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Schizophrenia Expert Studies New Biomarker

For more than a decade, Anissa Abi-Dargham, MD, and colleagues at Columbia University College of Physicians and Surgeons have conducted seminal research using molecular imaging to study the pathophysiology of schizophrenia, schizophrenia-related spectrum disorders, and addiction. The research studies have tested the dopamine hypothesis of schizophrenia, and ultimately are being used to develop biomarkers for risk and more focused treatment options.

"What's characteristic of the imaging work we've done is that it's very methodologically rigorous," said Dr. Abi-Dargham, emphasizing that imaging research requires a team of specialists with wide-ranging expertise, from mathematicians to radiochemists, physicists, and physicians.

The dopamine hypothesis of schizophrenia first emerged in the early 1960s, when researchers observed that psychostimulants could activate dopamine receptors and that nonreserpine neuroleptics acted as dopamine antagonists. Over time, they discovered that antipsychotic drugs blocked dopamine's D_2 receptors, whereas dopamine-enhancing drugs could in turn be psychotogenic. In the 1990s, more technologically advanced methods such as molecular imaging techniques became available to validate these clinical findings.

One of Dr. Abi-Dargham's early studies measured D_2 receptor availability in untreated patients with schizophrenia and in healthy subjects, first at baseline and then after an acute amphetamine challenge (*Am J Psychiatry* 1998;155[6]:761-767). Single photon emission computed tomography (SPECT) imaging and D_2 receptor radiotracer [123I]IBZM revealed excessive striatal dopaminergic transmission in patients with schizophrenia who were exposed to a psychostimulant.

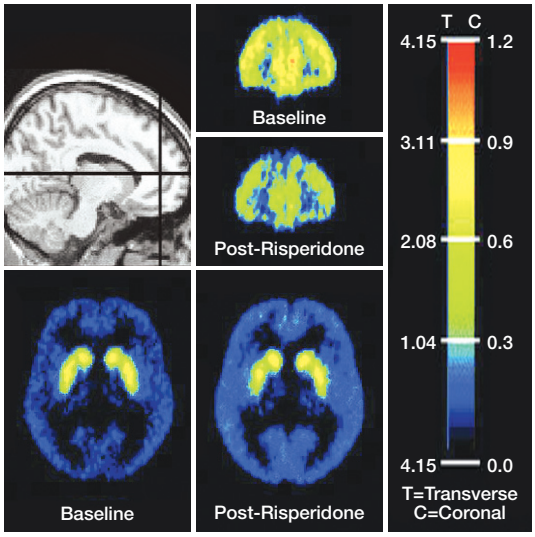

Photo courtesy of Anissa Abi-Dargham, MD.

Positron emission tomography displacement study to characterize in vivo binding of a radiotracer.

"Psychostimulants are more psychotogenic in schizophrenic patients than in the normal population, and this vulnerability to psychosis is related to more subcortical dopamine release," said Dr. Abi-Dargham.

In order to evaluate patients who were not exposed to psychostimulants, Dr. Abi-Dargham and her research team again used SPECT and the same radiotracer, this time to measure D_2 receptors at baseline and after acute dopamine depletion. The investigation revealed that dopamine depletion caused a larger unmasking of D_2 receptors among schizophrenic patients compared with healthy subjects (*Proc Natl Acad Sci USA* 2000;97[14]:8104-8109).

Notably, the researchers found that patients with high dopamine levels at baseline subsequently had a

see Schizophrenia, page 7

Suicide Rate Among Young People on the Rise

The debate over antidepressant medications and suicidal behavior among young people continues to take center stage. Some experts worry that a reduction in selective serotonin reuptake inhibitor (SSRI) prescriptions following the FDA's black box warning may be leading to unintended negative consequences, namely an increase in the suicide rate among young people in the United States. J. John Mann, MD, a researcher from NewYork-Presbyterian Hospital/Columbia University Medical Center, collaborated with researchers from the University of Illinois at Chicago to investigate the relationship between antidepressant treatment and suicidal behavior in a number of different studies.

"My colleagues and I predicted that the danger of the FDA's black box warning was that if prescription rates began to drop in the younger age group then

see SSRIs, page 2

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there would be an increase in suicide rates in that group. Indeed, that is exactly what happened," said Dr. Mann, citing the Centers for Disease Control and Prevention's (CDC) statistics from 2004. The CDC's *Morbidity and Mortality Weekly Report* (2007;56:905-908) showed an 8% increase in the suicide rate for 10 to 24 year olds from 2003 to 2004, representing the biggest jump in suicide rates recorded for young people since the CDC began collecting age-specific data almost a quarter of a century ago.

