

FOCUS ON PEDIATRIC NEUROLOGY AND NEUROSURGERY

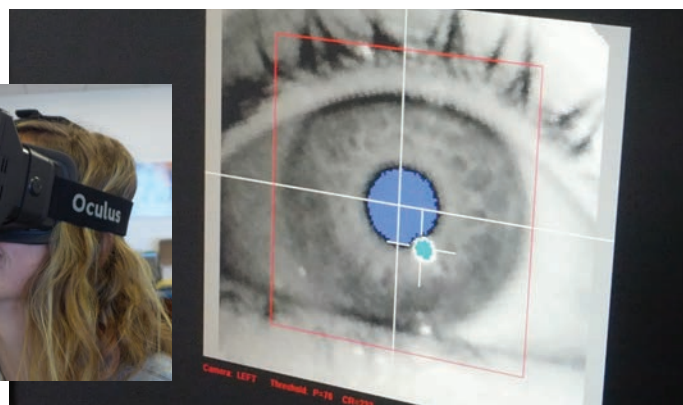
Affiliated with Columbia University College of Physicians and Surgeons and Weill Cornell Medical College

Post-Concussion Syndrome: Not Just Another Headache

In school gyms and on sports fields across the country, there's been growing attention to the risk of concussion and the need to carefully assess and manage children who may have suffered one during a game. But less attention has been paid to the headaches and/or dizziness that can last for several weeks or even a few months after the concussion: so-called "post-concussion syndrome."

At NewYork-Presbyterian Hospital/Phyllis and David Komansky Center for Children's Health and NewYork-Presbyterian/Morgan Stanley Children's Hospital, clinical researchers are studying pediatric patients who have had a concussion to identify factors that raise the risk of post-concussion syndrome. Armed with that information, physicians can then go on to explore therapeutic interventions that may relieve or prevent post-concussion symptoms in these patients, such as early administration of anti-inflammatory medications, anti-oxidants, and other agents to promote cellular energetics.

Eighty to ninety percent of children who have had a concussion recover in seven to ten days. But at least 10 percent continue to have lingering symptoms. "There has been surprisingly



Portable EYE-SYNC goggles — a component of the EYE-TRAC Advance system — could someday be used on the sidelines at sports games to assess athletes who have sustained a blow to the head.

little research on who gets post-concussion syndrome and who does not," asserts Robert Fryer, MD, PhD, Assistant Attending Physician at the Columbia University Headache Center and Assistant Professor of Neurology at Columbia University College

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Wide-Scale Brain Tumor Tissue Banking Effort Aims High

While the overall survival rate for children with cancer has improved over the last 50 years, enormous challenges still exist for those with brain tumors. Pediatric neuro-oncologists and neurosurgeons understand that a different tack is needed to make progress against these cancers. At NewYork-Presbyterian Hospital/Phyllis and David Komansky Center for Children's Health, the pediatric brain tumor team has embarked on an ambitious effort to collect brain tumor tissue for molecular analysis — not only from NewYork-Presbyterian Hospital/Weill Cornell Medical Center, but from other regional centers, too. Their goal: to identify new therapeutic targets and customize treatment for each patient.

Through Weill Cornell Medical College's NeuroBank, researchers are collecting pediatric and adult brain tumor tissue (extra tissue not needed for diagnosis and acquired with the consent of the patient or his/her parents), cou-

pling it with clinical data and storing it for use by researchers from participating institutions who may apply for tissue needed for brain tumor studies.

**An understanding
of the molecular
biology of pediatric
brain tumors is
essential for progress
to be made.**

"Because pediatric tumors are rare, it is especially important to bank as many tissue samples as possible," notes David Pisapia, MD, Assistant Professor of Pathology and Laboratory Medicine at Weill Cornell Medical College and a neuropathologist at NewYork-Presbyterian/Weill Cornell who is overseeing the pathology side of the NeuroBank initiative. "Our goal is to make the Weill Cornell NeuroBank a central brain tumor tissue bank for the region."

"The ability to understand brain tumor biology starts with having tissue you can analyze," adds Mark Souweidane, MD, Chief of Pediatric Neurological Surgery at NYP/Komansky Center and Professor

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The Tuberous Sclerosis Center: Expert Care for a Rare Disease

There's a new Tuberous Sclerosis Center in New York City, at NewYork-Presbyterian/Columbia University Medical Center. The Tuberous Sclerosis Alliance recently designated NewYork-Presbyterian/Columbia as a Tuberous Sclerosis Center for its commitment to and expertise in diagnosing and treating tuberous sclerosis complex (TSC) — a rare genetic disorder that causes tubers to form in vital organs, primarily the brain, heart, skin, kidneys, lungs, and eyes. Children with TSC receive care from an interdisciplinary team of specialists at NewYork-Presbyterian/Morgan Stanley Children's Hospital.

