The early detection of cerebral palsy in high-risk neonates: identification, intervention, and advocacy

Colleen Peyton, PT, DPT, PCS

WE SAVE BABIES

NEONATAL NURSES WEEK

Happy Neonatal Nurses Week!

Celebrating those who care for the most vulnerable patients and their families.

September 9 - 15, 2019

National Association of Neonatal Nurses

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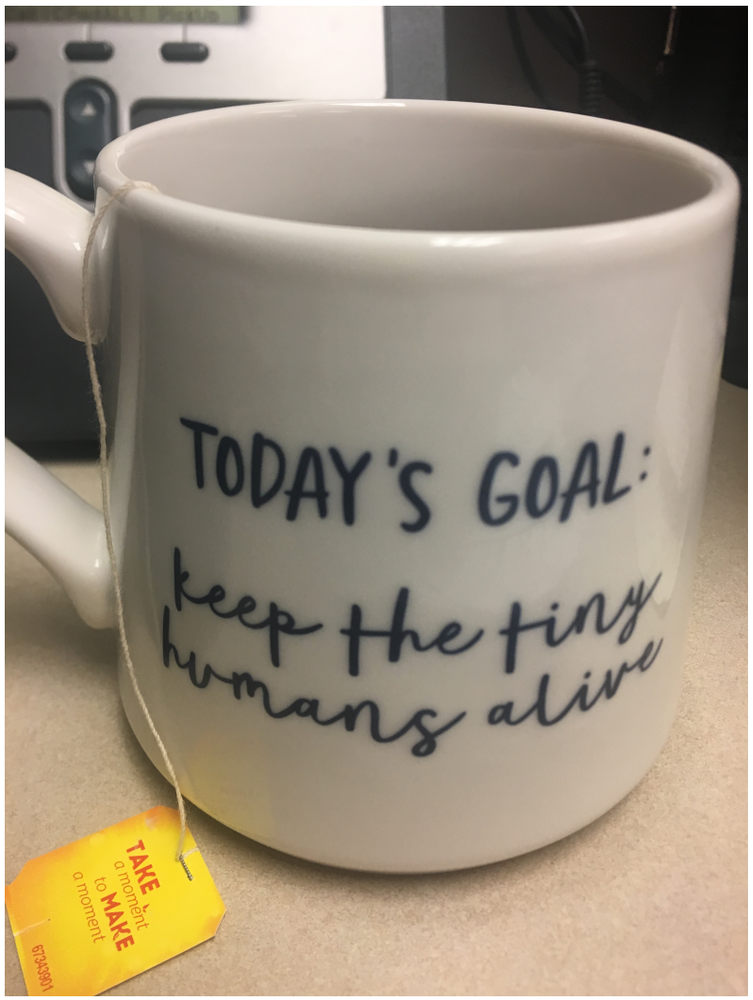

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Background

The problem

- Children aren’t commonly diagnosed with cerebral palsy until they are 2+ years old

Clinical questions...

- Is it possible to predict cerebral palsy in the young infant?

- How do we effectively deliver early intervention to those infants at highest risk after discharge?

DEVELOPMENTAL MEDICINE & CHILD NEUROLOGY REVIEW

A systematic review of tests to predict cerebral palsy in young children

MARGOT BOSANQUET[1,2,3] | LISA COPELAND[1] | ROBERT WARE[3,4] | ROSLYN BOYD[2,3,5]

	Sensitivity (Correctly detects cerebral palsy)	Specificity (Correctly detects normal)
Option A	98%	91%
Option B	74%	92%
Option C	86%	89-97%
Option D	88%	87%

Bosanquet, 2013

	Sensitivity (Correctly detects cerebral palsy)	Specificity (Correctly detects normal)
General movement assessment	98%	91%
Cranial ultrasound	74%	92%
MRI	86%	89-97%
Neurologic examination	88%	87%

