put together
- Every experience-- riding a bike, reading a book, etc excites certain neural circuits and leaves others inactive
- Those consistently turned on over time will be strengthened, while those that are rarely excited may be dropped away
- “Cells that fire together, wire together”
- “Use it or lose it”
Prenatal Period: Nervous system development

- Neuronal and glial cell proliferation, cell migration, neural apoptosis, axon and dendrite formation
Fetal movement

- Overt behavior is indicative of neurologic function
- Fetal environment affects brain wiring
Fetal movement

- Essential for development of skeletal, muscular, and neural systems
- Function is integral part of normal development
  - Prenatal use of structure is necessary for continuing and normal development of that structure
- Number of neurons undergoing apoptosis is closely related to muscle activity
NOTHING HAPPENS UNTIL SOMETHING MOVES

ALBERT EINSTEIN
Fetal movement prunes neurons

- Chick embryos immobilized by medication - increase in motor neurons in brachial and lumbar lateral motor columns that would otherwise degenerate.

- When chicks are allowed to move again, excess neurons undergo a delayed cell death and total cell number falls below control levels.

- Function at developing neuromuscular junction are critical in controlling cell death.

Oppenheim, Ronald W., et al. 1978
Fetal movement

* Prolonged experimental blocking of neuromuscular junction of the chick embryo leads to malformation of the joints

* Initial buds can differentiate, but adequate development of joint cavities and proper shaping of synovial plates require motion of the limb

Fetal movement

- Continuously change position of fetus
- Prevent adhesions and local stasis of the blood, especially in early fetus whose skin is fragile

Einsieler, Prayer, Prechtl, *Fetal Behavior: A Neurodevelopmental Approach* 2012
Fetal movements

- Mechanical forces generated in the embryo or fetus also have influence on how differentiating tissues respond to gene organization.

- Lack or impairment of physical forces changes the state of the organs.
Fetal hiccups

- Begin decreasing when fetal breathing movements increase at 12 weeks

- Hiccups cause repeat contractions of diaphragm smooth progress of subsequent diaphragmatic motions necessary to fetal breathing

Einsieler, Prayer, Prechtl 2012
Fetal breathing

- Lack of fetal breathing movements associated with decreased proliferation and apoptosis of pulmonary cells
- Required for lung growth and maturation
  - If abnormal, surfactant-active material is only partially released into alveolar or amniotic fluid
  - Required for differentiation of type I and type II pneumocytes

* Einsieler, Prayer, Prechtl 2012
Fetal eye movements

- Observed as early as 16 weeks gestation present until term

- Most eye movements are horizontal and conjugate

Einskieler, Prayer, Prechtl 2012
Fetal eye movements

- Opening and closing of eyelids can be observed from 23-26 weeks onward
- If eye does not move at all, motion capture cells do not develop

Einsieler, Prayer, Prechtl 2012
Fetal environment

- Rich with stimulation
  - Sounds
  - Smells
  - Tastes
  - Pressure
  - Movement
Infancy: Nervous system development

* Dendrite formation, synapse production and myelination
Form and pattern of movements largely unchanged in first weeks after birth

GMs at 27 weeks gestation

GMs at 34 weeks gestation

Einspieler, Prayer, Prechtl 2012
Humans vs. other mammals
Humans are less developed at birth

* Compared to primates, human neonate less adapted to extra-uterine environment

* Human pregnancy is relatively short

* Compensated by effectiveness of higher intelligence of caregivers
Human brain size

- Larger brain to body size than most creatures on the planet. If we stayed inside womb much longer, brains would not fit through birth canal

- If we were born later, we’d be less helpless, but heads wouldn’t fit through birth canal

- Born earlier easier to deliver, but higher risk for brain damage

2nd-3rd month- neural transformation

- Muscle power increases
- Body posture changes to space-oriented postural control
- Sucking pattern changes from tongue peristaltic movements to a new pattern with open corners
- Control of visual attention and binocular vision develops
- Social smiling and vocalization
- Intentional and antigravity movements occur and start to dominate
100 Days Celebration
Humans vs. insects

- Bugs have all the information they need for survival at time of birth
- They don’t need to learn from their environment
- Born with a range of natural instincts
While human babies are helpless at first, it is this state of immaturity that helps us learn from the world around us in ways other animals can’t.