> **"It is more important for physicians to know how to use [antidepressant] medications safely and well instead of the other option, which is to be afraid of the medications and not treat patients."**
>
> —J. John Mann, MD

Because of the difficulty in obtaining enough data on suicides via a prospective clinical trial, Dr. Mann and his colleagues have turned to large epidemiologic studies to measure the relationship between SSRIs and lethal suicide attempts.

In one study, Dr. Mann and his colleagues examined the relationship between antidepressant treatment and suicide attempts by analyzing records from the Veterans Health Administration for 226,866 veterans who had been diagnosed with depression in 2003 or 2004, had at least 6 months of follow-up, and had no history of depression from 2000 to 2002 (*Am J Psychiatry* 2007;164(9):1044-1049). The researchers compared suicide attempts in subjects who received SSRIs, new-generation non–serotonergic-specific (non-SSRI) antidepressants, tricyclic antidepressants, or no antidepressants.

Across all adult age ranges, rates of suicide attempts were significantly lower among patients receiving SSRIs versus those who were not taking antidepressant medication. Patients also taking SSRIs had a lower rate of suicide attempts while receiving treatment compared with before they received treatment. This benefit was also present, although not statistically significant, in young adults.

In another study (*Am J Psychiatry* 2007;164:1356-1363), the authors examined US and Dutch prescription rates for SSRIs in children and adolescents and found a 22% decrease from 2003 to 2005 and an increase in youth suicide in both countries in 2004 and an increase in the Netherlands in 2005 (when data were available). This corresponded to a time when the "US Food and Drug Administration and European regulators issued public health warnings about a possible association between antidepressants and suicidal thinking and behavior," wrote the study authors.

"Suicide is an important cause of death in one of the most vital portions of our society," said Dr. Mann, stressing that suicide is the third-leading cause of death for young people in the United States. "It is more important for physicians to know how to use these medications safely and well instead of the other option, which is to be afraid of the medications and not treat patients."

Initially, concerns related to SSRI safety arose about a decade ago from case reports. In mid-2003, evidence showed that children and adolescents taking paroxetine were reported to have increased incidence of suicide attempts compared with placebo. Based on these reports, first the United Kingdom Medicines and Healthcare Products Regulatory Agency and then the FDA reviewed the data. In 2004, the FDA introduced a black box warning for SSRIs and other antidepressants because of a risk of suicidal ideation and behavior among children and adolescents. In 2007, the warning was extended to young adults aged 18 to 24 years. This action has spurred a debate in the medical community and the public at large about how the drugs impact suicide risk.

Dr. Mann became increasingly interested in how SSRIs affect the suicide risk to young adults in light of the FDA's latest extension of the black box warning. He was initially drawn to understanding the connection between suicide and SSRIs after research by his group and others showed that people who commit suicide or make serious attempts appear to have deficiencies in serotonin transmission in the brain. The hope was that SSRIs might correct that imbalance and reduce the risk of suicide. Dr. Mann has found that the overwhelming majority of people who commit suicide are not receiving treatment, making him question the idea that SSRIs, rather than the mental illness itself, trigger suicide.

To better monitor data across the country, Dr. Mann advocates a reporting system so that suicides and suicide attempts become a reported event. His research team has also obtained a National Institutes of Health grant to conduct a controlled study on how brain imaging and genetic profiling might be used to predict clinical outcome on SSRIs.

Contributing faculty for this article:
J. John Mann, MD

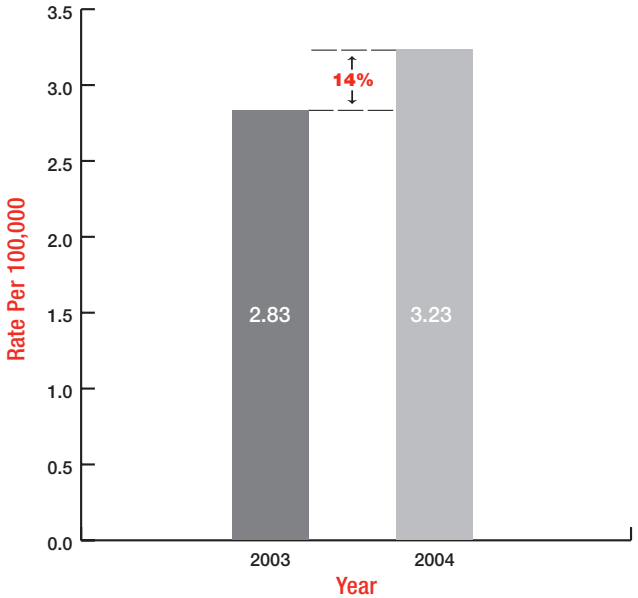

Figure. Suicide rate in children and adolescents (aged 5-19 years) in the United States.
Adapted from Gibbons RD et al. *Am J Psychiatry.* 2007;164(9):1356-1363.