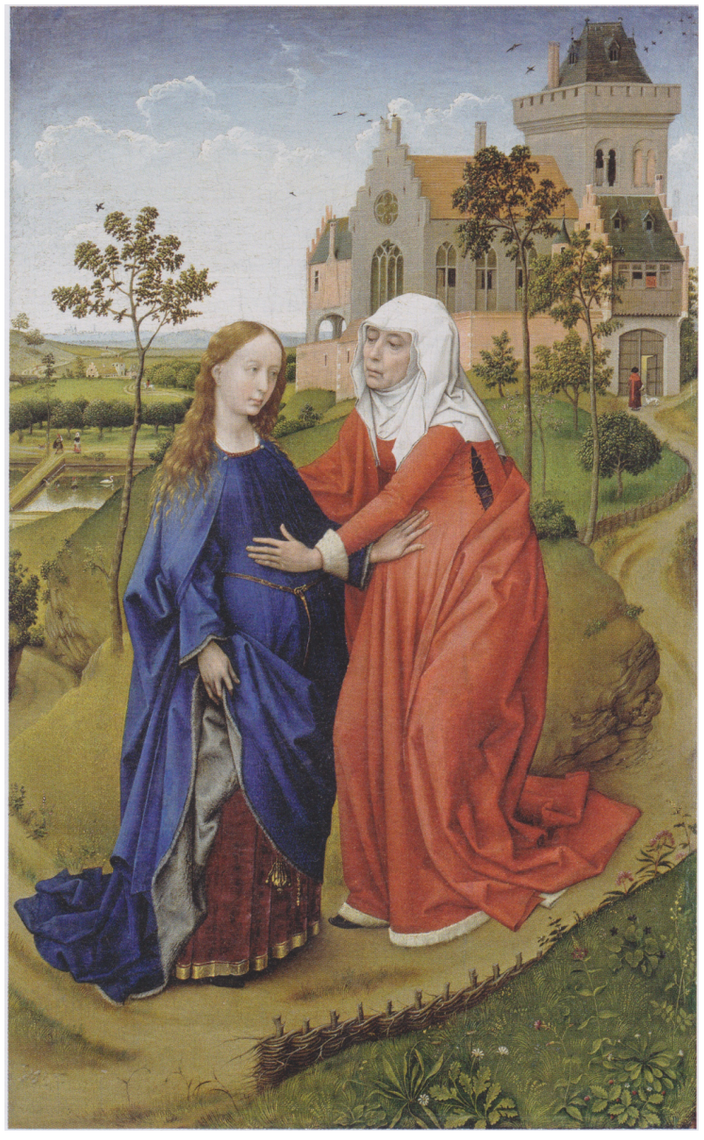
Bosanquet, 2013

Background

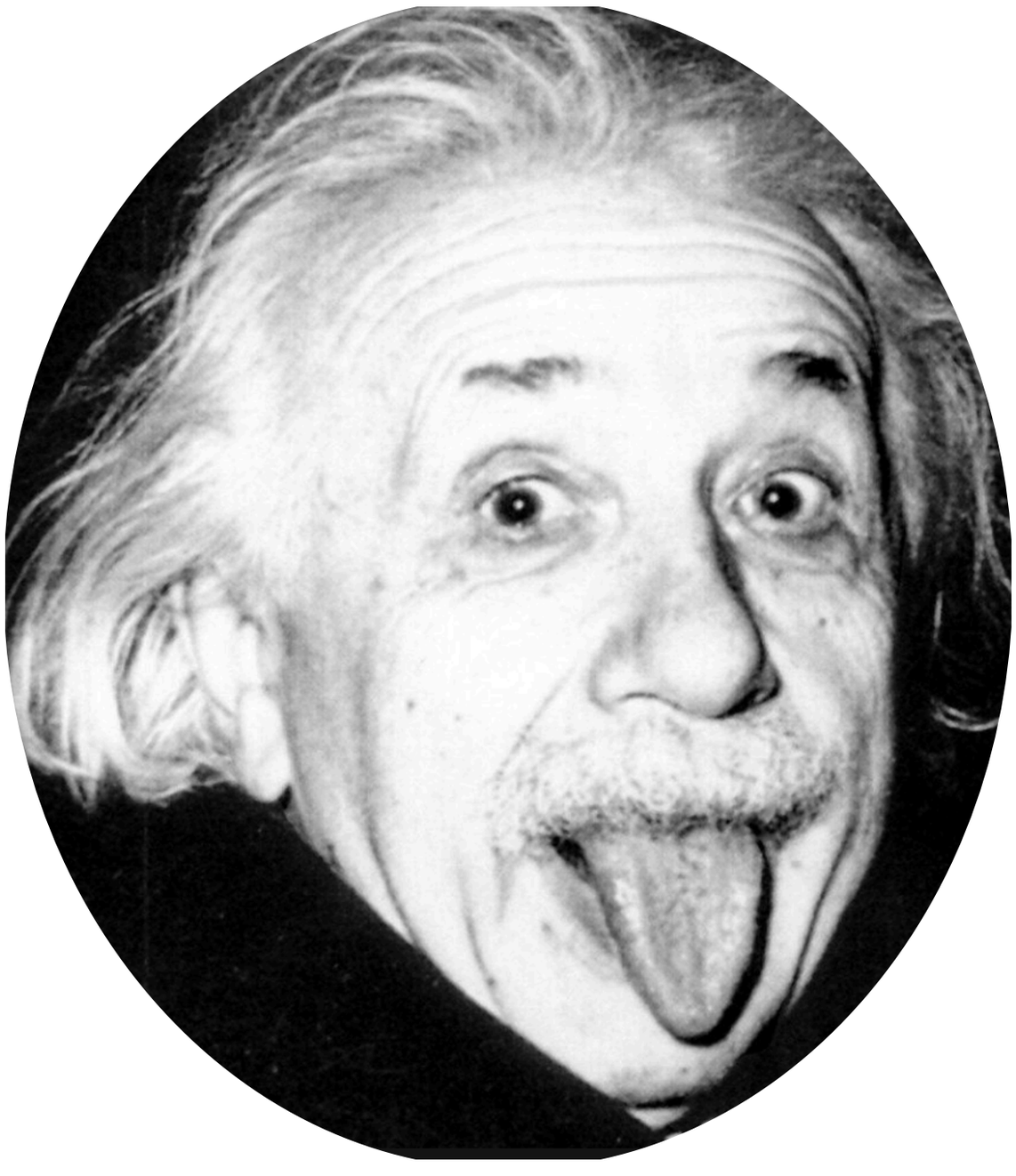
- The young human nervous system generates a wide variety of spontaneous movement patterns in the fetus and young infant

- General movements are the most frequently occurring pattern and involves the whole body in a variable sequence

Why does the fetus move?

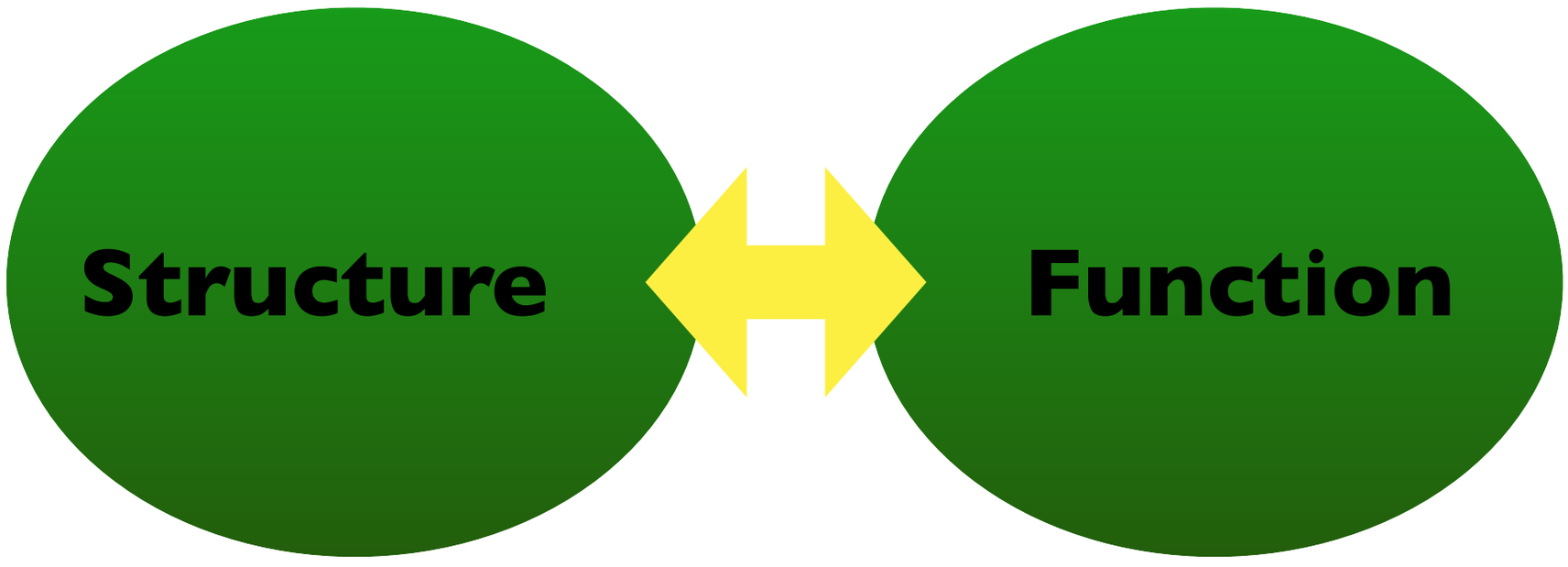


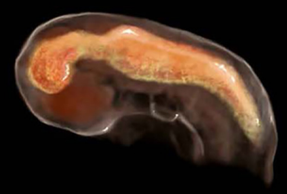
Movement is essential to life!