Evaluation at a medical center with expertise in the treatment of TSC is critical. The other medical problems that patients with TSC may develop later in life may be missed at centers unfamiliar with the disorder. "Our team consists of a group of accomplished subspecialists who can provide comprehensive care to TSC patients," says Dr. James Riviello, Director of the NewYork-Presbyterian/Columbia Tuberous Sclerosis Center, Chief of Child Neurology at NYP/Morgan Stanley Children's, and Sergievsky Family Professor of Pediatric Neurology at Columbia University College of Physicians and Surgeons. "The prompt treatment of TSC in children is especially important, since uncontrolled seizures over a period of time can lead to developmental problems. We tailor the management of TSC to each patient's needs while following the Tuberous Sclerosis Alliance's consensus guidelines."



Tuberous sclerosis complex causes tubers to form in vital organs — primarily the brain, heart, skin, kidneys, lungs, and eyes. (Photo provided by Tuberous Sclerosis Alliance.)



Tuberous Sclerosis Alliance

NewYork-Presbyterian/Columbia was designated by the Tuberous Sclerosis Alliance as a Tuberous Sclerosis Center.

About TSC

TSC is diagnosed in about one of every 6,000 births and affects one million people worldwide. It can result from an inherited or acquired mutation in one of two tumor suppressor genes *TSC1* or *TSC2*. It is often detected at or before birth by the presence of rhabdomyomas in the heart, visible on routine ultrasound.

Other patients are diagnosed later in life, when they experience seizures and/or developmental delays. Seizures occur in 70 percent of people with TSC. Other symptoms may include abnormal skin growths or skin pigmentation; cognitive impairment, behavioral problems, and autism; respiratory disease; and renal dysfunction.

Comprehensive Care

Although there is currently no cure for TSC, advances are being made in treating and managing the disorder. Anticonvulsant medications are typically the first intervention used to control seizures. Patients whose seizures are not well controlled with medication may be candidates for surgery to remove tubers in

the brain triggering the seizures. Neurosurgeons at NYP/Morgan Stanley Children's use the results of brain mapping and functional MRI to resect only the tuber(s) responsible for seizures, with the goal of preserving a child's vital functions, such as speech and motor function.

Patients also undergo regular surveillance to monitor their health and to see if their TSC has progressed to other organ systems. The NewYork-Presbyterian/Columbia Tuberous Sclerosis Center's collaborating neurologists, neurosurgeons, cardiologists, geneticists, pulmonologists, dermatologists, ophthalmologists, and others work together to manage each patient's health in one center. The team also provides transitional care from childhood to adolescence and then adulthood. "Parents can feel at ease knowing that all of their child's medical needs can be addressed in one location, with the highest level of care and expertise. And that includes transitional care into adulthood," says Dr. Riviello.

A Commitment to Research

Ongoing TSC research continues to be promising — not only for this disorder, but also for autism, epilepsy, and even cancer, because of the shared genetic mTOR pathway. Patients treated at the Tuberous Sclerosis Center may have the opportunity to participate in clinical trials of promising new approaches. Examples of current research by the Tuberous Sclerosis Alliance include:

- Studies of the chronic use of everolimus to treat TSC lesions in the brain and kidneys.
- The use of everolimus to improve cognitive function in patients age six and older.
- Assessment of everolimus to see if it can improve the control of seizures when given with other antiseizure medications.

For more information or to refer a patient to the Tuberous Sclerosis Center at NYP/Morgan Stanley Children's, call the Division of Child Neurology at (212) 342-6867.

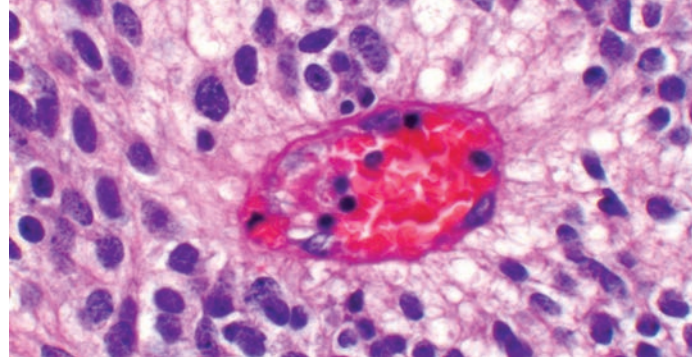
Wide-Scale Brain Tumor Tissue Banking Effort Aims High (continued from page 1)

of Neurological Surgery at Weill Cornell. “Conventional treatments target cells growing at an increased rate, but they do not address the cell type and biology. Only by studying the molecular and genomic signals driving brain tumor growth will we be able to make progress.” He and Jeffrey Greenfield, MD, Assistant Professor of Neurological Surgery, are co-directing the effort, with a team of other brain tumor experts at Weill Cornell.