Renowned Psychiatric Facility Strengthens Existing Program

Specialized psychiatric care, collaboration with other NewYork-Presbyterian Hospital institutions, and an innovative program to resocialize patients after long periods of hospitalization are among the innovations that make the Westchester Division of NewYork-Presbyterian Hospital/Weill Cornell Medical Center among the top psychiatric programs in the country, and one that has received recognition from New York State and the National Institutes of Health (NIH).

"We have a very prominent geriatric institute, one of the nation's 3 NIH-accredited geriatric institutes, where we research geriatric disorders as well as provide clinical services and teaching," said Philip J. Wilner, MD. "We have one of the nation's most prominent eating disorders programs, designated by New York state as a center of excellence in eating disorders. We combine comprehensive eating disorder treatment with research and education. We have a long history of research into psychotherapy and have an extremely prominent personality disorder institute under the leadership of Otto Kernberg, MD, who's one of the world's leading figures in the research and treatment of borderline personality disorder."

The wide array of specialists working at the Westchester Division provide comprehensive diagnosis and treatment of rare, unusually acute, treatment-resistant, and comorbid mental illnesses. "Patients receive a very thorough evaluation," Dr. Wilner said.

"If patients have comorbidities, such as psychiatric illness combined with an addiction problem or an eating disorder, we can treat them for both. For geriatric patients who have a particular neurologic concern or medical concern, specialists provide diagnostics and treatment for whatever comorbidities they have. We are a tertiary care facility, so we also get patients who are very treatment-refractory, and patients whose previous doctors have not been able to develop a definitive diagnosis that would lead to an effective treatment plan," added Dr. Wilner.

Many patients who are referred to the Westchester Division have spent time in New York state hospitals. Patients who have been a resident at a New York state hospital for 5 or more years are eligible for the Second Chance program, which offers psychosocial rehabilitation as well as reevaluation of the patient's psychopharmacologic needs. "These patients have profound chronic illness, profound psychosocial disability, and functional disability," said Dr. Wilner. "We teach them how to live in a community, how to eat properly, how to attend to their personal hygiene, things that really do fall away when people are institutionalized for a long time," he said. The Westchester Division is now working to bring elements of the program to community residences, offering educational "boosters" to support patients so that the effects of the rehabilitation are not lost over time. "Two thirds of our patients leave us to go to community residences, an astounding number," added Dr. Wilner.

The facility's size has led to the development of several specialized divisions, which combine treatment with cutting-edge research and training for medical residents, physicians, psychologists, nurses, and social workers. There are dedicated programs for child, adolescent, adult, and geriatric psychiatry, depression and bipolar disorder, psychoses, and addiction and rehabilitation. "We have an inpatient component and corresponding ambulatory programs along various levels of care," Dr. Wilner said, citing some patients who receive services at the hospital every day but reside at home, whereas others come in for treatment only during acute phases of chronic illness.

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is published by NewYork-Presbyterian Hospital. The Department of Psychiatry at NewYork-Presbyterian Hospital is at the forefront of research and practice in the diagnosis and treatment of patients with psychiatric diseases. The Department of Psychiatry at NewYork-Presbyterian Hospital/Columbia University Medical Center and NewYork-Presbyterian Hospital/Weill Cornell Medical Center is affiliated with Columbia University College of Physicians and Surgeons, Weill Cornell Medical College, and the New York State Psychiatric Institute.

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Sleep Lab Finds Napping Improves Cognitive Function

Ongoing research from the Human Chronobiology Laboratory at NewYork-Presbyterian Hospital/Weill Cornell Medical Center has found that a midday nap may improve daytime cognitive function.

"Research has shown that humans have a biological tendency to nap in the middle of the day, and that's why there are siesta cultures," said Scott S. Campbell, PhD. "We used to think of napping as a postprandial phenomenon. It turns out that the relationship is not as clear-cut, and the likelihood of having a nap is going to be there regardless of what you eat," he added.

In a National Institutes of Health (NIH)-sponsored study, Dr. Campbell and Patricia Murphy, PhD, examined the effect of napping on waking and cognitive function in older adults. The researchers studied daytime napping and its relationship to nighttime sleep in 32 healthy men and women aged 55 to 85 years (*J Am Geriatr Soc* 2005;53(1):48-53). Participants attended 2 sessions at the Human Chronobiology Laboratory. Each session was separated by at least 1 week and included 3 nights and the following day.

"We found that a nap of up to 2 hours does *not* disturb subsequent nighttime sleep," said Dr. Campbell, "as long as you end the nap by about 6 PM. The findings are important because it means that napping increases the total amount of sleep per 24 hours, which significantly improves waking performance in these older people," he said (Table).

"In [a] 72-hour experiment, healthy young adults ... have an average total 24-hour sleep duration of about 9.5 hours. So it looks like if the brain had its way, it would sleep a lot longer than most of us sleep."

