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New Leadership at NewYork-Presbyterian Hospital



Dr. Steven Corwin

On September 6, 2011, Steven J. Corwin, MD, took over the helm of NewYork-Presbyterian Hospital as its new Chief Executive Officer. Dr. Corwin succeeds Herbert Pardes, MD, who served as President and Chief Executive Officer for the past 11 years and is now Executive Vice Chairman of the Board of Trustees.

“We have created a patient-centered culture and achieved a level of excellence in patient care that has become the absolute bedrock of NewYork-Presbyterian,” said Dr. Corwin. “We are an institution dedicated to comprehensiveness – to treating any medical problem or disease across every age of the human life span. Beginning the next chapter of our history is a great milestone – for me personally, and for the entire NewYork-Presbyterian team. Our Hospital enjoys a special and powerful partnership with Columbia University’s College of Physicians and Surgeons and Weill Cornell Medical College, and I am committed to further strengthening these collaborations.”

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Diagnoses of Autism Spectrum Disorders Vary Widely Across Clinics

Contributing faculty for this article: **Catherine E. Lord, PhD**

To diagnose autism spectrum disorders, clinicians typically administer a variety of tests or scales and use information from observations and parent interviews to classify individuals into subcategories listed in standard psychiatric diagnostic manuals. This process of forming “best-estimate clinical diagnoses” has long been considered the gold standard, but a new study demonstrates that these diagnoses are widely variable across centers, suggesting that this may not be the best method for making diagnoses.

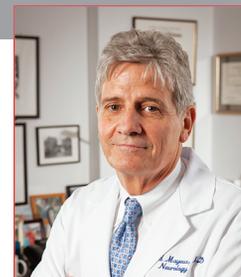
“Clinicians at one center may use a label like Asperger syndrome to describe a set of symptoms, while those at another center may use an entirely different label for the same symptoms. This is not a good way to make a diagnosis,” says the study’s lead investigator, Catherine E. Lord, PhD, Director of the Institute for Brain Development, a partnership of NewYork-Presbyterian Hospital, Columbia University College of Physicians and Surgeons, and Weill Cornell Medical College. “Autism spectrum disorders are just that – a spectrum of disorders. Instead of subcategories based on differing clinical impressions (such as Asperger syndrome), it would be better if clinicians measure and report the specific factors that contribute to the subcategories. These factors aren’t compiled from the standardized diagnostic instruments, rather they are factors such as

how well the child can talk, how severe is the child’s repetitive behavior, how limited is the child’s social behavior, and how good is the child’s nonverbal problem-solving?”

The new study, published in *Archives of General Psychiatry*, adds to previous evidence that standardized diagnostic instruments accurately predict who has autism and will continue to have it over time. It is also in line with recent skepticism about the value of categorical groupings of autism spectrum disorders in standard diagnostic manuals. “There has been a lot of controversy about whether there should be separate diagnoses for autism spectrum disorder, especially Asperger syndrome,” Dr. Lord says. “Most of the research has suggested that Asperger syndrome really isn’t different from other autism spectrum disorders.”

see **Autism Spectrum Disorders**, page 5

Dr. Richard Mayeux Leads Neurology at NewYork-Presbyterian/Columbia



Dr. Richard Mayeux

On March 1, 2011, Richard P. Mayeux, MD, MSc, was named Chairman of the Department of Neurology at Columbia University and Neurologist-in-Chief at NewYork-Presbyterian Hospital/Columbia University Medical Center. Dr. Mayeux, the Gertrude H. Sergievsky Professor of Neurology, Psychiatry and Epidemiology at Columbia, serves as Director of the Gertrude H. Sergievsky Center for Neuroepidemiology and Genetics and Co-Director of the Taub Institute for Research on Alzheimer’s Disease and the Aging Brain. Dr. Mayeux succeeded Timothy A. Pedley, MD, a renowned expert in epilepsy, who had served as Chairman and Neurologist-in-Chief since 1998.