The NeuroBank brings together a number of separate initiatives launched over the past couple of years into one cooperative effort. Individual laboratory interest, participation in the Children’s Oncology Group (COG), and the recent launch of the Institute for Precision Medicine at Weill Cornell Medical College and the New York Genome Center are now converging into a centralized process that will facilitate important scientific quests.

The mission of the Institute for Precision Medicine is to replace the traditional “one-size-fits-all” medicine paradigm with one that focuses on targeted, individualized patient care using a patient’s own genetic profile and medical history. The identification of molecular signaling pathways driving cancer growth and progression can be used to design innovative therapies targeting these molecules, which may differ from one patient to the next.

In its first full year of participation in the COG protocol, Weill Cornell ranked eighth out of 142 global member institutions. This year, Weill Cornell remains poised for the highest accrual of patients on study to date. Within the institution, strong collaborative efforts between the Department of Neurological Surgery and the Division of Surgical Pathology have served as a platform



The analysis of brain tumor tissue — such as this perivascular pseudorosette in a pediatric anaplastic ependymoma — may help investigators identify new therapeutic targets.

for the success of such national protocols and the development of the now institution-wide NeuroBank. Researchers from participating institutions may apply to use the tissue in studies determined by a governance committee to be of scientific merit. “The world has recognized that pediatric brain tumors are genetically unique and can’t all just be considered ‘children’s brain tumors,’” concludes Dr. Souweidane. “There’s a great show of force, unity, and thought driving the NeuroBank effort. The promise of this initiative is huge.”

Physicians interested in contributing tissue to the Weill Cornell Medical College NeuroBank may contact the Department of Pathology and Laboratory Medicine at (212) 746-2700.

Post-Concussion Syndrome: Not Just Another Headache (continued from page 1)

of Physicians and Surgeons. “Normally when kids have a concussion, we prescribe rest. But if we know a child has a greater risk of post-concussion syndrome, we may treat them differently at the beginning to reduce their symptoms.”

Dr. Fryer and his colleagues performed a retrospective chart review and identified two predictors of post-concussion syndrome: a history of a previous concussion and a personal or family history of migraines. The team recently embarked on a prospective study of acute concussion to identify post-concussion syndrome risk factors.

Barry Kosofsky, MD, PhD, Chief of Pediatric Neurology at NYP/Komansky Center and Horace W. Goldsmith Foundation Professor of Pediatrics at Weill Cornell Medical College, is co-directing a prospective longitudinal clinical research study called EYE-TRAC Advance to see how eye tracking, brain imaging with MRI, and neurocognitive performance can predict the risk of post-concussion syndrome. The study, which is run by the Brain Trauma Foundation and directed by Jamshid Ghajar, MD, PhD, includes children ages 7 and older (as well as adults) presenting at the hospital’s emergency department, and is part of a research program funded by the U.S. Department of Defense. “Our goal is to determine the extent to which we can use these tools to predict who may need early treatment for post-concussion syndrome,” explains Dr. Kosofsky.

For EYE-TRAC Advance, the Brain Trauma Foundation developed customized portable EYE-SYNC goggles (see cover

photo) and selected sensitive tests to explore the relationship between eye-tracking and cognitive domains such as processing speed, predictive timing, reaction time, and attention. Participants are evaluated within two weeks of the concussion and then again at one month, and the results are compared with testing data from individuals who have not sustained a concussion. In the future, it might also be possible to use the EYE-SYNC goggles on the sidelines at sports games to assess athletes who have sustained a blow to the head.

Future planned studies include those identifying “actionable” serum biomarkers that could be used to diagnose a concussion soon after brain injury, predict concussion outcome, and identify specific therapeutic interventions to prevent ongoing symptoms. “The hardest part of concussion care is identifying who has sustained a significant brain injury — that’s why biomarker studies are so important,” says Dr. Kosofsky. The goal of all of these investigations is to improve the clinical diagnosis and management of patients with concussion.

The Weill Cornell Concussion and Brain Injury Clinic
weillcornellconcussion.org • (212) 746-1112

Columbia Concussion and Sports-Related Head Injury Program
columbianeurology.org • (212) 305-3472

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