—Scott S. Campbell, PhD

About 50% of people older than 60 years of age are not getting enough sleep at night, he noted. "The average sleep duration for healthy young adults is about 7.5 hours. The average sleep duration for people over 60 is about just a little more than 6 hours," said Dr. Campbell.

At the Human Chronobiology Laboratory, Drs. Campbell, Murphy, and their colleagues continue to explore the phenomenon of human sleep and temporal regulation. They have conducted a number of studies showing that people are more likely to nap when their body temperature is at its maximum—typically occurring between 4 and 5 PM. Conversely, the time in one's daily cycle when body temperature is at its lowest is between 4 and 5 AM.

"We put people in bed around 2 PM, and have them sleep until 4 PM," said Dr. Campbell, "because that tends to be the time when people are most likely to be able to fall asleep and stay asleep for a nap. And that's why in siesta cultures, after lunch, things shut down; it doesn't have anything much to do with eating, but rather with the biological tendency to nap at that time," he added.

Under a current NIH grant, the investigators are examining whether napping may serve as an intervention for older people over the long term. In the study, participants are directed to take daily naps at home for a 1-month period. "We're looking at whether the participants are willing to nap, whether their brains will allow them to nap, and how napping affects their waking performance," said Dr. Campbell.

Interestingly, the researchers also found that people who sleep well at night tend to be good nappers and people who don't sleep well at night may have a difficult time napping. "And that's a bit disappointing, because the very people whom you wish you could help with a nap may not be the people who are able to do it," said Dr. Campbell.

The researchers also collaborate with geneticists at Rockefeller University to study genetic links to sleep behaviors, including napping and delayed sleep phase disorder. "We have already found that there are nappers and non-nappers, just like there are late-night people and early-morning people and long-sleepers and short-sleepers," said Dr. Campbell.

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Table. Effects of Afternoon Nap on Sleep Quality and Composition

EEG Sleep Variable	Nap	Postnap Night	Nap + Postnap Night	Postsedentary Night
	Mean ± Standard Deviation			
Total sleep time, min	81.0 ± 25.9	362.8 ± 65.9	443.8 ± 67.1[b]	373.3 ± 51.8
Sleep efficiency	77.1% ± 21.3%	81.2% ± 10.9%	80.1% ± 9.4%	83.0% ± 9.7%
Sleep onset latency, min	12.8 ± 18.8	21.8 ± 16.8[a]	N/A	15.5 ± 14.2

Significantly different from sedentary condition: [a] $P<.01$; [b] $P<.001$.
EEG, electroencephalogram; **NA,** not applicable.

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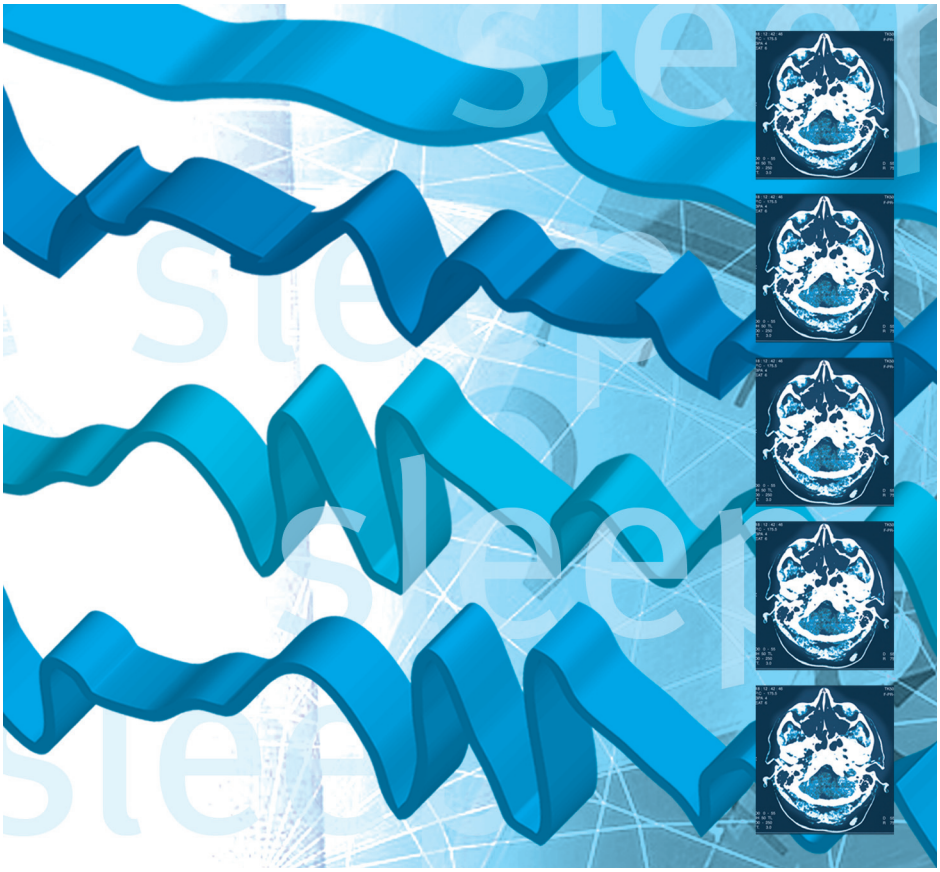
In a recently published study, Drs. Campbell and Murphy examined the nature of spontaneous sleep in adulthood (*J Sleep Res* 2007;16(1):24-32). Participants slept in an isolation apartment in the Human Chronobiology Laboratory for 72 hours. Each apartment was equipped with a kitchen supplied with food that participants prepared for themselves. "In these particular studies, we destructure the day as much as possible," said Dr. Campbell. Participants are directed to eat when they're hungry and sleep when they're sleepy, rather than focusing on preparing 3 meals a day.



