

SHAKE, RATTLE AND ROLL: THE PEDIATRIC BRAIN (PART 1)



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Background

The brain is an amazing organ with over 2½ billion cells split between neural cells and glial cells. Neural cells, or neurons, are the electrical conducting cells which make up the grey matter of the brain. The glial cells, on the other hand, surround the neurons, providing support and insulation. Each neuron consists of one to several dendrites, branch-like structures which conduct electrical activity into the cell, and only one axon, a long thread-like extension which conducts electrical impulses out of the cell. Components of the white matter of the brain, axons are coated in myelin sheaths made up of Schwann cells, a fatty insulation that speeds up impulse conduction. Impulses are conducted at the synapses where the axon meets the dendrite. Neurotransmitters are released from the axon, cross the synaptic cleft, and attach at receptor sites on the dendrite, where they activate the cell. The activation may cause either excitation or inhibition of the receiving cell. There are a number of different neurotransmitters, and more than one type can be released at each synapse. Many psychoactive medications, drugs and neurotoxins can change the properties of neurotransmitter release, neurotransmitter reuptake and the availability of binding sites. This is how they are used to change the brain's response.

Locations in the brain are identified in several different manners. Technical language used in describing locations on brain imaging include: horizontal/transverse plane, which describes a section of the brain as if being sliced from front to back, looking up from the toes to the head; coronal plane, which is a slice separating the front from the back; and sagittal plane, which separates the left from the right. Locations on the brain itself are identified using the terms *gyrus*, *sulcus* and *fissure*. A gyrus is a ridge, while a sulcus is a shallow groove and a fissure is a deep groove. The brain can also be described by its lobes, of which there is a left and right of each with the bones above them named the same. While these are generalities and

Executive Summary *This is part one of a two-part series on the pediatric brain. The described illnesses, conditions and syndromes may be seen on insurance applications and attending physician statements of children and young adults. Part one includes a general overview of brain anatomy and function, and explores common pediatric neurologic impairments. The various conditions are reviewed in chronological order of common presentation, and include craniosynostosis, plagiocephaly, febrile seizures, epilepsy and concussions.*

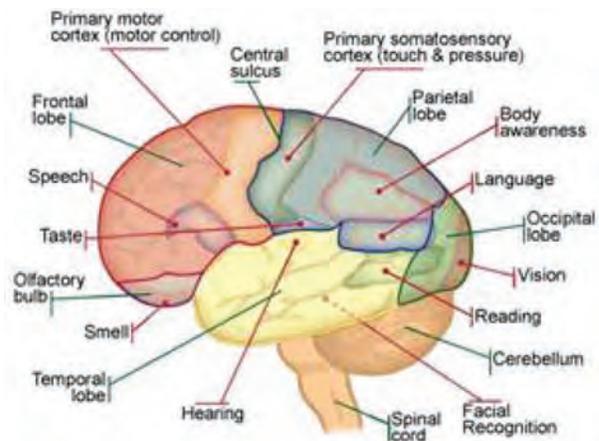
there is some overlap, the occipital lobe is responsible for vision, the temporal lobe for hearing and memory, the parietal lobe for sensation, and the frontal lobe for executive function. Also, most of the right side of the brain processes and controls the left side of the body and vice versa. Primarily, in both the spine and the brain, posterior areas are involved in sensation while anterior areas handle motor control. The brainstem controls more vital functions, such as the autonomic nervous system including breathing and heartbeat, level of alertness, sleep regulation, and the swallowing of solids and liquids. Hence, any pathology affecting the brainstem is quite dire in nature.

An adult brain weighs approximately 1350g or 3 lb, and consists of 2% of an adult's mass. The adult brain utilizes 20% of the body's total energy and oxygen intake. The brain consists of 73% water, but only 2% dehydration is enough to affect attention, memory and cognitive skills, an effect that is more pronounced in the very young and very old.

