Mechanisms of Injury in Dyskinetic Cerebral Palsy

Alec Hoon, MD
Associate Professor of Pediatrics
Johns Hopkins University School of Medicine
Director, Phelps Center for Cerebral Palsy
Kennedy Krieger Institute

Key Concepts in Cerebral Palsy

- Motor control: tone, posture, movement
- 2-3/1000 children
- Risk factors include infection, inflammation, low birth weight, prematurity, genetic
- Secondary to brain dysgenesis or injury
- “Non-progressive” manifestations can change
- Unilateral and bilateral phenotypes
- A range of associated disorders
- Etiology links to phenotype links to treatment
Cerebral Palsy - Clinical Phenotypes

Cascade of events in brain injury

1. Prenatal antecedents may be suspected - (Freud)
2. Final common pathways often involve hypoxia-ischemia and infection-inflammation
3. Injury may have a protracted time course
4. Injury may lead to myelin abnormalities, reduced plasticity and decreased cell number
5. Injury changes both developmental trajectory and may sensitive brain to later injury

The Evolving Nature of Injury
### Dyskinetic Disorders

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Etiology/Risk Factors</th>
<th>Neuroimaging</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute HIE</td>
<td>Hypoxia-Ischemia</td>
<td>Putamen, VI, Thalamus, Perirolandic Motor Strip</td>
</tr>
<tr>
<td>Kernicterus</td>
<td>Bilirubin toxicity</td>
<td>Globus Pallidus, Subthalamic Nucleus, Substantia Nigra, Brainstem</td>
</tr>
<tr>
<td>PVCL+</td>
<td>Hypoxia-Ischemia, Infection-Inflammation</td>
<td>Pulvinar, Periventricular White Matter</td>
</tr>
<tr>
<td>PKAN</td>
<td>PKAN</td>
<td>Globus Pallidus (“Eye of the Tiger”)</td>
</tr>
<tr>
<td>GA1</td>
<td>GC0H</td>
<td>Caudate and Putamen</td>
</tr>
<tr>
<td>Leigh Syndrome</td>
<td>Nuclear, Mitochondrial genes</td>
<td>Basal Ganglia, Brainstem, other</td>
</tr>
<tr>
<td>Proprionic Acidemia</td>
<td>PCCA, PCCB</td>
<td>Globus Pallidus</td>
</tr>
<tr>
<td>Striatal Necrosis</td>
<td>Neuroinflammatory</td>
<td>Caudate and Putamen</td>
</tr>
</tbody>
</table>

### Basal Ganglia Circuitry

- **Basal Ganglia Circuitry**

### Neonatal Encephalopathy- Term Infant: A Cause of CP in 15-20% of Cases

- A constellation of findings including abnormal consciousness, tone, reflexes, feeding, respiration or seizures and can result from myriad conditions.
- May/may not result in permanent neurologic impairment.
- Pathway from intrapartum hypoxic-ischemic injury to CP must progress through NE.

ACOG Task Force on Neonatal Encephalopathy, 2003
Term infant with HIE:
Energy Failure Impairs Glutamate Pump

Exito-oxidative Cascade

Acute HIE: Images in Newborn Period
Asphyxia Damages Structures Connected by Excitatory Pathways

Involvement of GP in Kernicterus

Periventricular Leukomalacia (PVL)

Periventricular White Matter Injury (PVL) in premature infants: the most common cause of CP

Selective Vulnerability - Immature Oligodendroglia

- Immature vascularity - impaired autoregulation
- Oligodendroglia vulnerable to ischemia/inflammation
- Free radical pathway to destruction
Periventricular Leukomalacia (PVL)

Thalamic Lesions in HIE and PVL

MRI: Striatal Necrosis