"We were studying how the brain would sleep and wake if it weren't inundated with societal demands and other distractions," Dr. Campbell explained. "And it turned out to be a very good way of seeing whether people could or couldn't sleep, as well as when they couldn't sleep.

"Even in this 72-hour experiment, healthy young adults in that kind of environment have an average total 24-hour sleep duration of about 9.5 hours. So it looks like if the brain had its way, it would sleep a lot longer than most of us sleep."

Other studies include Dr. Murphy's work exploring sleep disturbance in postmenopausal women and whether the administration of melatonin may be effective in reducing hot flashes and improving sleep. She has also begun a study looking at sleep disturbance in children with bipolar disorder. Drs. Campbell and Murphy are currently collaborating on a study examining recovery from sleep loss in healthy young subjects.

"We're helping people in our culture to understand that napping is not a bad thing," he said. "We think of people as lazy or not very good people if they nap, and it turns out that napping can be extremely helpful for waking function, which is one of the findings we emphasize," added Dr. Campbell.

Contributing faculty for this article:
Scott S. Campbell, PhD

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The Westchester Division works closely with other institutions at NewYork-Presbyterian Hospital. Three years ago, Columbia University College of Physicians and Surgeons, Weill Cornell Medical College, and the Westchester Division closed their individual child and adolescent psychiatry residency training programs and started an integrated program drawing on the best faculty and facilities from all 3 institutions. "We recognized that if we brought the programs together, we could give trainees exposure to the best that each campus has," said Dr. Wilner.

Future endeavors at the Westchester Division will focus on strengthening collaborations and increasing the emphasis on ambulatory care. "In all of our programs, we want to make sure that our practice continues to be evidence-based and that we conduct research to find better, more effective, and more efficient treatments," Dr. Wilner explained. "We hope to collaborate with others so that we can take the best of what we have and meld that with other people and programs that also have outstanding resources or knowledge. Our goal is to maintain our leadership role and integrate ourselves into the latest and most innovative areas in the field."

The wide array of specialists working at the Westchester Division provide comprehensive diagnosis and treatment of rare, unusually acute, treatment-resistant, and comorbid mental illnesses.

Contributing faculty for this article:
Philip J. Wilner, MD

Correction

The new book by George J. Makari, MD, described on page 5 of the Fall 2007 issue of this newsletter, should have been cited as *Revolution in Mind: The Creation of Psychoanalysis* (HarperCollins Publishers, 2008). Dr. Makari is Associate Professor of Psychiatry and Director of the Institute for the History of Psychiatry at Weill Cornell Medical College.

Mental Health Programs Cater to Unique Needs of Women

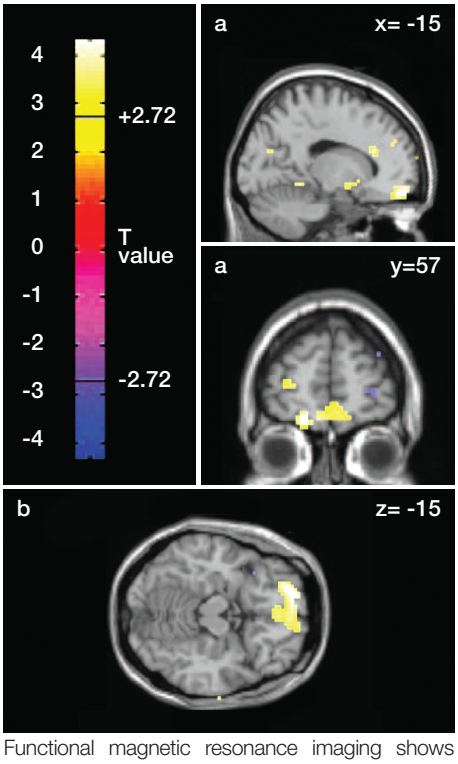
Columbia and Weill Cornell psychiatrists at NewYork-Presbyterian Hospital are involved in several treatment and research initiatives dedicated to women's mental health and the reproductive life cycle. The first initiative, the Payne Whitney Manhattan Women's Program at NewYork-Presbyterian Hospital/Weill Cornell Medical Center, was established in 2002. Two additional programs followed: The Center for Women's Mental Health at NewYork-Presbyterian Hospital/Columbia University Medical Center and the Women's Program at NewYork-Presbyterian/Payne Whitney Westchester. The programs offer mental health services to women who are trying to become pregnant, are pregnant, or have recently delivered, as well as to women coping with issues such as pregnancy loss, menstruation-related mood disorders, and menopause.