The pediatric brain differs from the adult brain in several ways. At birth, an infant's brain is a much larger percentage, 12%, of the total mass than an adult's brain, 2%. The average newborn's brain weighs approximately 350-400g or 12-15oz, and be-

gins growing immediately with an initial 1% increase in size per day. By 90 days old, the infant's brain has reached 55% of adult size. Growth, architectural changes, myelination and synaptic development are all occurring simultaneously. Initially, there is very little myelination and complexity. The folds, gyri and sulci, occur from the 700 new neural connections that are formed every second during the first 2-3 years of life. Throughout life, synaptic formation and pruning occur, but in different proportions at different stages. Initially, formation dominates, until 2-3 years of age, when the maximum of synaptic connections during a person's lifetime exist, after which pruning increases. Adult size of brain tissue is generally reached during adolescence. However, the brain is not thought to be fully developed until an average age of 25 years, when the frontal lobe finally reaches adult potential. This explains much of the impulsive actions and poor decision making that is often seen in adolescents and young adults. Twenty-five years is an average age; some reach maturity sooner than others.

The brain is the organ responsible for most neurologic and nearly all psychiatric disorders in children. The spine and the peripheral nervous system are the remaining portions of the neurologic system, and pediatric impairments regarding these are rare and will not be discussed here. Some neurologic and psychiatric disorders are treated with the same medications and medication classes. A solid understanding of the brain aids in the understanding of these impairments.



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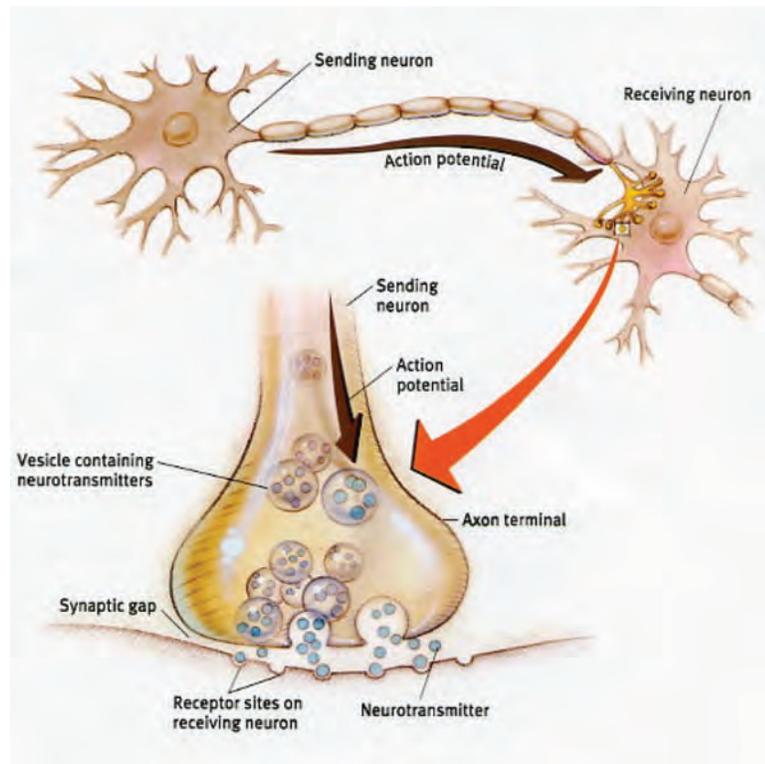
Neurologic Impairments

Craniosynostosis

Craniosynostosis is the premature fusion of the sutures in the skull. Technically, this is not a neurologic disorder, but a skeletal issue. However, neurosurgeons and neurologists handle this clinically. When a baby is born, the skull is made up of multiple unfused bones that fuse with age. If one of the sutures fuses prematurely, the skull will grow in an abnormal fashion. Surgical repair is performed, usually in infancy, rarely to prevent or treat increased intracranial pressure and, more commonly, to correct or prevent cosmetic deformities. As long as the craniosynostosis is present without a syndrome (genetic abnormality or group of associated malformations), the standardized mortality ratio (SMR) 1 year after repair is essentially normal. These children tend to do very well after recovering from surgery.