Nothing happens until something moves

Fetal movement drives development of body and brain

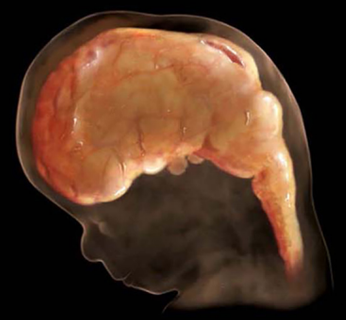




29 days

33 days

52 days



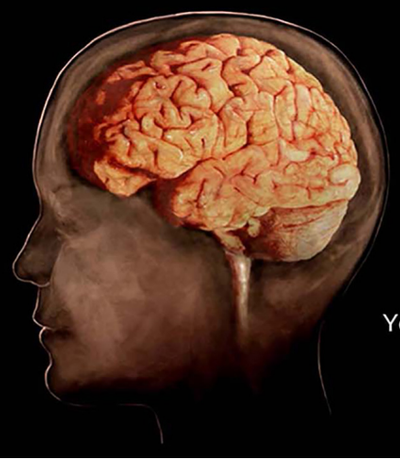
59 days

70 days

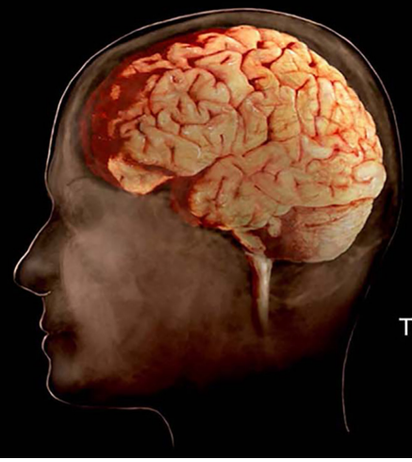
20 weeks

6 months

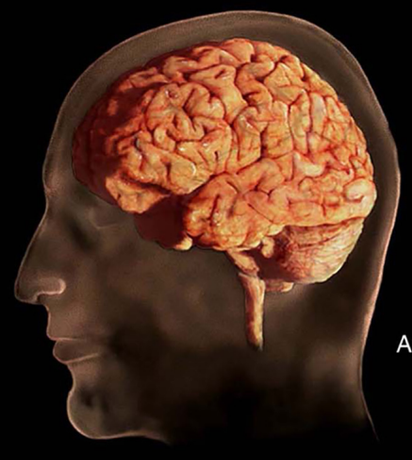
9 months



Young child

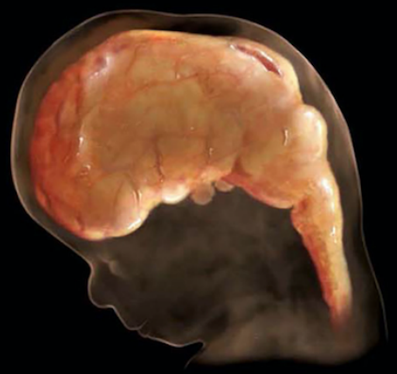


Teenager



Adult

The VisualMD/ScienceSource



59 days

70 days

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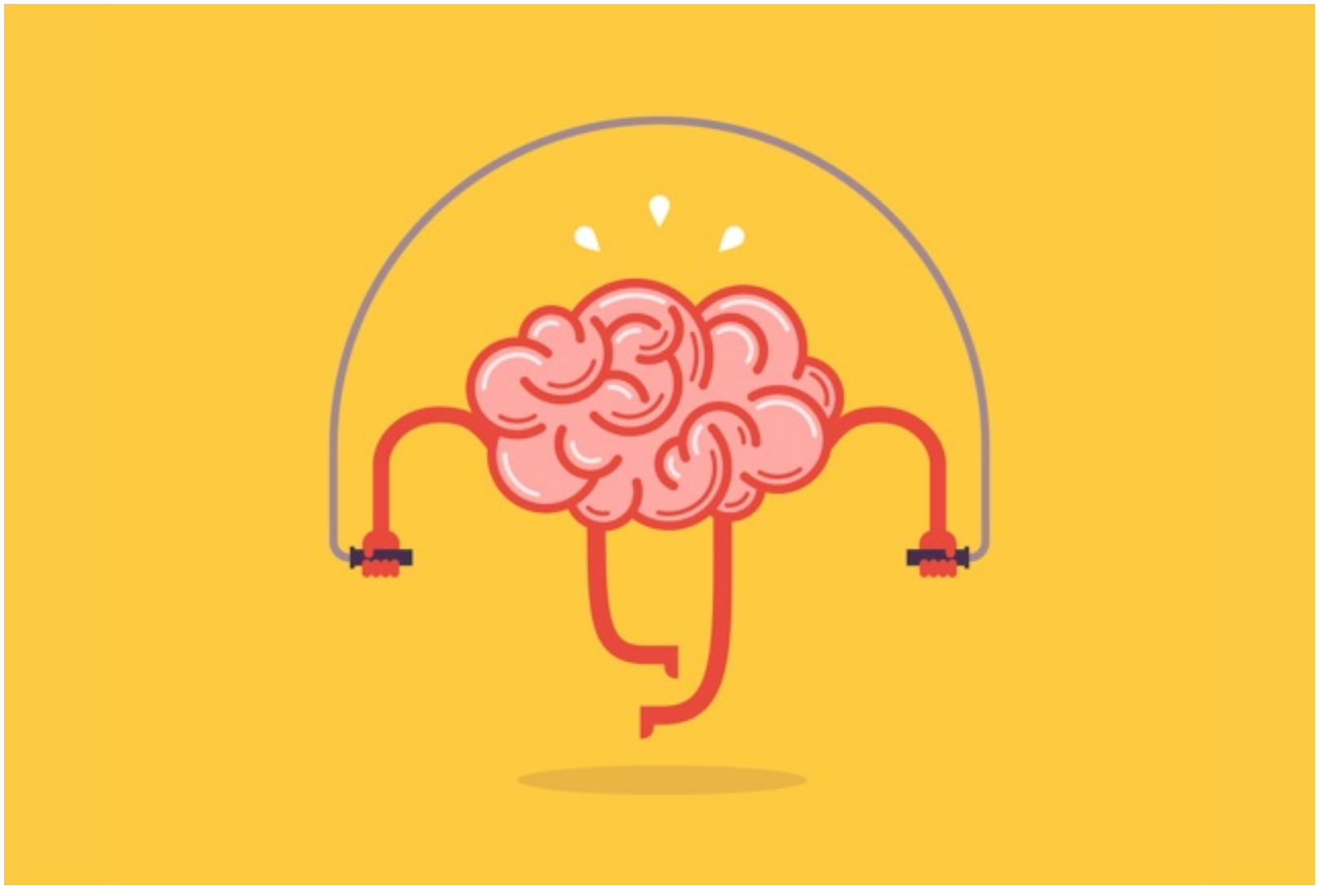
Fetal movement drives development of body and brain