Dr. Mayeux is an internationally recognized authority on Alzheimer’s disease and other dementias. Since 1989, he has led the Washington Heights-Inwood Community Aging Project – a multidisciplinary, population-based, epidemiological investigation of Alzheimer’s disease and related conditions. This body of work, which now spans more than 20 years, has provided most of our current knowledge about the rates and risk factors for Alzheimer’s disease among elderly individuals in African-American and Caribbean Hispanic populations. The study has also

provided information on the relationship between Alzheimer’s disease and numerous risk factors, including genotypic variability of apolipoprotein-ε4 risk in different ethnic groups and the relationship of alterations in lipid metabolism to risk of dementia. Dr. Mayeux also directs a genetic linkage study of Alzheimer’s disease in Caribbean Hispanic families in which he and his colleagues have completed two full genome-wide scans and are now fine mapping regions of interest. They have recently identified genetic variants in the sortilin-related receptor, SORL1, that are related to Alzheimer’s disease.

Dr. Mayeux received his medical degree from the University of Oklahoma Health Sciences School of Medicine and a master’s degree in epidemiology from Columbia. He completed a residency in internal medicine at Boston City Hospital, Boston University, and in neurology at The Neurological Institute, Columbia University Medical Center, as well as a postdoctoral clinical fellowship in behavioral neurology at the Boston Veterans Administration Medical Center, Boston University.

Neurosurgical Challenges: A Case Study

Contributing faculty for this article: **Robert A. Solomon, MD**

With a particular interest in identifying and defining the treatment of cerebral aneurysms and cerebral AVMs before rupture, Robert A. Solomon, MD, Chief of Neurological Surgery at NewYork-Presbyterian/Columbia, works closely with neuroradiologists and experts in non-surgical endovascular treatment of cerebral vascular diseases. Here Dr. Solomon discusses the treatment approach to a large arteriovenous malformation.

A 32-year-old woman who had been having migraine-type headaches most of her adult life visited her family doctor for a bad headache and drooping eyelid. An angiogram confirmed a four-centimeter arteriovenous malformation on the surface of the right frontal lobe, showing that the blood supply going to the malformation from the middle cerebral arteries, and the veins that were draining the malformation, were going up superficially to the superior sagittal sinus. “We’re usually reluctant to operate on AVMs that are this big,” says Dr. Solomon, “but because it was in a favorable location and she was so young, we decided to resect it.”

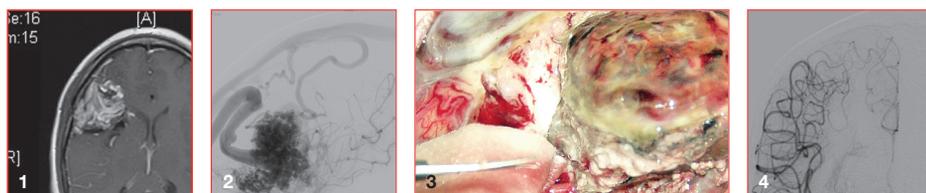
The patient’s treatment began with three

embolizations by Philip M. Meyers, MD, Clinical Co-Director, Neuroendovascular Services, to close off the major arteries feeding the AVM and reduce its blood flow. A few weeks later, Dr. Solomon and his team mapped out the exact coordinates of the malformation with stereotactic-guided craniotomy and then resected the malformation in a six-hour surgery. “Immediately after surgery, while the patient was still under anesthesia, we took her to Dr. Meyers who performed another angiogram,” describes Dr. Solomon. “It appeared that the AVM was obliterated – but because the AVM was so big and she had had it her whole life, the angiogram also showed a lot of abnormal blood vessels

around the margins. It was unclear if these were really an abnormal part of the malformation or just abnormal vessels that had grown up in response to the malformation, which are common in patients with AVMs.”

A follow-up angiogram almost two months after surgery showed that the malformation was completely obliterated and all the blood vessels were back to normal. The patient had recovered completely and returned to all her regular activities. “Since the AVM is a sink – a path of least resistance for blood – the vessels around it dilate over time as more and more blood shunts through it rather than through the normal brain, and eventually these vessels rupture,” explains Dr. Solomon. “This patient was just approaching the age when AVMs typically rupture, in the 30s and 40s.”