Positional Plagiocephaly

Positional plagiocephaly is a similar appearing yet very different condition. The skull of infants with this impairment are slightly misshapen, but for a different, more benign reason. Years ago, positional plagiocephaly was recognized, but had a very low prevalence and, therefore, received very little attention. Since 1992 when the American Academy of Pediatrics instituted its Back to Sleep campaign, which recommended that infants only be put to sleep on their backs to help combat sudden infant death syndrome (SIDS), the prevalence of positional plagiocephaly has increased to nearly 20% by 4 months of age. This is simply caused from a child's head being in the same position for prolonged periods of time. There is



no premature fusion of sutures and, thus, no need for corrective surgery. This is treated by repositioning and occasional orthotic devices such as cranial bands or helmets. There is no mortality implication to this condition whatsoever.

Febrile Seizures

KEY Febrile seizures are the most common neurologic disorder in infants and children, with a prevalence of 2-5% of children under 6 years of age. Most commonly they occur between 12-18 months, often but not always run in families, and are a response to the rapid rate of rise of the temperature, rather than the height of a fever.

Definition:

- Seizure.
- Temperature $>38^{\circ}\text{C}$ or 100.4°F .
- Age >3 months and <6 years old.
- Absence of CNS infection.
- Absence of a metabolic abnormality that may produce seizures (i.e., hyponatremia or hypoglycemia).
- No history of previous afebrile seizure.

Simple febrile seizures last less than 15 minutes and do not recur within 24 hours. All of the rest would be classified as complex febrile seizures.

Approximately one-third of children are at risk for a recurrent febrile seizure after their first. The majority recur within the first year, and nearly all within 2 years. The risk is increased in those with a younger age at onset, febrile seizures in first-degree relatives, a low degree of fever in the ER, and a brief duration of fever. The risk of developing epilepsy (afebrile seizures) is increased in those children who have abnormal neurologic development, complex febrile seizures, a family history of epilepsy and multiple febrile seizures.

According to a very large study published in *The Lancet* 2008 by Vestergaard et al., following singletons with febrile seizures from 1977-2005, the SMR for those with simple febrile seizures is 1.0, while those with complex febrile seizures have a slightly higher SMR of 1.28.

Epilepsy

The definition of a seizure is the clinical expression of abnormal, excessive synchronous discharges in the cerebral cortex. A seizure can be idiopathic or provoked by a cause. Seizures can be described as focal (partial) or generalized. To be classified as a seizure, abnormal electrical activity on an EEG must accompany the abnormal paroxysmal clinical activity. However, a normal EEG between potential seizures

means absolutely nothing. If the EEG is abnormal between the episodes of clinical behavior in question, it makes the paroxysmal activity more likely to have been a seizure. Sleep-deprived EEGs are common, as sleep deprivation can lower the seizure threshold, making it more likely to catch abnormal seizure discharges on EEG. Oftentimes, video EEGs are performed, overnight or even for days, as an attempt to catch the behavior in question on video and EEG.

The definition of epilepsy is two or more unprovoked seizures > 24 hours apart. The seizures may be idiopathic or arise from a variety of genetic (i.e., chromosomal abnormalities), structural (i.e., malformations) or metabolic (i.e., sodium channel disorders, etc.) causes. They may not be reactive or provoked seizures, i.e., caused by hyponatremia, hypoglycemia, toxins, bleeds, infections, etc.

The mortality rate for idiopathic epilepsy (no cause is found) in those who are otherwise asymptomatic is close to the general population. Risk factors for increased mortality include: abnormal neurologic exam, intellectual disability, structural or metabolic etiology of seizures, history of status epilepticus, and poorly controlled epilepsy with the use of more than one antiepileptic drug (AED), continued frequent seizures and/ or the diagnosis of intractable epilepsy. **KEY**

Sudden unexplained death in epilepsy is a feared outcome of an adolescent or young adult. It is a diagnosis of exclusion, and occurs most often in a patient's early 20s. Risk factors include: > 1 seizure/ month, poly-drug therapy, subtherapeutic AED levels, greater than 10 years duration of epilepsy, and severe cognitive impairment. The etiology is unknown, and it causes between 2-18% of all epilepsy deaths, depending on the age range of the study.

Concussions

Traumatic brain injuries can be divided into open head injuries and closed head injuries. Open head injuries, such as open skull fractures, gunshot wounds (GSW) and other penetrating injuries, clearly are grave injuries which can have dire consequences and mortality implications. Closed head injuries include shaken baby syndrome, brain bleeds (subdural or epidural hematomas), contusions, closed skull fractures and concussions.