Autopoietic

Fetal movements influence muscle and joint formation

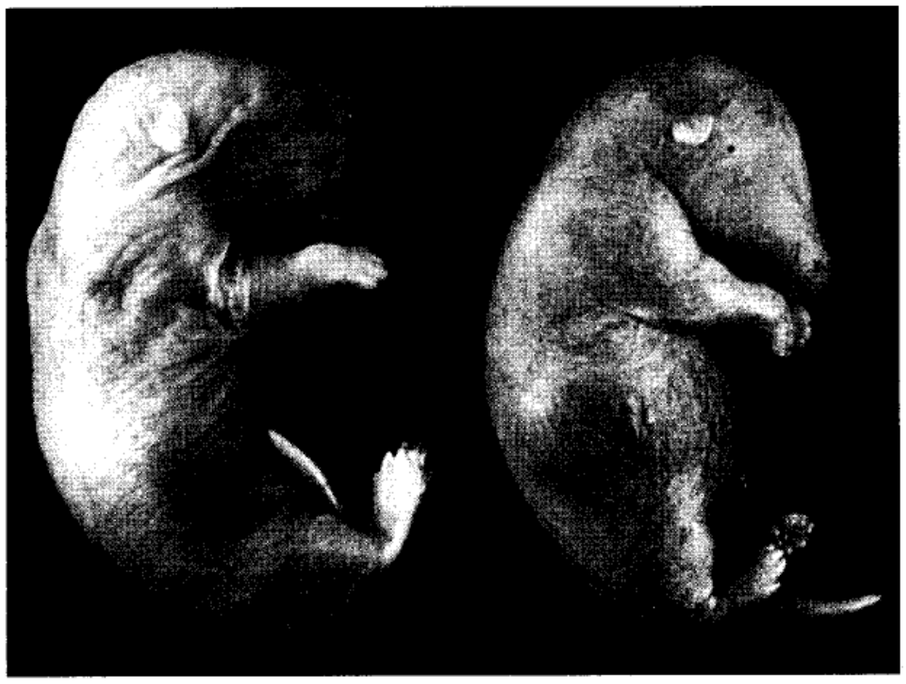


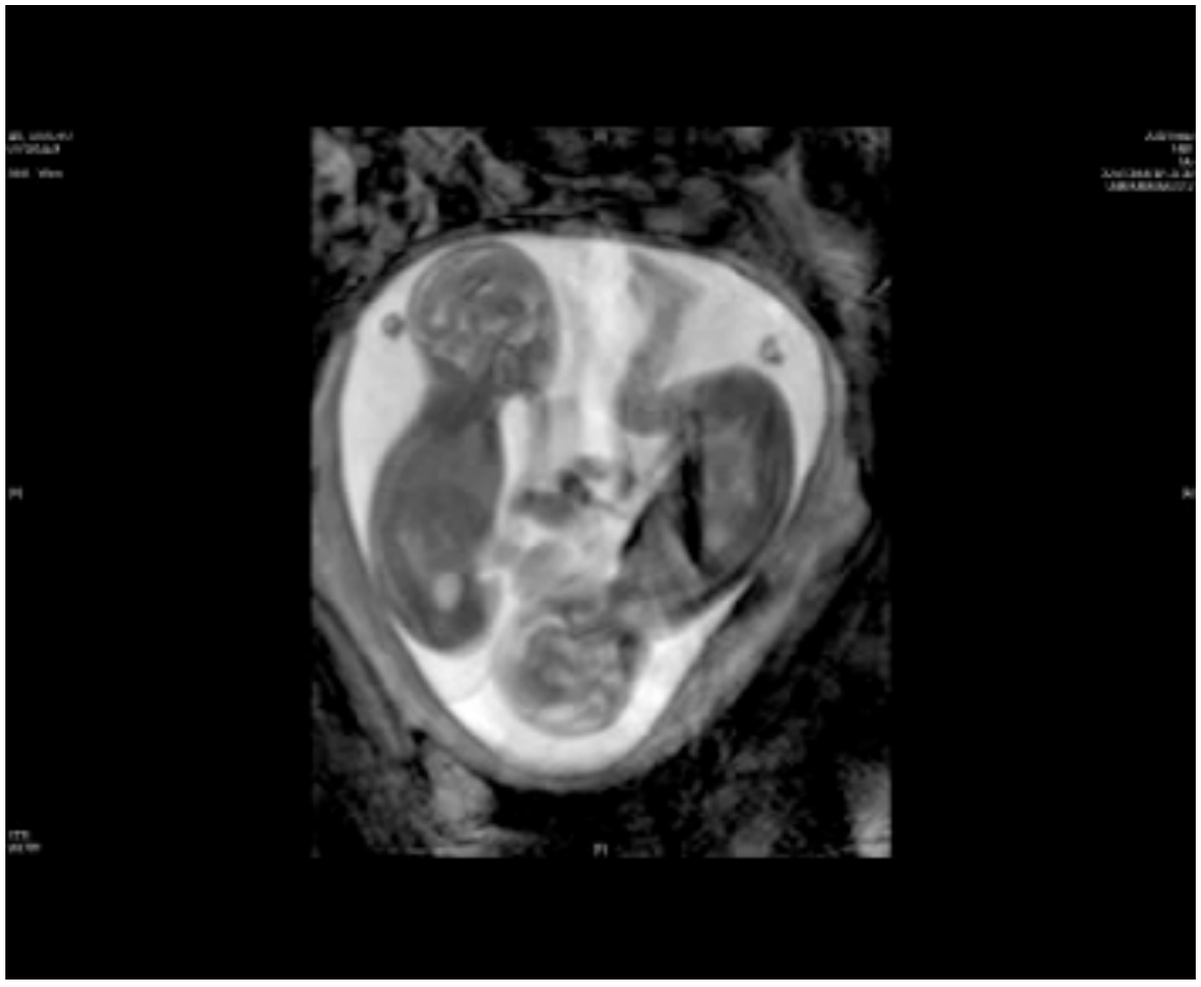
FIGURE 5.4 Rat fetuses after normal gestation (left photo) and after being immobilized by curare during the last three days of gestation (right photo). The curarized fetus exhibits fused joints, underdeveloped hind limbs, a small mouth, thin, tight skin, and a shortened umbilical cord. Reproduced with permission from *Pediatrics*, 72, 858–859. Copyright © 1983.

Moessinger, Adrien C. "Fetal akinesia deformation sequence: an animal model." *Pediatrics* 72.6 (1983): 857-863.

- Less movement leads to malformation of the joints Oppenheim, Ronald W., et al. J*ournal of Comparative Neurology* 179.3 (1978): 619-640.

Fetal movements continuously change position of the 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 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

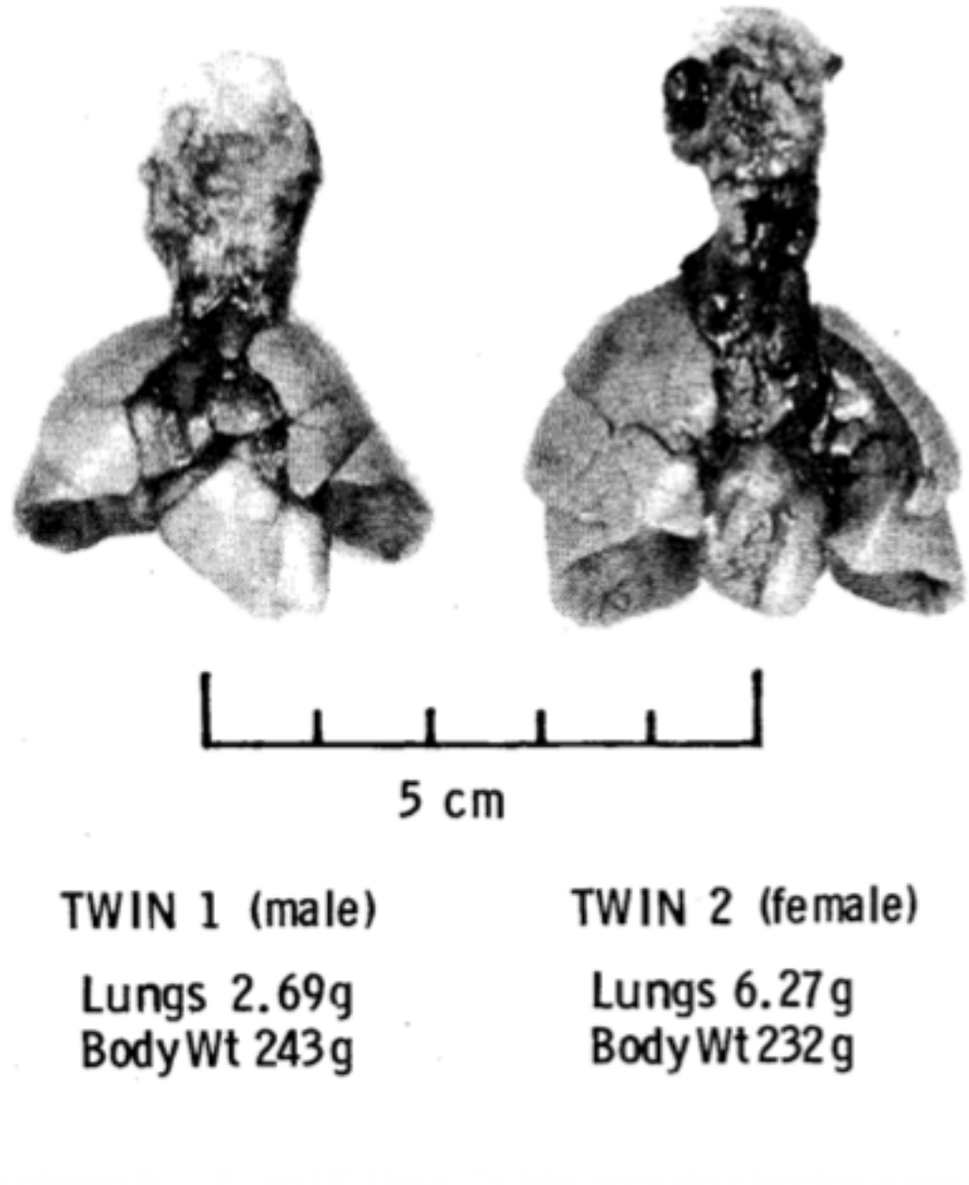
- Function at developing neuromuscular junction are critical in controlling cell death