Humans have opportunity to learn which other animals don’t have.
The brain that wires itself

- Brains double in size in the first year
- Brain builds itself to adapt to its environment
- One hundred billion neurons (at birth)
- Neurons communicate across synapses
- Adds connections to eventually have a quadrillion
How do babies learn?

- Babies have to lose certain abilities in order to master others.
- They are selectively learning things that are most relevant to their environment and unique circumstances.
Elimination of synapses in developing nervous system

- Nervous system competes for limited resources
- Survival of the fittest

Figure 1. Expression of Different Fluorescent Proteins in Different Motor Axons in Double Transgenic Mice
In this muscle, all motor axons express YFP (yellow), and a small random subset expresses CFP (blue). A red-shifted fluorescent α-btx was added to label the AChRs in the postsynaptic membrane (red).
(A) Low-power image of part of an excised and fixed sternomastoid muscle at P8 in which only one motor axon expressed CFP. Both singly innervated (s) and multiply innervated (m) junctions are visible.
(B) High-power image of the neuromuscular junction shown in box in (A). The CFP containing axonal input is segregated to the right half of the junction. Scale bars equal 10 μm.

Synaptic takeover

Figure 2. Synaptic Takeover

In vivo imaging of the same multiply innervated junctions in neonates provides evidence both for the gradual relinquishment of synaptic territory by the losing axon before it is eliminated and takeover by the winning axon of synaptic territory that previously was occupied by the losing axon.

(A–E) Five views of the same junction imaged between P8 and P15. The subset CFP axon (blue) comes to occupy the sites in the upper parts of the junction that were formerly innervated by the YFP axon (yellow; 100% expresser), which completely withdrew (E, asterisk). At P12, a process of the CFP axon had begun to invade the territory of the YFP axon (D, circle and arrow in inset).

(F–J) Although in this case the subset CFP axon (blue and insets) has greater terminal area (~70%) at the first view, it progressively withdraws from the junction (arrows). The withdrawn axon can be seen in (I) and (J) (asterisks). Insets, 70% size reduction. Scale bars equal 10 μm.

These battles repeat billions of times as a baby grows. Every move a baby makes helps strengthen certain connections and weakens others.
Critical periods

- Phase during life span during which an organism has heightened sensitivity to exogenous stimuli that are compulsory for development of a particular skill.

- Failure to learn a particular skill allows the cortical areas normally allocated for that function to fall into disuse.

- Unused brain areas will eventually adapt to perform a different function and therefore will no longer be able to perform other functions.
Critical periods
How do babies learn?

- Babies can recognize subtle differences between monkey faces at 6 months, at 9 months unable to differentiate monkey faces.
- Adults and older babies (9 months) only able to differentiate faces of own species.
- Human faces are most important in environment.

Between 6 and 10 months infants ability to discriminate among native speech sounds improve.

Same ability to discriminate among foreign speech sounds decrease.

Language

The early catastrophe

* Hart and Risley, 1995
Language: the early catastrophe
The early catastrophe

- Vocabulary significantly different by age 3
- Predictive of reading and writing skills at age 9
Enriched environment in relationship to standard laboratory conditions

EE is complex and is varied over period of experiments: tunnels nesting materials, toys and food locations are changed frequently. Animals given opportunity for voluntary physical activity on running wheels.

Enriched environments have higher rates of synaptogenesis and more complex dendrite arbors leading to increased brain activity.

Lack of stimulation delays and impairs cognitive development.

Romanian orphanages

- 80s and 90s orphanages were overcrowded, understaffed. Children were abused and neglected.

- Children have smaller white and grey matter

- See faces less often, have difficulty reading expressions, abnormal input.