According to Margaret Altemus, MD, the Women's Program offers both consultations and ongoing care through its faculty practice and resident clinic. Its team includes psychiatrists, psychologists, social workers, and a nurse practitioner, all with expertise in women's mental health issues. One key feature of the resident clinic is that it is in network with several insurance plans, including Medicare and Medicaid. Theresa Nguyen, NP, runs a free postpartum support group for women with depression and anxiety on Thursdays at NewYork-Presbyterian/Weill Cornell. The women's health specialists also advise women who are already taking medication about the risks and benefits of continuing their treatment, and provide guidance about starting new medications or alternative treatments during pregnancy and the postpartum period.

In addition to offering clinical services, psychiatrists at the Women's Program are conducting innovative research. One area of research interest is premenstrual dysphoric disorder (PMDD), a severe form of premenstrual syndrome that causes intense anger, mood swings, and impaired concentration in about 5% of women. "The severe symptoms can impact women's ability to work and get along with their family," Dr. Altemus said. "It is a chronic illness. If you add all the days together, they amount to 7 to 9 years of symptomatic days."

The FDA has approved only 2 types of treatment for PMDD: certain selective serotonin reuptake inhibitors (SSRIs) and the oral contraceptive drospirenone-ethinyl estradiol. Both treatments have limitations. Although SSRIs are effective in 70% of women, they do not relieve symptoms of PMDD in all patients, and many women who take SSRIs experience sexual side effects. Conversely, some women are not able to take drospirenone-ethinyl estradiol because they cannot tolerate the side effects or do not want to take a daily hormonal medication.

In an attempt to find alternative treatments for PMDD, psychiatrists at the Women's Program are currently conducting 2 clinical trials funded by the National Institutes of Health (NIH). One trial, a 3-site study being carried out in cooperation with Yale University and Virginia Commonwealth University, is investigating whether women can take the SSRI sertraline only on days when they have PMDD symptoms. Most patients have these symptoms 5 to 10 days per month. Study participants undergo a 2-month evaluation period to determine whether they have PMDD and then enter a 6-month phase during which they receive sertraline or placebo only on symptomatic days. Preliminary evidence suggests that the treatment is effective and that stopping the medication at the onset of menses each month does not produce withdrawal symptoms.



Functional magnetic resonance imaging shows increased brain activity in areas of the brain responsible for behavioral control in the premenstrual vs postmenstrual phases of the menstrual cycle. The women were performing a task that involved inhibiting behavior in the context of emotional stimuli.

The other trial is examining whether flutamide, a drug that blocks androgen receptors, can alleviate PMDD by reducing the activity of testosterone and other androgen hormones. Dr. Altemus proposes that in some women with PMDD, the progesterone normally produced during the luteal phase may be converted to testosterone in the brain and other tissues. The study includes a 2-month evaluation phase and a 2-month treatment phase during which participants receive the androgen blocker flutamide or placebo. After completion of the study, investigators will continue to meet with subjects for several cycles to help to establish the best treatment for each patient.

A third NIH-funded study of PMDD, led by Emily Stern, MD, co-director of the Functional Neuroimaging Laboratory at NewYork-Presbyterian/Weill Cornell, is using functional magnetic resonance imaging (fMRI) to study changes in brain function across the menstrual cycle. Women who participate in the study undergo a 2-month evaluation to establish a diagnosis of PMDD and then receive fMRI scans early in the cycle (when they are not symptomatic) and again during the symptomatic premenstrual phase. Initial work by Dr. Stern's research group has shown that healthy women undergo changes in emotion regulation pathways in the brain during the premenstrual period, but that these changes are disrupted in women with PMDD.