Dr. Solomon points out that earlier imaging would have revealed the AVM. “Everybody who is diagnosed with migraines should at least have one MRI because there are several things that can mimic migraine headaches, and AVMs are one of them.”



(1) an MRI of the patient’s brain shows a four centimeter arterial venous malformation on the surface of her right frontal lobe; (2) a preoperative angiogram confirms the AVM, showing that the flow of the blood supply to and from the malformation were going up superficially to the superior sagittal sinus; (3) resecting the AVM; (4) the two-month follow-up angiogram shows completely normal blood vessels and no evidence of residual arteriovenous malformation

Weill Cornell Researchers Identify Target for Gene Therapy and New Drug Development in Depression

Contributing faculty for this article: **Michael G. Kaplitt, MD, PhD**

Almost 15 million Americans suffer from serious depression, which affects their ability to work and enjoy life. Depression places huge costs on the healthcare system and on the workplace: It is the leading cause of disability in the country in those ages 15-44, and costs U.S. businesses \$70 billion annually in medical expenses and lost productivity. In 10 to 30 percent of people with major depression, currently available medications provide only partial or no relief.

The researchers used gene therapy techniques in mice to demonstrate a link between depression and a specific serotonin receptor-binding protein, and to identify the brain region where the protein is active.

In a study published in fall 2010 by Michael G. Kaplitt, MD, PhD, and colleagues in *Science Translational Medicine*, the researchers used gene therapy techniques in mice to demonstrate a link between depression and a specific serotonin receptor-binding protein, and to identify the brain region where the protein is active. They also showed that brain tissue in humans with depression has lower levels of this protein than that of people without a history of the disorder. Their work not only demonstrates that gene therapy may be a viable approach for treating depression, but also identifies a protein target for new drug development.

Dr. Kaplitt, a neurosurgeon and Director of the Laboratory of Molecular Neurosurgery at Weill Cornell Medical College, and his colleagues focused their research on a serotonin receptor-binding protein called p11 (a 5HT_{1A} family member), which “seems to act like a tugboat that bring ships into port,” says Dr. Kaplitt. “It binds to serotonin receptors inside the cell and brings them to the cell surface, where they can be seen and bound by serotonin circulating outside. In the absence of p11 these receptors simply float around inside the cell.”

Building on earlier research, the team focused on the brain region where p11 was thought to be active, the nucleus accumbens, a neuronal region in the striatum, which is known to play an important role in reward or satisfaction. “The nucleus accumbens is most highly studied in addiction,” notes Dr. Kaplitt, “because there are significant abnormalities in this part of the brain in people who are addicted to drugs in response to those drugs.”

In the first phase of the study, the researchers transferred a small interfering

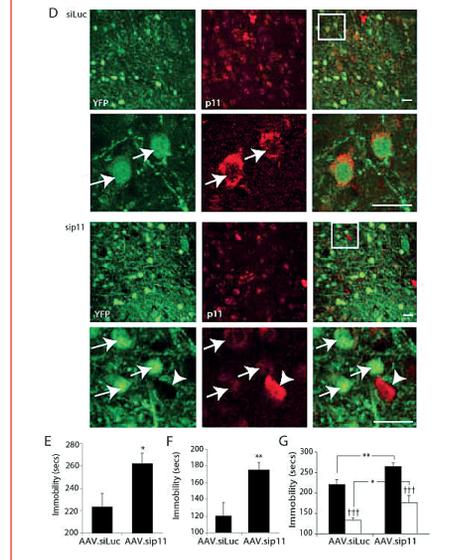
RNA to the nucleus accumbens using an adeno-associated virus (AAV) vector. The RNA was designed to specifically target and block cell machinery from producing p11. “We took normal mice with no behavioral problems and knocked out p11 production in the nucleus accumbens,” explains Dr. Kaplitt. The mice then exhibited a variety of depression-like behaviors, which are measured by the amount of time they spend immobile when suspended by the tail or in a ‘forced swim test,’ and by the amount of interest they express in a sugar-water solution. “The more time they spend in an inactive state, the more depressed they are considered to be.”