- Have more difficulty forming attachments

- Abused children with smaller hippocampal volumes

Poverty

The Effects of Poverty on Childhood Brain Development: The Mediating Effect of Caregiving and Stressful Life Events

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Development is individualized and variable from the beginning of human movement

Einsieler, Prayer, Prechtl 2012
Variability is key in motor development
Challenging assumptions about motor milestones

- Standardizing children’s motor development began 100 years ago

- Focused on “typical child” rather than on within-individual variability and individual difference

- Gesell 1928 scales of motor development based on small sample of 51 infants, Northern European distraction from New Haven CT

- Inspiration for Bayley and Denver
Challenging milestones

- Milestones are a poor way to think about development
- Ignores individuality and variability
- “Infants do not lift their heads roll over, or walk simply because of age” Adolph, Berger 2011.
- Acquire skills with help of caregivers in environment of objects, surfaces and places
Motor

FIGURE 1:
An 18-month-old baby skillfully cuts a fruit with a knife, under the watchful eye of a relative (in the far corner of the Democratic Republic of Congo).
Onset ages

How infants are held, carried, bathed, fed, placed for sleep, etc affects timing of motor milestones by providing varying amounts of stimulation and opportunities for spontaneous movement.

Contextual factors that restrict practice can delay onset ages.

Cultural factors that augment practice and enrich or intensify stimulation can accelerate developmental timing.

Adolph et al 2009
Cultural differences

A. 
B. 
C. 

D. 
E. 
F. 

* Hopkins, Westra 1988
Mother tosses the infant into the air, shakes and swings the infant while holding the baby under the arms, around the head, or upside down by the ankles.

Keller, et al. 2002
Among Caribbean and African cultures, childcare routines are designed to stimulate development of particular skills.

At 3 months of age, mothers sit babies on floors supported by hole in the ground, mound of sand, a basin with clothes wrapped around or supported by cushions. Adolph et al 2009
To facilitate walking, Kenyans stand children in their laps and bounce them vigorously, infant responds with stepping movements, sometimes walking up the caregivers body.

In Bali, parents set up a bamboo rail to hold as they practice taking independent steps. Adolph et al 2009
Cultural practices

* Informal handling:

  * French infants spend 50-60% of time lying down Bril, 1997
  
  * Riding in sling of an active person promotes vestibular, visual proprioceptive input
  
  * Typical Mali woman bends down 1.5 times/minute to tend to fire or prepare food Bril, 1986
Do handling practices make a difference?

- Dose-response relation with onset age to formal training
- Facilitative effects are limited to the skills that receive special practice
- The frequency of formal exercise predicted ages at which infants sat and walked
Formal experiments

• Confirm facilitative effects of exercise and handling

• 4 weeks of vestibular stim (20 biweekly spins in an office chair) resulted in higher scores for infants on the Denver Clark, et al 1977
Formal experiments

- 3 weeks of enhanced handling and positioning (15 min/day) at 2 months of age showed
  - Immediate advances in prone skills
  - Short-term advancements in head control, reaching and sitting behaviors

- Long term advances in object transfer, crawling and walking

Figure 1: Congenital cerebral palsy intervention group (1) were asked to place their infants in supine and engage them in face-to-face interaction with objects for 15 min daily. Congenital cerebral palsy experimental intervention group were asked to perform activities for 1 hr daily to encourage and assist reaching, up and out, pulling up and reaching, prone to supine, supine to sitting (d), maintaining head and upper body control in sustained sitting and standing (e-g), and moving hands to midline (i-j).

Lobo, Galloway 2012
Expectations

- Cultural differences in timing of motor milestones often accompany culture-specific expectations about when children should acquire various milestones.

- Expectations can feed into childrearing practices and thereby affect the ages at which children in the culture acquire the skills.

- Mothers hear about age of onset from own mothers, midwives, pediatricians and parenting books and observe ages at which children in culture acquire various skills important to the culture. 
  Hopkins, Westra 1988
Restricted practice delays onset of motor development.