Concussions have been at the forefront of the media in the last several years. The CDC estimates that between 1.6 million and 3.8 million concussions occur per year. For 15-24-year-olds, sports are second only to motor vehicle crashes as the leading cause of traumatic brain injuries. All states in the United

States have enacted some form of Return to Play/Concussion Safety law.

The definition of concussion is a form of mild traumatic brain injury (mTBI) recognized as a clinical syndrome of traumatically induced alteration of brain function which is generally self-limited. There may or may not be a loss of consciousness (LOC). Symptoms may appear immediately, or not present for hours, days or weeks. There is no generally accepted objective test for diagnosis. Brain MRI or CT may be performed to rule out more significant pathology, but a concussion cannot be diagnosed nor excluded based on these scans. Symptoms can be subtle and include: cognitive/fatigue, vestibular (balance), ocular (vision), mood or anxiety, migraine headaches and cervical discomfort leading to headaches. As a result of the heightened education of lay people and professionals and expansive media coverage of concussions, there appears to be an increase in concussion incidence. However, this may be an actual increase in the incidence of concussions, an improvement in recognition and reporting of these minor head injuries, or a combination of the two.

There are signs and symptoms during physical exams that can be suggestive of a concussion, and there are tests that are diagnostic aids (concussion tests) such as ImPACT and SCAT-3, that also are tools in assisting in the diagnosis. However, there is no definitive test, such as a blood test or a brain scan, to make the diagnosis. If LOC has occurred, by definition, the patient has suffered a concussion. But without LOC, the diagnosis is made on the patient's subjective symptoms, and objective signs if present. Difficulty or variability in diagnosis leads to uncertainty of incidence. This also leads to difficulty in long-term follow-up of mortality.

Potential complications of concussions include post-concussion syndrome, which is persistent post-concussive symptoms lasting ≥ 3 months. It is difficult to determine the percentage that fall into this category. It appears that pre-existing neurologic disease, psychiatric disease and life stressors may be factors, and on occasion, malingering may be present. The vast majority of concussions, however, have resolved by 3 months. Second impact syndrome is a frightening concern, and the instigator behind the Return to Play laws. By definition, this syndrome is a second concussion while still symptomatic from a first concussion. It can result in diffuse brain swelling and death. It is extremely rare and somewhat controversial, as more boxers would be expected to suffer from this.

Finally, chronic traumatic encephalopathy (CTE) is also a recently publicized complication of multiple

concussive and/or subconcussive blows that was brought to light via the NFL controversy. Concussions in the NHL and NASCAR have also made the media recently. A study published by Lehman et al., in *Neurology* 2012, indicated that while the overall mortality rate for former NFL players is less than in the general population (SMR = 0.53), the incidence of neurologic diseases and the SMR from diseases such as amyotrophic lateral sclerosis (ALS) and Alzheimer's dementia (AD) is approximately 4 times that of the general population. There exist very few, if any, studies on the long-term effect of concussion in younger people. Currently, it is held that a simple concussion with complete resolution has little effect on mortality.

Key Underwriting Points

- Craniosynostosis without an associated syndrome is usually a benign condition and risk is approximately standard a year after repair.
- Positional plagiocephaly has become quite common and in itself is a benign condition without mortality risk.
- Simple febrile seizures are the most common childhood neurologic disorder and have very little mortality risk.
- Epilepsy in children is quite similar to adults. If well controlled and no developmental delays or neurologic deficits, mortality risk approaches standard.
- A simple concussion with complete resolution has very little effect on mortality.

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About the Author

Regina Rosace, MD, FAAP, is an AVP and Medical Director at Scor Global Life Americas. She graduated from Northeast Ohio Medical University, completed a pediatric residency in Phoenix, AZ, and spent 20 years practicing pediatric emergency medicine in Cleveland, OH. She is currently on the 2017 Program Committee and the Professional and Public Relations Committee for American Academy of Insurance Medicine, and is the secretary/treasurer for the Midwestern Medical Directors Association. Now that she has left clinical practice, she gets her “kid fix” hanging out with her nine children.