The group next studied p11 knockout mice, which lack the ability to produce p11 throughout the body and express all of the depression-like behaviors above, to determine whether they could reverse the behavioral consequences of p11 loss. Using the same AAV vector, they transferred an active form of the p11 gene into the nucleus accumbens. The transferred gene restored p11 production specifically in the nucleus accumbens and restored normal behaviors in these mice.

In the last phase, the investigators examined nucleus accumbens tissue from the University of Texas Southwestern brain tissue bank, and compared tissue from patients with known depression to those with no history of depression. “The level of p11 in the depressed patients was significantly lower,” says Dr. Kaplitt, again underscoring the link between p11 and depression. “We’re now collaborating with researchers at the National Institute of Mental Health to better understand the role of p11, and are studying this approach in primates for safety purposes.”

Dr. Kaplitt’s group is building on its

Focal inhibition of p11 expression in adult mouse NAcc induces depression-like behaviors



Confocal micrographs of YFP (green) and p11 (red) immunofluorescence in the NAcc after injection of control virus (AAV.silLuc.YFP, top 2 panels) and knock-down virus (AAV.sip11.YFP, bottom 2 panels) in vivo. Arrows, YFP-positive cells; arrowhead, YFP-negative cell still expressing p11 at normal levels (scale bars, 20 μm). (E-G) Induction of depression-like behaviors in adult mice following AAV shRNA-mediated focal knockdown of p11 in NAcc

extensive experience using gene therapy for neurologic diseases. “Our major research interest is in gene therapy for the brain, and we’ve had a long interest in doing this clinically,” he said. “We did the first gene therapy for Parkinson’s disease here at Weill Cornell, and over the past decade we have created a body of work that demonstrates the safety of this approach in humans. When you break down the list of diseases that cause most suffering around the world you see that treatment-resistant depression is at the top of the list,” concludes Dr. Kaplitt. “This is a difficult and morbid disease and there is a great need for new treatment approaches.”

For more information, see the original journal article: Alexander B, Warner-Schmidt J, Eriksson T, Tamminga C, Arango-Lievano M, Ghose S, Vernov M, Stavarache M, Musatov S, Flajolet M, Svenningsson P, Greengard P, Kaplitt MG. Reversal of depressed behaviors in mice by p11 gene therapy in the nucleus accumbens. *Science Translational Medicine*. 2010 Oct 20; 2(54):54ra76.



Dr. Richard Kogan

Musical Masters Give Insight into Mental Health

Contributing faculty for this article: **Richard Kogan, MD**

If you are an accomplished, Juilliard-trained concert pianist and you also have a very successful psychiatric practice, what do you do for an encore? In the case of Richard Kogan, MD, you combine the two to bring new insights into mental health and musical creativity.

This journey began over 12 years ago when Dr. Kogan was asked to give a symposium on music and mental illness at the American Psychiatric Association. In preparation he researched classical musicians with an eye toward understanding the creative elements that may have gone into making a masterpiece. Looking through the lens of a psychiatrist himself, Dr. Kogan was able to surmise the nature of the mental illness experienced by some of the world's greatest musicians, including Schumann, Tchaikovsky, Beethoven, Mozart, Chopin, and Gershwin. "Doing a retrospective diagnosis on historical figures is very difficult," cautions Dr. Kogan. "However, they often kept extensive diaries or wrote detailed letters to trusted relatives and friends describing their emotional state that allow us to speculate."

"If a 21st century Tchaikovsky came in for treatment, we could give him an antidepressant, but would he no longer be able to write *Swan Lake* or *The Nutcracker*? This is a profoundly important question for which there is no simple answer." — Richard Kogan, MD

What better way to describe the characteristics of a musician's mental state than within a recital of the musical pieces of that master? The result is a kaleidoscope of insights into the composer, the composition, the potential role of mental health in the creative process, the effect on audiences, implications for mental health professionals, and unanswered questions begging for neuroscience research. "It is certainly more enjoyable to partake of a great composition with educated ears," says Dr. Kogan. "Information about the life of the composer and events that might be behind a composition adds richness to the listening experience."