- Impoverished conditions in orphanages can delay onset of motor development.
Endpoint of development

- Endpoint of development can be higher or lower depending on cultural expectation
- Begin practicing while playing at young age
Environment affects movement

- Speed of everyday activity is related to population density

- “Pace of life” is culture specific; people walk at a faster pace and conduct transactions more rapidly in areas of higher population density

Bornstein 1979
Children are not in a vacuum; culture, environment, and childrearing play a role in development.
Universals

- Healthy children in all cultures acquire basic motor functions including sitting, reaching and walking

- Some stages are reached in varying orders or skipped all together - crawling

- Most forms of crawling are omitted from milestone charts
Why do infants walk?

- Why do expert crawlers abandon a presumably stable, quadrupedal posture that takes months to master in order to move in a precarious upright posture where falling is rampant?
How Do You Learn to Walk? Thousands of Steps and Dozens of Falls Per Day


New York University
Experience matters!

- Average toddler in one hour:
  - takes 2368 steps
  - travels 701m (length of 7.7 American football fields)
  - falls 17 times/hour

- Practice, practice, practice! Adolph et al 2012
Early walking is variable

- Although infants accumulated thousands of steps/session, spent most of time stationary

- Average walking 32.3% of time

- Walking was distributed over time in primarily short bursts

- Sometimes infants will skip days where they walk

- Adolph et al 2012
Babies don’t walk in straight lines!

- Infants started and stopped at will, traveled in winding paths over varying surfaces, took sideways and backward steps, varied walking speed, switched from upright to other postures, and misstepped and fell.

- They visited multiple locations and engaged in different activities therein.

Adolph et al. 2012
Clinical relevance

- Traveling over a uniform path at a steady pace encourages infants to execute the same movements over and over.

- Navigating through a cluttered environment while adapting to changing goals and varying destinations requires infants to change their movements from step to step.

- At every point in the development of stance and mobility, infants must use perceptual information to detect the changing constraints on balance and locomotion.

Adolph et al 2012
Early walking

- Practice is variable!!
- Leads to greater flexibility and broader transfer of skills to varied environments
- Implications for children with cerebral palsy...

Do children with cerebral palsy change their gait when walking over uneven ground?

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Cortical representation and synaptic enrichment and pruning for specific movement are enhanced through:

- Active problem solving
- Variability
- Task specific practice
- Intensity of practice
- Errors
Navigating challenging terrain

- Infants find multiple and variable solutions for navigating challenging terrain, rather than a single, fixed approach.

- On steep slopes and stairs abandoned typical crawling and walking methods in favor of alternative strategies that lowered their center of mass and provided more balance control.

Adolph, 1997
Navigating challenging terrain

- Wobbly handrail experiment: infants required to cross a narrow bridge with only foam and rubber handrails designed to give way when infants weight placed on them

Berger et al 2005
Navigating challenging terrain

* Wobbly handrail experiment: infants required to cross a narrow bridge with only foam and rubber handrails designed to give way when infants weight placed on them

* Infants came up with multiple strategies to successfully cross bridge

Berger et al. 2005

Navigating challenging terrain

- Many infants use multiple strategies on different trials and within the same test session and multiple means on the same trial.

- Acquire alternative locomotor strategies by process of exploration and construction.

- In test trials, when experienced infants faced steep slopes and narrow bridges, they rarely rested quietly.

- Infants concertedly sought out information, weighed whether a particular posture afforded traversal and continued to try out different combinations of postures.

- Berger et al. 2005
Specificity

- Avoidance of real cliff experiment
- Experience does not transfer from earlier developing skills to later developing ones
- Infants who have learned not to crawl over cliff will attempt to walk over cliff initially

Adolph 2000
Babies learn through exploration

- Exploratory learning
- Babies don’t know hands are for grasping and feet are for walking
- Infants can reach and contact objects with feet one month earlier than with hands

Galloway, Thelen 2004
Take home points

- Development is individualized and variable
- Plasticity is driven by activity and experience
- Experience and activity are influenced by culture, caregivers, and environment
- Need flexibility because bodies, skills and environments change
References

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