Oppenheim, Ronald W., et al.1978

Fetal movements facilitate gene organization

- Influences how differentiating tissues respond to gene organization

- Lack or impairment of physical forces changes the state of the organs



Fetal repertoire by week

8 weeks	10 weeks
Startles	Startles
General movements	General movements
Hiccups	Hiccups
	Breathing movements
	Isolated arm and leg movements

Formation of the diaphragm begins at 8 weeks and is complete by 10 weeks

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

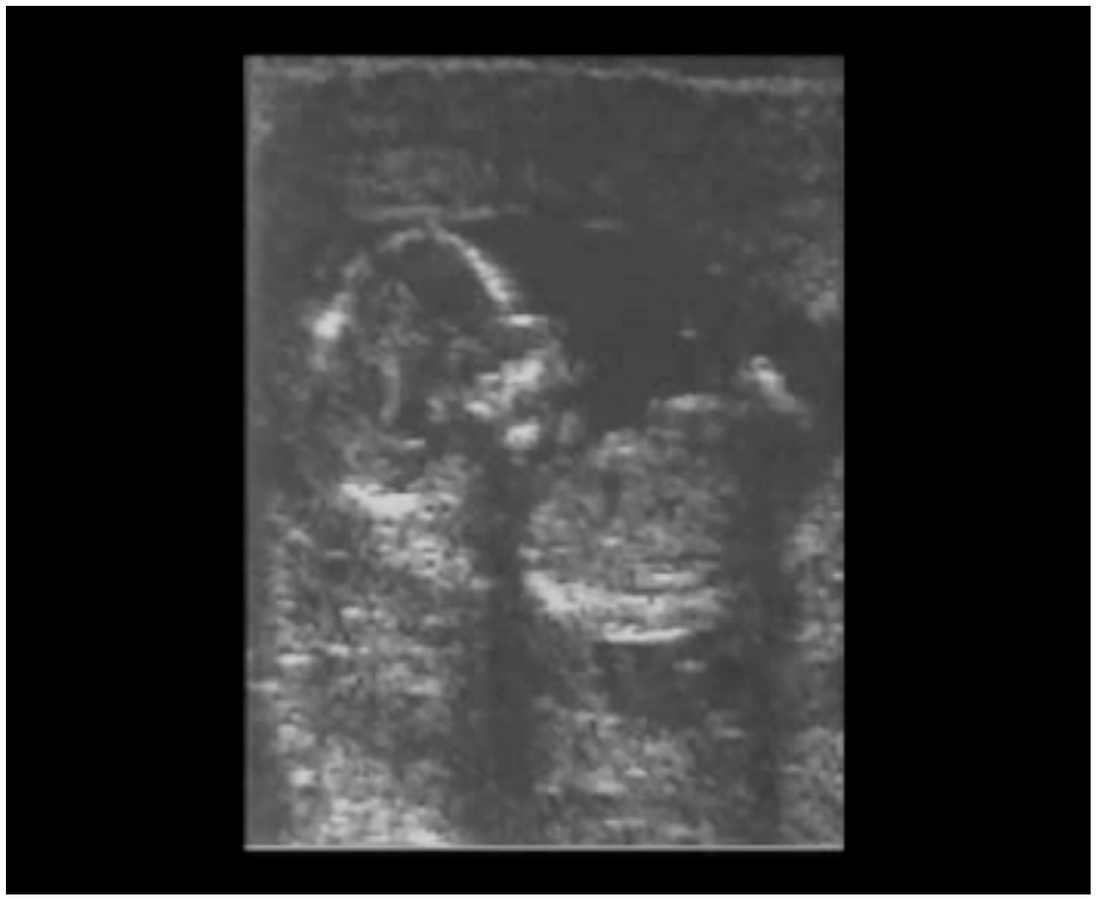
Fetal hiccups

- Frequent in early gestation
- Begin decreasing when fetal breathing movements increase at 12 weeks
- Precursor of fetal breathing
- Hiccups cause repeat contractions of diaphragm smooth progress of subsequent diaphragmatic motions necessary to fetal breathing

Einsieler, Prayer, Prechtl 2012

Fetal breathing

- Occur episodically with either regular or irregular pattern
- 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

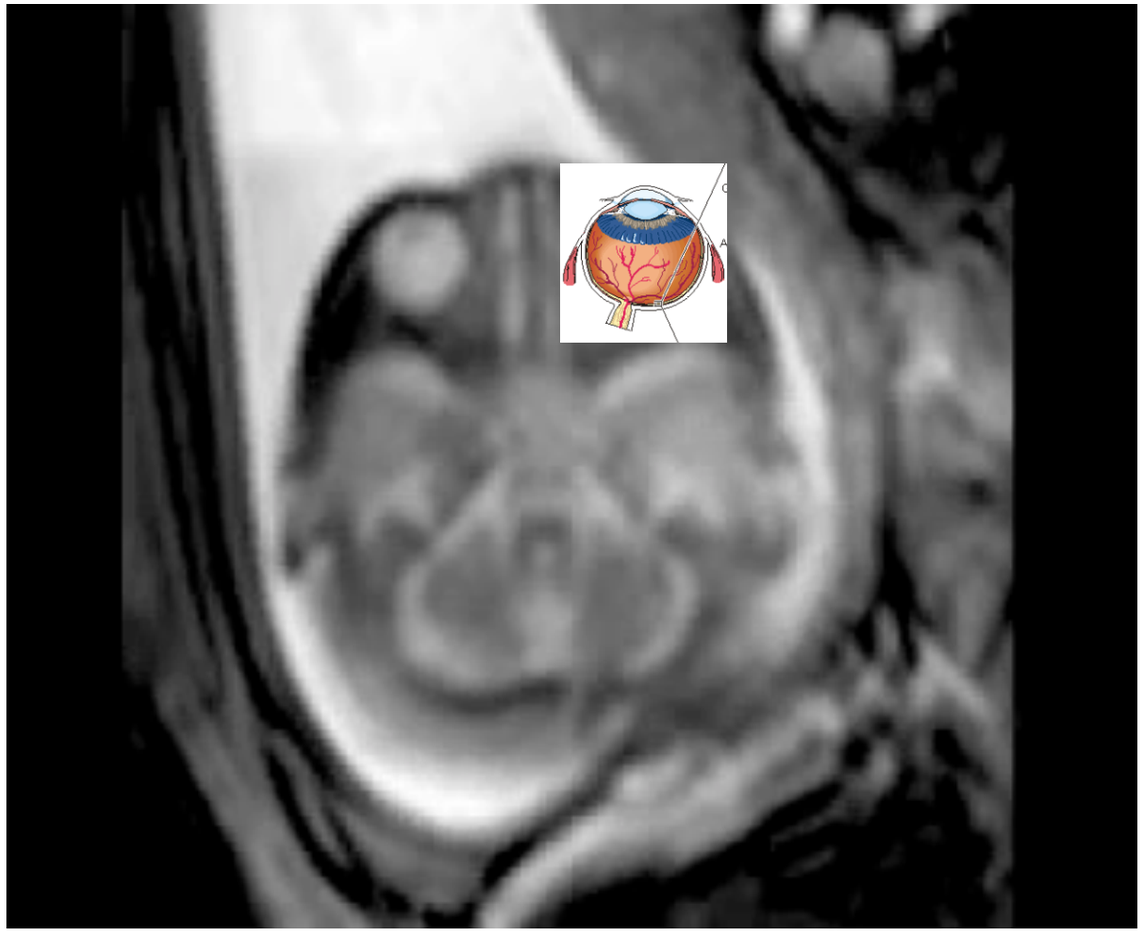
- Observed as early as 16 weeks gestation present until term