Dr. Kogan uses the filter of his psychiatric training to highlight the lives and works of

some of the most famous composers. For example, Robert Schumann died at the age of 46 after having spent the last two years of his life in an insane asylum following a suicide attempt. "In his writings, Schumann described many of the symptoms of what today we would call bipolar disorder," notes Dr. Kogan. "He was given to vast mood swings from deep depressions and periods of inactivity to hypomanic episodes characterized by sharpened imagination, increased energy, and the decreased need for sleep." Dr. Kogan has demonstrated these swings when playing Schumann's famous work *Carnaval*, which contains movements of great energy and excitement, as well as those of deep melancholy.

What insights might we gain into mental health from an examination of the masters? "Scientists who have conducted epidemiological

research suggest what we intuitively sense – the incidence of mental illness, particularly the mood disorders, is greater in populations of writers, musicians, artists, poets, and painters than in the general population," says Dr. Kogan. "Having said that, it's important not to overromanticize the notion of mental illness because most individuals in these creative professions will tell you that when they are in the throes of mental illness they are not especially creative. People having manic episodes often are too disorganized to actually create."

Would modern treatment have helped or destroyed the works of the great masters? It is impossible to be sure, but it certainly gives one pause when considering the role of treatment for mental illness. "It is appropriate to

be concerned about whether an intervention will dampen creativity," Dr. Kogan continues. "On the other hand, it is important to provide treatment because often creativity is blocked by the mental illness. As a clinician you have to walk a fine line. You don't want to overtreat because that can lead to blunting of the creative process. You also don't want to undertreat because individuals who are in the grips of mental illness often don't have the resources to be creative. My goal in telling these stories and looking at these cases is to get people thinking about these issues in a more complex way."

And perhaps music itself was a treatment for the mental illnesses that these composers experienced. Tchaikovsky said "without music I would go insane."

"Tchaikovsky, according to writings about him, was clearly depressed but antidepressants didn't exist in the 19th century," adds Dr. Kogan. "If a 21st century Tchaikovsky came in for treatment, we could give him an antidepressant, but would he no longer be able to write *Swan Lake* or *The Nutcracker*? This is a profoundly important question for which there is no simple answer." In many cases Dr. Kogan states that the great masters "used music to make sense of their universe." Does this healing power translate to today? Dr. Kogan would suggest that there is a great healing power in music, one that is largely untapped and is just beginning to be understood through neuroscience research. "Music has a profound healing impact on groups of individuals and patients who can't be reached by any other means... physicians should be thinking about that regularly," he says.



Robert Schumann

continued from **New Leadership**, page 1

A cardiologist and internist, Dr. Corwin received his undergraduate and medical degrees from Northwestern University. He completed training in internal medicine and cardiology at Columbia-Presbyterian Medical Center, and, in 1986, was named to the faculty of Columbia University College of Physicians and Surgeons. Dr. Corwin joined the management team of Columbia-Presbyterian Medical Center in 1991 and served in various management capacities. From 1998 to 2005, he was Senior Vice President and Chief Medical Officer at NewYork-Presbyterian, becoming the Chief Operating Officer in 2005.

Robert E. Kelly, MD, who has been affiliated with NewYork-Presbyterian Hospital for nearly three decades, was named President of the Hospital. In 1995, Dr. Kelly joined the management team of The New York Hospital serving in various administrative capacities. In 1999, he moved to the uptown campus as Senior Vice President, Chief Operating Officer, and Chief Medical Officer at NewYork-Presbyterian/Columbia, taking on the additional role as Group Senior Vice President in 2007.