Researchers are also examining anxiety disorders during pregnancy and the postpartum period to determine whether particular subtypes of anxiety abate or worsen during pregnancy, lactation, and weaning. Prior work by Dr. Altemus' laboratory has shown that brain levels of several hormones that influence anxiety and depression are altered in humans during pregnancy (*Biol Psychiatry* 2004;56[6]:386-392). In her current research study, patients rate anxiety symptom severity during pregnancy or the first year postpartum. Information obtained by the study should help patients and their clinicians anticipate any symptom changes and better plan prevention and treatment efforts during pregnancy and the postpartum period.

Contributing faculty for this article:
Margaret Altemus, MD

continued from Schizophrenia, page 1

better response to antipsychotic treatment. In other words, patients' response to antidopaminergic drugs depends on the degree of dopamine dysregulation they start with.

The study earned widespread recognition and provided solid evidence that schizophrenia involves an underlying dopaminergic abnormality.

Another area of Dr. Abi-Dargham's research delves into the longstanding theory that, although schizophrenia's positive symptoms relate to excess subcortical dopamine transmission, the disease's negative symptoms and cognitive dysfunction relate instead to a deficit in cortical dopamine transmission. In a study using positron emission tomography (PET) and the radiotracer [^{11}C]NNC 112 to measure D_1 receptor availability, she and colleagues found that patients with schizophrenia had significantly elevated cortical D_1 levels (*J Neurosci* 2002;22[9]:3708-3719). In fact, increased levels were associated with poorer working memory performance.

Dr. Abi-Dargham described similar D_1 elevations in other conditions associated with low cortical dopamine. One of the most creative studies, funded by the National Alliance for Research on Schizophrenia and Depression Independent Investigator Award, showed that users of ketamine also have elevated D_1 levels (*Am J Psychiatry* 2005;162[12]:2352-2359). The study bridged the 2 leading hypotheses of schizophrenia by demonstrating that a glutamate dysfunction, as induced by chronic recreational use of ketamine, can result in a dopaminergic dysfunction in otherwise healthy individuals.

A related study currently in press (*Molecular Psychiatry*) discusses the effect of val158met, a common polymorphism in the gene encoding catechol-*O*-methyltransferase (COMT), on the expression of D_1 receptors. Results show that subjects with val/val alleles had significantly higher cortical [^{11}C]NNC 112 binding compared with met carriers, but they did not differ in striatal binding.

The results confirm the prominent role of COMT in regulating dopamine transmission in the cortex but not the striatum. Because D_1 is a critical mediator of dopamine transmission in these brain regions, the findings further our understanding of the relationship between genes and their underlying cellular function. The study also shows how molecular PET imaging can play a central role in understanding this process.

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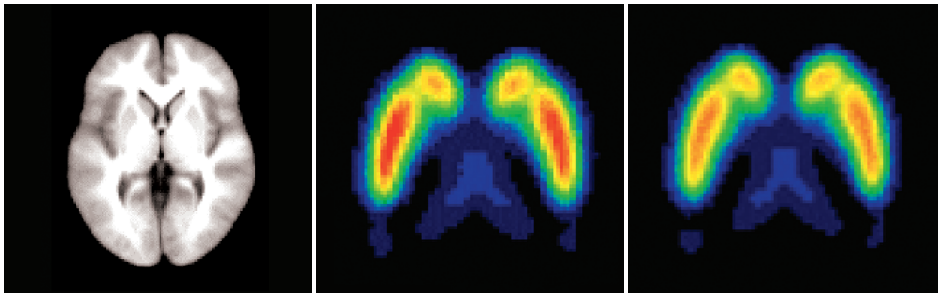
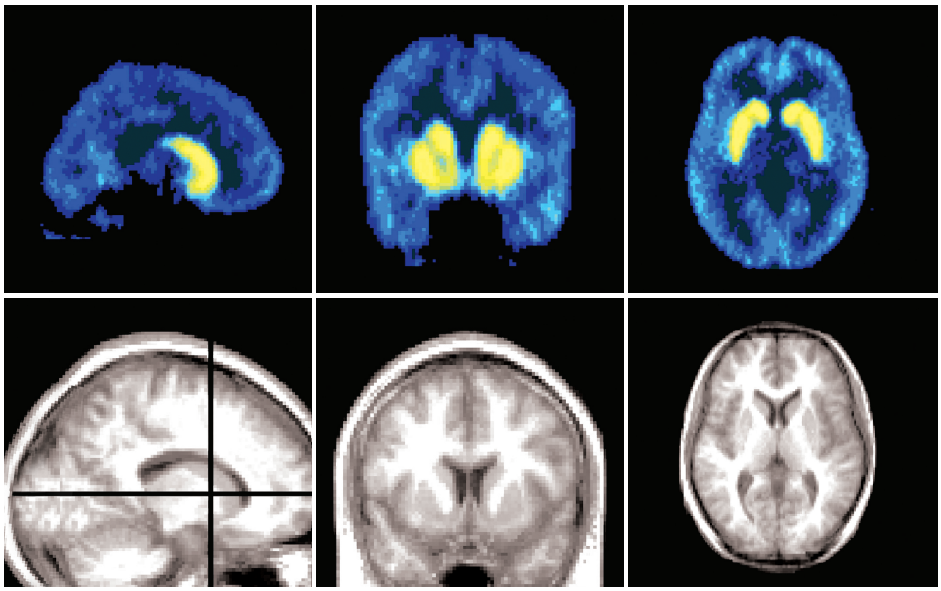
"When we're characterizing the pathophysiology [of schizophrenia], we are developing phenotypes that could be used as early markers for risk or as therapeutic targets."