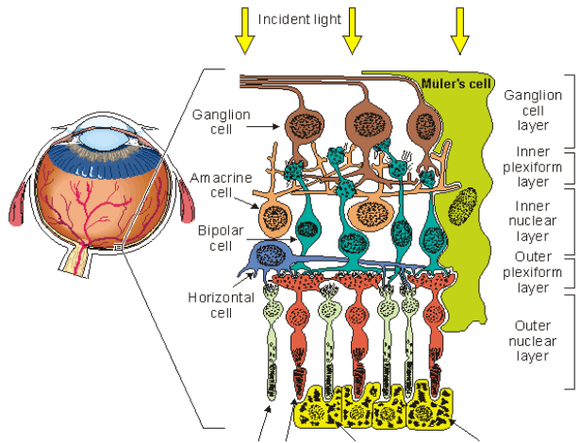
- Most eye movements are horizontal and conjugate

- Important in differentiation of cholinergic amacrine cells

- Non-moving eyes do not develop a type of retinal cell involved in motion detection

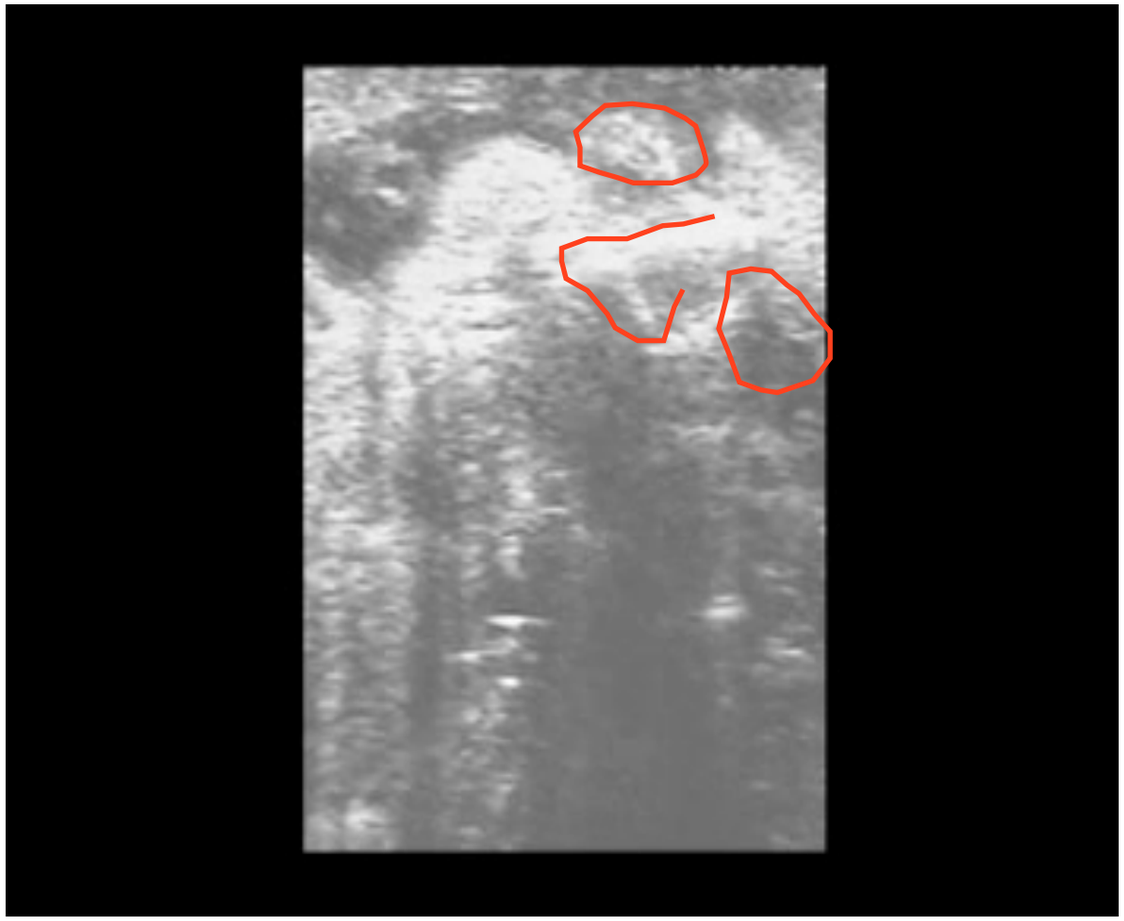
Baguma-Nibasheka, M., et al. (2006).