Dr. Robert Kelly

“This is a time of great achievement for our Hospital, but it is also a time when medicine and the entire health care industry are facing challenges that must be addressed head-

on,” said Dr. Kelly. “We will always be committed to providing the best possible experience for our patients and delivering the safest and highest quality care.” Dr. Kelly received his medical degree from the University of Cincinnati College of Medicine and completed his internship at The Christ Hospital in Cincinnati. He completed his residency in anesthesiology and fellowship in cardiac anesthesiology at New York Hospital-Cornell Medical Center.

“Dr. Corwin and Dr. Kelly represent the next generation of leadership for this remarkable institution,” said John J. Mack, Chairman of the Board of Trustees, NewYork-Presbyterian Hospital.



Dr. Laurie Glimcher

New Dean to Lead Weill Cornell Medical College

Laurie H. Glimcher, MD, one of the nation's leading physician-scientists and researchers, has been named the Cornell University Provost for Medical Affairs and the Stephen and Suzanne Weiss Dean at Weill Cornell Medical College, effective January 1, 2012.

Dr. Glimcher was the Irene Heinz Given Professor of Immunology at the Harvard School of Public Health and Professor of Medicine at Harvard Medical School. Her pioneering research laboratory at Harvard is known for its many discoveries, ranging from the T-bet transcription factor, which regulates a variety of immune functions, to the Schnurri-3 adapter protein that controls adult bone mass. Her research has been unusually interdisciplinary and has given her a very broad perspective on many different key areas of biomedical science at the Medical College.

Dr. Glimcher succeeds Antonio M. Gotto Jr., MD, DPhil, who has served as Dean since 1997. Beginning in 2012, Dr. Gotto will become Co-Chairman of the Board of Overseers for Weill Cornell Medical College and Vice President of Cornell University.

continued from **Autism Spectrum Disorders**, page 1

In the new study, Dr. Lord and co-author Eva Petkova, PhD, Director of the Division of Biostatistics at the NYU Child Study Center, studied about 2,100 people between the ages of 4 and 18 who were given a diagnosis of autism spectrum disorder by clinicians at 12 university-based centers. The participants were recruited from the Simons Simplex Collection, a multi-site project aimed at studying de novo genetic variations in families affected by autism spectrum disorders.

Because of the inconsistencies in best-estimate clinical diagnoses, the use of standard diagnostic manuals to classify individuals into subcategories of autism spectrum disorder should be reconsidered.

The researchers found that diagnoses of specific categories of autism spectrum disorder varied dramatically from site to site across the country. “The labels are pretty meaningless, because people are using the same general terms as if they mean the same thing, when they really don’t,” Dr. Lord says. “Because clinicians may not be using labels

appropriately or diagnosing accurately, they may not be getting a sense of children’s strengths and weaknesses and what therapy is best for them.”

Because of the inconsistencies in best-estimate clinical diagnoses, the use of standard diagnostic manuals to classify individuals into subcategories of autism spectrum disorder should be reconsidered, Dr. Lord says. “It’s very important for clinicians to use information from dimensions that directly relate to autism spectrum disorders, in

addition to verbal IQ and the level of irritability and hyperactivity. The take-home message is that there really should be just a general category of autism spectrum disorder, and then clinicians should be able to describe a child’s severity on these separate dimensions.”

“This is an extremely important paper regarding our understanding of the various

components of autism spectrum disorder from a group that has been crucial in defining the features of autism over many years,” says Gerald D. Fischbach, MD, Scientific Director of the Simons Foundation Autism Research Initiative. “They call attention to quantifiable traits rather than existing diagnostic categories.”

In future research, Dr. Lord will work on improving diagnostic instruments – making them shorter, easier to use, and more appropriate for a wider variety of patients – and assessing whether certain dimensions are really distinct from one another. This work will build on her previous pioneering efforts in developing these commonly used scales.

This research was funded by the Simons Foundation and the National Institute of Mental Health. For more information, see the original journal article: A multisite study of the clinical diagnosis of different autism spectrum disorders. *Archives of General Psychiatry*. 2011 Nov 7. [Epub ahead of print]



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