Prediction of CP in Young Infants: Current Concepts and Research

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General movements

- Early identification of cerebral palsy can be achieved through analysis of spontaneous movements

Traditional neonatal neurologic examination

- Classic neurophysiology
- Sir Charles Sherrington 1906
- Studied de-cerebrated animals and spinal preparations
- Able to study in detail stable, quantitative relationship between sensory input and reflexive motor output

Traditional neonatal neurologic examination

- Early studies on human fetal movements done on exteriorized fetuses (Minkowski 1928, Hazel 1952)
- Survival limited to a few minutes during which fetus was stimulated with tactile stimulation
- Studies conducted with principals of reflexology and behaviorism
- Described abnormal movement patterns of dying fetuses
- Used as basis for future neonatal neurological examination
Traditional neonatal neurologic examination

- Concept of tonus/tone introduced into neurology by adult neurologist Andre-Thomas
- Later brought ideas of tonus testing to infant neurology (Thomas and Saint-Anne Dargassies 1952)

The problem with traditional exam

- Severe cases of hypotonia and hypertonia are clinically important
- In most cases, there is an inconsistent character of tonus in young infants
- Inter-observer agreement is weak
- During first weeks of life- hypotonia and hypertonia are not specific signs of later neurologic dysfunction (Prechtl 1997, 2001)

Traditional examination components:
- Reflexes
- Responses to elicited stimulation
- Tonus

Classic neurophysiologists studied neural functions in experimentally impaired neural systems
- Focus of attention was on quantitative relationship between sensory input and reflex (motor) output
- Excluded spontaneous movements to get clear cut results
The problem with traditional exam

- Led to distortions of concept of neural functions

Classic stimulus-response

The problem with traditional exam

- Can reveal acute condition of infants nervous system, but lacks power to make a specific prognosis
- At level of individual infant and its parents, can be more of a gamble and burden, then a help

Prechtl’s conclusion

- Reflexes are performed more consistently by decerebrated animals than by humans
- Therefore, reflexes cannot be the best way to study the consequences of brain development

Prechtl’s conclusion

- Spontaneous motility is an expression of spontaneous neural activity
- Qualitative assessment of spontaneous activity is a sensitive indicator of neurological impairment
- A window into the brain!
Paradigm shift

- Reflex-based
- Passive nervous system
- Response to elicited stimuli

- CNS is active and endogenously-generating
- Spontaneous movements indicate neurologic function

Central pattern generators

- 1913 Graham-Brown discovered locomotor movements in kittens are not based on reflex activity, but on intraspinal generation
- Well-known CPGs include mechanisms for breathing, sucking and chewing, locomotion: swimming, crawling, walking

Rhythmical patterns

- Can be generated continuously
  - Breathing
- Can be generated episodically
  - Locomotion
  - When long or short bouts of rhythmic activity are interspersed with periods of quiescence
- Arises from active, maintained inhibition of otherwise active network (Staras et al 2003)

Non-rhythmical patterns

- Many exhibited in human fetus and young infant without any recognizable stimulus
- Prechtl suggests these generating neural mechanisms should also be called CPGs because the relevant motor patterns are constant in form and recognizable when they occur (e.g., general movements, yawns, stretches, startles) (Forsberg, 1999)
Non-rhythmical patterns

- Their periodical or episodical rate of occurrence suggests CPG, as documented in studies of fetal motility actograms (de Vries JIP et al 1985, 1988)
- The similarity between fetal and unstimulated preterm infants (at the same PMA) actograms indicate CPG vs. outside influence on motility (Prechtl 1997)

Central Pattern Generator

- Animal studies isolate brainstem and spinal cord preparations in vitro and obtain direct extra- and intracellular recordings from various neurons, transmitters, and receptor blocks in CPG network
- Most CPGs consist of neurons which act as pacemaker-like structures

Central Pattern Generator

- Isolated CPGs generate fictive locomotor rhythms (recorded in absence of movements)
- Indicates fundamental pattern of motor output depends on intrinsic connectivity and electric properties of central circuits
- Sensory inputs are required to modify pattern of motor activity in response to the actual circumstances of real movement (Suster and Bates 2002)
Early movement

- First movement occurs at 7.5-8 weeks PMA
- Sideward bending of the head

Early movement myth-busters

- Tonic and phasic movements emerge at same time 9-10 weeks
- All early and later fetal movement patterns are differentiated from first appearance onward
- Stretches and yawns complex movements that do not change throughout entire life-begin at 10 weeks PMA (Prechtl 1989)

Form and pattern of movements largely unchanged in first weeks after birth

- 9-10 weeks PMA complex and generalized movements and startles occur
- General movements slower than startles and have complex sequence of involved body parts

Yawn at 14 weeks gestation

GMs at 27 weeks gestation

GMs at 34 weeks gestation
• Some of motor patterns come under sensory control after birth
• Rooting, sucking, breathing movements
• At birth new motor repertoire functions of lung ventilation- (sneezing, coughing) and vestibular responses (VOR, Moro) (von Bernuth and Prechtl 1969, Cioni et al 1984)

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• Continuation of prenatal repertoire during first two months post-term age (Prechtl 1984, Cioni et al 1989, Hadders-Algra and Prechtl 1992)
• In healthy preterm infant, continuation lasts until the same PMA as the infant born at term (Cioni and Prechtl 1990)
• 3rd month of life (PMA) transformation of motor and sensory patterns occurs (Prechtl 1984)

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• Preterm general movements
• Prior to term age
• Writhing general movements
• Term age to 6-9 weeks

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• Fidgety general movements
• Emerge at 6-9 weeks as writhing movements gradually disappear