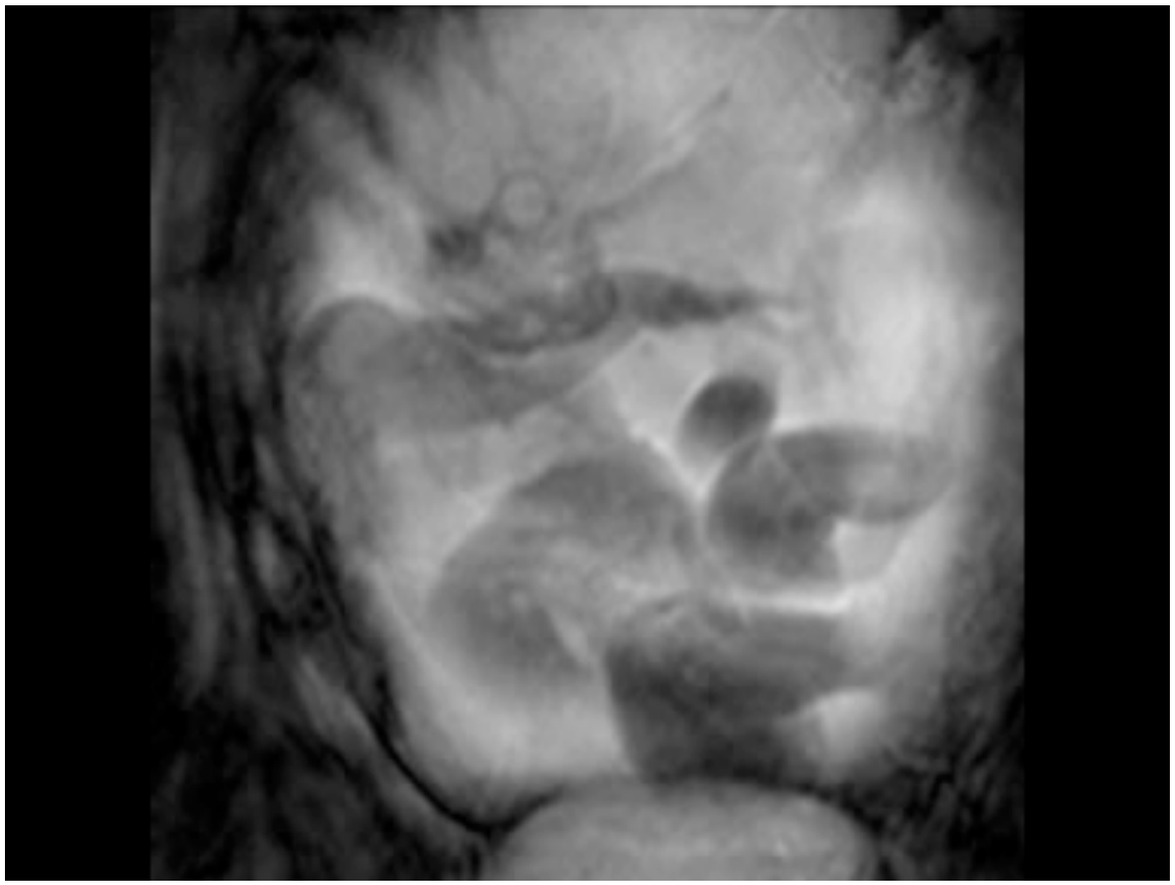
Fetal eye movements

- If eye does not move at all, motion capture cells do not develop



- **Einsieler, Prayer, Prechtl 2012**

Fetal movements *may* develop sensory pathways in the brain



Developmental 'awakening' of primary motor cortex to the sensory consequences of movement

James C Dooley[1,2]*, Mark S Blumberg[1,2,3,4,5]

General Movements

- 9-10 weeks PMA complex and generalized movements and startles occur

- General movements slower than startles and have complex sequence of involved body parts

Einspieler, Prayer, Prechtl 2012

10 weeks gestation

Why?

- Period of more activation of the cortical areas of the brain

- Shift from subcortical to cortical modalities of neural mechanisms (Chugani and Phelps, 1986)

100 Days Celebration

Normal Fidgety Movements

↓

Normal Neurologic Development

Absent Fidgety Movements

↓

Cerebral Palsy

How can we use this information?

Early detection

- 27 week preterm infant
- BPD
- Normal head ultrasound

So what?

Elimination of synapses in developing nervous system

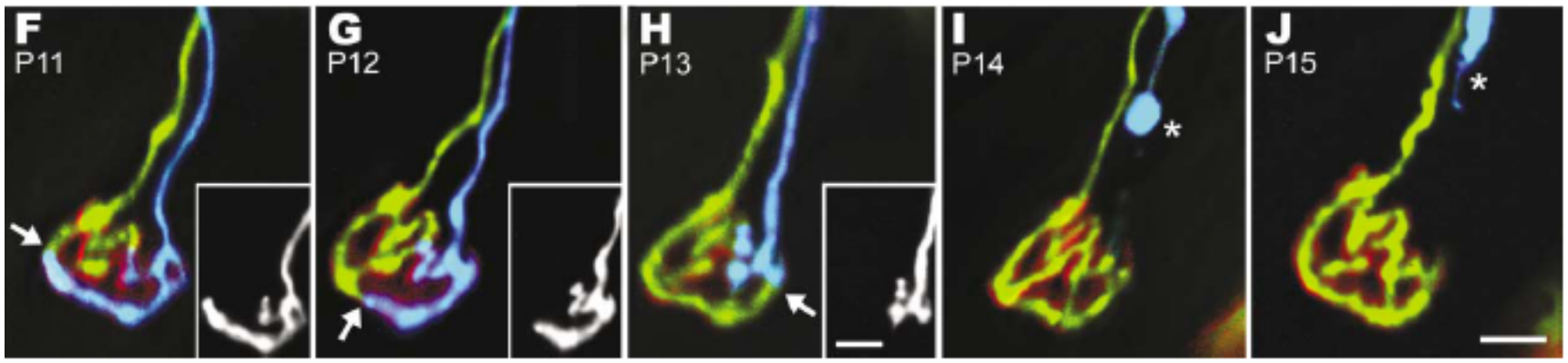


Figure 2. Synaptic Takeover

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.

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

Critical Periods

- Most common in early childhood

- Certain windows of time during which the young especially sensitive to their environment

- “If you don’t use it, you lose it”

  - Babies with amblyopia will fail to develop full acuity and depth perception if the problem is not corrected

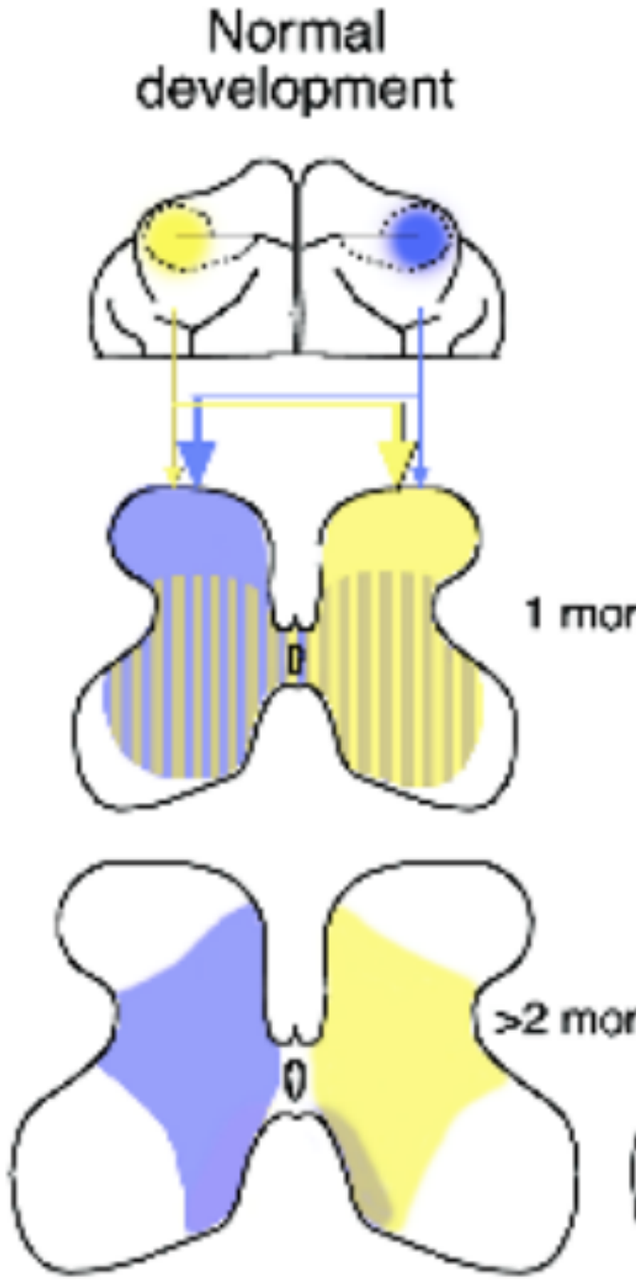
  - Patch good eye to compete for neurons

CST development

- Corticospinal tract (CST) principal motor control pathway for skilled movements

- Has a protracted development, matching development of skilled movements

- Prolonged period of vulnerability when damage to CST (or its cortical origins) can have long term consequences to motor function



Eyre et al, 2007

Is Hemiplegic Cerebral Palsy Equivalent to Amblyopia of the Corticospinal System?

Janet A. Eyre, DPhil, MBChB,[1] Martin Smith, PhD, MBBS,[1] Lyvia Dabydeen, MBBS,[1]
Gavin J. Clowry, DPhil,[1] Eliza Petacchi, MD,[2,3] Roberta Battini, MD, PhD,[2] Andrea Guzzetta, MD, PhD,[2]
and Giovanni Cioni, MD[2,3]

Newborn
6-12 months
2-3 months
Right
Left

When do babies show signs of hemiplegia?