—Anissa Abi-Dargham, MD

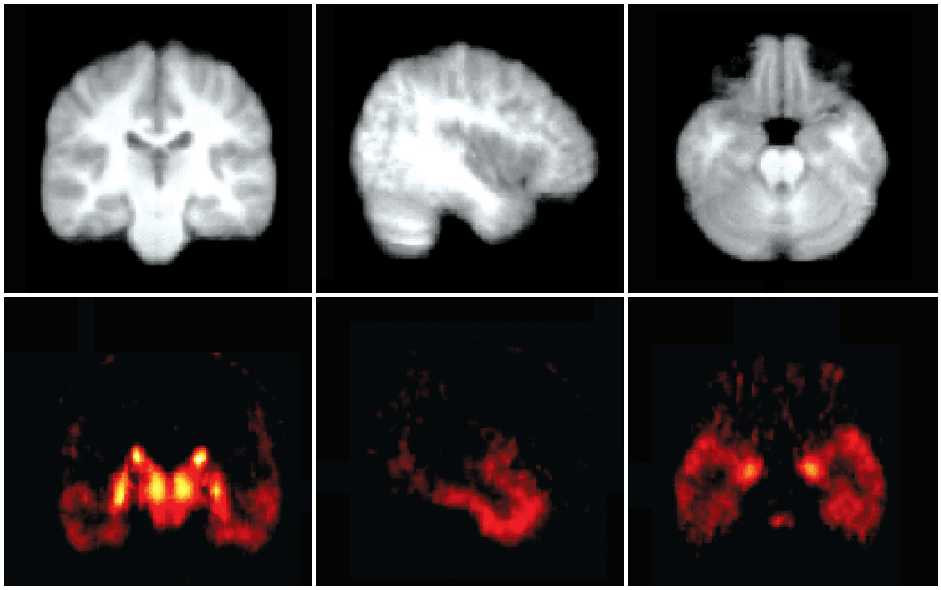


Photos courtesy of Anissa Abi-Dargham, MD.

Occupancy by antipsychotic medication: D_2 scan before and after low-dose aripiprazole.



Images of dopamine D_1 receptors in a human brain: Positron emission tomography scans with corresponding magnetic resonance imaging slices.



Imaging low-density D_2 outside the striatum with a high-affinity D_2 radiotracer labeled with [F-18]-fallypride: Positron emission tomography scans with corresponding magnetic resonance imaging scans.

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Other work by Columbia researchers focuses on the intersection of addiction and schizophrenia. Studies conducted with recently detoxified alcoholics show, as has been previously demonstrated in cocaine-dependent subjects, that addiction involves an opposite set of findings than those described in schizophrenia regarding dopaminergic indices in the striatum. In one study, Dr. Abi-Dargham and colleagues found that alcohol dependence was associated with a decrease in D_2 receptors and decreased dopamine release (*Biol Psychiatry* 2005;58[10]:779-786).

Because 60% of patients with schizophrenia have significant substance abuse, Dr. Abi-Dargham is now investigating this comorbidity. She is currently funded by the National Institute on Drug Abuse to assess the effects of cannabis use as well as to examine the impact of cannabis comorbidity with schizophrenia on dopamine transmission.

Her group's next project will investigate whether increased striatal dopamine synthesis, measured with [18F]DOPA, can predict which young prodromal patients are at risk for developing schizophrenia. If the idea is validated, physicians may be able to use PET scans to distinguish whom should be treated early with antipsychotics.

A central goal—better treatment based on better understanding—unifies these diverse research projects. "In a way, when we're characterizing the pathophysiology, we are developing phenotypes that could be used as early markers for risk or as therapeutic targets," she said.

Dr. Abi-Dargham serves as vice president for the Brain Imaging Council for the Society of Nuclear Medicine and associate editor for *Neuropsychopharmacology for Brain Imaging.*

Contributing faculty for this article:
Anissa Abi-Dargham, MD

Contributing Faculty

The following is a list of the doctors quoted in this issue of the *NewYork-Presbyterian Hospital Psychiatry* Newsletter. For more information on their work, please contact them at the e-mail addresses listed.

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