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General movements

• Believed to be generated supraspinally
• Both startles and GM include activity of all segments from cervical to lumbar spinal cord
• Movements emerge in the fetus at 9-10 weeks PMA, unlikely to have involvement higher than brainstem

• GMs of writhing quality and fidgety movements likely come from different CPGs
• Temporal overlap during transition between writhing and fidgety GMs
• Writhing movements still present at 6 months during infants sleep
Pre-term GMs

- No difference observed between fetal and preterm movements, suggesting neither force of gravity after birth nor maturation has an influence on the appearance of preterm GMs
- Occasionally have large amplitudes and are often of fast speeds
- Extremely variable movements

Writhing movements

- Term age to first two months post-term
- Small to moderate amplitude
- Slow to moderate speed
- Typically ellipsoid in form, creates impression of writhing quality
- Something forceful has been added to variable preterm movements

2nd-3rd month- neural transformation

- Compared to primates, human neonate less adapted to extra-uterine environment
- Human pregnancy is relatively short
- Compensated by effectiveness of higher intelligence of caregivers

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
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)

Fidgety movements

- Small movements of moderate speed and variable acceleration of neck, trunk and limbs, in all directions, continual in awake infant, except during fussing and crying
- Seen as early as 6 weeks, but usually occur at 9 weeks and continue to 20 weeks
- Early onset (6 weeks) mainly observed in preterm infants
- In all typical GMs - variation in onset of ms activity and large amount of co-activation in antagonistic ms groups

Fidgety movements

- Temporal organization of fidgety movements varies with age
- Initially occur as isolated events, gradually increase in frequency and then decrease once again
- Can be broken down into continual, intermittent, sporadic

Fidgety movements

- Usually equally present in the distal and proximal body parts
- Some infants with more activity in wrists and ankles than in the trunk and proximal joints, and vice versa
- Can be relevant in prediction of less optimal neurological outcome
Fidgety movements

Various other movements can occur with fidgety movements:
- Wiggling-oscillating
- Saccadic arm movements
- Swipes
- Mutual manipulation of fingers
- Manipulation of clothing
- reaching and touching
- Legs lift with or without hand-knee contact
- Trunk rotation
- Axial rolling

Abnormal GMs

- Quality of GMs probably modulated by cranial structures (cortico-spinal, reticulo-spinal)
- Disruption of cortico-spinal projections by periventricular lesions of the corona radiata or internal capsule (due to IVH or hypoxic-ischemic lesions) leads to abnormal GMs
- If the nervous system is impaired, GMs lose their complex and variable character
- Can have a poor repertoire, be cramped-synchronous, or chaotic
- True for preterm, post-term, and early post-term (2 months)
- Fidgety movements can be abnormal or absent

Poor repertoire GMs

- Occurs during preterm, term and early postnatal age
- Sequence of successive movement components are monotonous
- Movements of different body parts do not occur in complex way seen in normal
- Frequent in infants with abnormal HUS
- Can be followed by normal, abnormal, or absent fidgety movements
- Lower predictive value

Cramped-synchronized GMs

- Abnormal from preterm age onward
- Movements appear rigid and lack the normal smooth and fluent character
- If observed consistently over a number of weeks, is highly predictive for cerebral palsy
- All limb and trunk muscles contract and relax almost simultaneously
**Crammed-synchronized GMs**

*Prechtl et al 1997 conducted the largest longitudinal study to date of 130 high-risk infants.*

- All children (N=40) who consistently showed cramped-synchronized GMs developed severe spastic cerebral palsy.
- Consistent findings: biweekly preterm, one during term, two during postterm.

**Predictor of CP**

- Ferrari et al 2002 found that the earlier cramped synchronized GMs occur, the worse the later motor impairment.

**Chaotic GMs**

- Movements of all limbs are of large amplitude and occur in a chaotic order without any fluency or smoothness.
- Can be observed during preterm, term and early post-term age, but are rare.
- Consistently appear to be abrupt.
- Often develop cramped-synchronized GMs a few weeks later.
Abnormal fidgety movements

- Rare
- Predictive value low
- Look like normal but amplitude, speed and jerkiness are moderately or greatly exaggerated

Absence of fidgety movements

- If fidgety movements are never observed from 9-20 weeks post-term
- Other movements can be commonly observed
- Highly predictive for cerebral palsy, both spastic and dyskinetic forms
- If cramped - synchronized movements present at 3-4 months, fidgety movements are absent

Predictor of CP

- Prechtl et al 1997: 96% of infants with normal fidgety movements (67/70) were normal at the age of 2; none developed cerebral palsy
- 44/130 never showed fidgety movements and 43/44 (98%) developed CP
- Remaining infant had severe cognitive and motor impairment

Predictor of CP

- Ferrari et al 2002: 43/44 (98%) high-risk infants with absent fidgety movements developed spastic cerebral palsy
Interrater reliability

- 11 studies on 358 infants, assessed by 90 testers had agreement between 83-93%.
- Effectiveness of training at 3-4 day basic training course: 83% correct judgements.
- Additional training improved to 89%.
- Global discrimination between normal and abnormal, agreement 94%.
- More difficult to correctly judge infants at term.

Validity

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GMs vs. Ultrasound

- Brain US most frequently used imaging technique.
- Several studies have found that the GM assessment is superior to head ultrasound in predicting neurological outcome (Ferrari et al 1990, Cioni et al 1997, Prechtl 1997, Bos 1998, Ferrari et al 2002).

GMs vs. traditional neurological exam

- Superior predictive power of qualitative assessment of GMs to traditional neurological examination at all ages.