Pre-term infants with hemiplegia first show signs of bilateral abnormal movements

Cioni 2000, Guzetta 2003

They show asymmetry only at second month post-term

2 weeks old

Injury
Right

Newborn
6-12 months
2-3 months

Left

Corticospinal tracts

Competition

Activity Dependent Withdrawal

Increased ipsilateral projections from the noninfarcted cortex compound disability by competitively displacing surviving contralateral corticospinal projections from the infarcted cortex

Eyre et al, 2007

Vicious cycle whereby lesions reduce movement, which in turn prohibits normal neural development of the circuitry underlying movement

Eyre et al, 2007

Consequences of brain injury

- Child with mild hemiplegia will develop 1-3 cm of contracture in gastrocsoleus-Achilles tendon complex b/w birth and skeletal maturity

- Usually accompanied by 2cm shortening of the tibia on affected side

- 3cm reduction in circumference of calf muscle

Gage et al, 2009

Mirror movements may be caused by a strong connection between ipsilateral M1 and the mirror movements conveyed through a dominant ipsilateral corticospinal pathway

Why is this a problem?

Harnessing activity-dependent plasticity to repair the damaged corticospinal tract in an animal model of cerebral palsy

JOHN H MARTIN[1] | SAMIT CHAKRABARTY[1] | KATHLEEN M FRIEL[2]

The cats got better with early intervention!

Therapy worked!!

- Constrained the unimpaired limb and trained impaired limb x 4 weeks

- Restored normal CST spinal connections and behavior

Martin, Chakrabarty, Friel, 2011

Needed training to see change

- 4 weeks of constraint of unimpaired limb alone without training of affected limb- resulted in no reduction of step distance (compared to significant result with training)

- Suggests CST synaptic competition is at work in re-establishing normal connections after activity-based treatment

Martin, Chakrabarty, Friel, 2011

Pathophysiological mechanisms of impaired limb use and repair strategies for motor systems after unilateral injury of the developing brain

KATHLEEN M FRIEL[1,2,3] | SAMIT CHAKRABARTY[3,4] | JOHN H MARTIN[3,5]

- 3 Treatment groups:
  - Constraint only (immediately after injury)
  - Constraint and early reach training (immediately after injury 1hr/day)
  - Constraint and late reach training (feline adolescence 1hr/day)

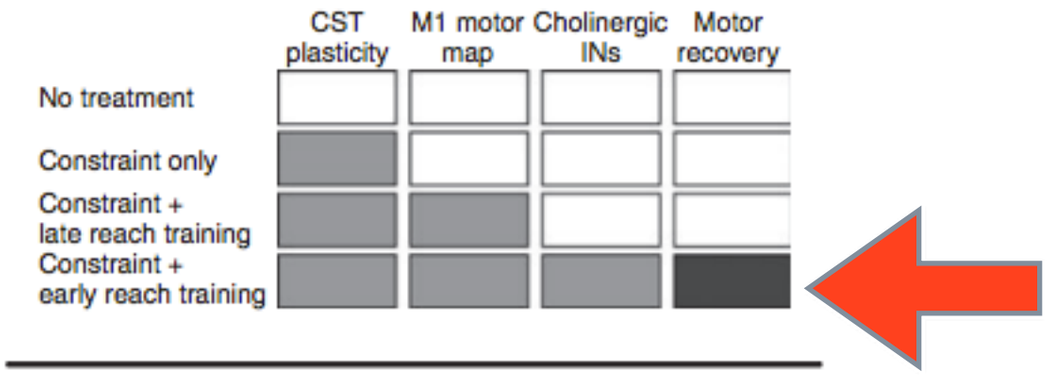


Figure 4: Summary of effects of the different behavioral interventions. Gray rectangles, conditions in which an effect was noted. Corticospinal tract (CST) plasticity is defined as the presence of axons/varicosities within the spinal intermediate gray matter or more ventrally. An effect of treatment on the M1 motor map is defined as a substantial increase in the number of sites from which stimulation evoked a limb motor response. A filled light gray rectangle in the cholinergic interneuron (INs) column indicates the presence of a robust increase in the ratio of spinal cholinergic interneurons on the affected and unaffected sides. The dark gray rectangle in the motor recovery column indicates a significant reduction in forward step distance (i.e. a reduction in overstepping the ladder rung during performance of the horizontal ladder task that achieves a normal step length).

Only early training group had motor recovery!

What does that mean for us?

- In cat study, the period of effective activity treatments immediately follows the period of CST refinement
- In humans this occurs between 3 months and 1 year of age
- This early age is optimal time to intervene in children at risk for developing CP

Martin, Chakrabarty, Friel, 2011

What does that mean for us?

- Problematic if cerebral palsy is not diagnosed until age 2 or later

What does that mean for us?

- If cat model theory is correct, altering balance in activity on two sides at an early age may normalize connectivity and help ameliorate or prevent development of impaired motor function!!!

Martin, Chakrabarty, Friel, 2011

How can we apply this information to our patients?

STUDY PROTOCOL | OPEN ACCESS | OPEN PEER REVIEW

Efficacy of baby-CIMT: study protocol for a randomised controlled trial on infants below age 12 months, with clinical signs of unilateral CP

Ann-Christin Eliasson ✉, Lena Sjöstrand, Linda Ek, Lena Krumlinde-Sundholm and Kristina Tedroff

BMC Pediatrics 2014 14:141 | DOI: 10.1186/1471-2431-14-141

Received: 2 May 2014 | Accepted: 22 May 2014 | Published: 5 June 2014

Eliasson, 2014

Baby CIMT study

- Underlying assumption: self-initiated motor actions CRUCIAL for motor development

- Randomized babies with hand asymmetry (ages 3-8m): massage group or CIMT

- Simple glove on babies (as early as 3m)

- Two 6 week training periods, 5-7 days/week by families at least 30 minutes/day

Eliasson, 2014

Training principles

- Encourage self-produced motor activities
- Activities need to be novel, challenging, and always fun!
- In pilot study, children are always permitted to take off “soft glove”
- Activities are never forced

Research in Developmental Disabilities 72 (2018) 191–201

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Research in Developmental Disabilities

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Research paper

The effectiveness of Baby-CIMT in infants younger than 12 months with clinical signs of unilateral-cerebral palsy; an explorative study with randomized design

Ann-Christin Eliasson[a,*], Linda Nordstrand[a], Linda Ek[a], Finn Lennartsson[b,c], Lena Sjöstrand[a], Kristina Tedroff[a], Lena Krumlinde-Sundholm[a]

[a] Department of Women's and Children's Health, Karolinska Institutet, Stockholm, Sweden
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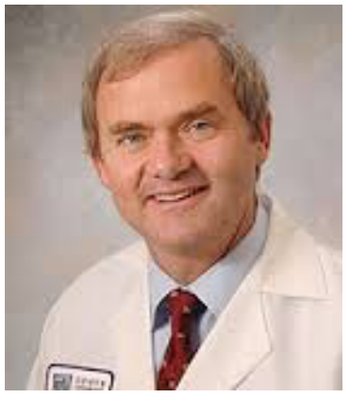
Case study

Acknowledgments

Michael Msall MD



Michael Schreiber, MD

Jeremy Marks, MD, PhD

General Movements Trust, Andrea Guzzetta MD, PhD, Arie Bos MD, PhD, Giovani Cioni MD, PhD, Christa Einspieler PhD, Alicia Spittle PT, PhD, Fabrizio Ferrari MD, PhD, Natasicia Bertonecelli PT

Alexander Drobyshevsky, PhD

Ragnhild Stoen, MD, PhD

Lars Adde, PT, PhD

Thank you!

Questions?

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