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NewYork-Presbyterian Psychiatry
ranks #1 in the nation.



Dr. Maria Oquendo Prepares for Presidency of APA

In May 2016 Maria A. Oquendo, MD, will become President of the American Psychiatric Association. Dr. Oquendo, Vice Chair for Education and Director of Residency Training at the New York State Psychiatric Institute and Columbia University, recently spoke with Advances about some of her plans as she begins her tenure in this prestigious position.

What issues do you intend to emphasize?

I would like to heighten attention to early detection and prevention. Most psychiatric conditions manifest around puberty. We need to identify young people before they get too far along in their illness and help them develop the skills and coping strategies they need to do well in life. In the last decade we've learned a lot about intervening early for individuals who look like they are headed toward schizophrenia. We are also getting better at identifying youngsters who appear to have depression, anxiety, and agitation but, in fact, have a bipolar disorder that is just starting to blossom.

We also need to improve access to psychiatric care. There are simply not enough psychiatrists to go around. About 25 percent of the population is afflicted with a significant mental disorder at some point in their lifetime, yet in this country we have 13 psychiatrists per 100,000 persons. We have to figure out ways of reaching more individuals. Some changes that are likely to be implemented in the next few years will result in psychiatrists being embedded in family medicine and primary care clinics. In this type of set-up, the psychiatrist plays more of a consultative role, supervising case managers and advising primary care doctors. The psychiatrist only sees the most challenging and refractory patients. Using physician extenders is another strategy to refocus the distribution of our human resources and reach more individuals who need care.

How important is research in your agenda?

Although mental disorders are at the very top of the list in terms of global burden of disease, they actually receive incredibly modest research dollars in our country and around the world. I would like to see a further strengthening of the APA's message around research. Most people understand that research for conditions such as autism, schizophrenia, and cancer is very important. But it might be hard for them to



Dr. Maria A. Oquendo

understand that depression, anxiety, and conditions that fall along the spectrum of the normal human experience also can benefit from research. We can make peoples' lives much better by building the knowledge base for prevention and also for treatments. We need to right size the research funding to be commensurate with the types of disability and mortality that are associated with the conditions that we treat.

Will you be working to influence legislation?

The APA is very active in Washington, DC, advocating for better access to care for individuals with mental disorders. Even though the Mental Health Parity Act was passed two decades ago, many insurance companies are not quite following the spirit of the law. Also, combating stigma against psychiatric conditions is very important. Stigma makes it harder for people to acknowledge that they have a condition or seek care for it. Physicians are also affected. For example, for years some state licensing bureaus would ask if a physician had ever had a mental health condition. This is starting to change, but the threat of not being able to practice medicine because you've had a depression, anxiety disorder, or a substance abuse disorder was very, very real. That is something that the APA has been active in trying to expunge from our legal and regulatory framework and we will continue to pursue.

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Alternative Treatment Approaches to Agitation and Depression in the Elderly

“To say a patient is agitated means nothing if you don’t assess its cause,” says **Nabil Kotbi, MD**, a geriatric psychiatrist and Unit Chief of The Haven and the Addiction and Recovery Unit at NewYork-Presbyterian/Westchester Division.

“Agitation is a common but challenging complication of Alzheimer’s and related disorders. In the elderly, you’re generally dealing with co-morbid conditions in addition to a neurodegenerative illness. So before we reach for an antipsychotic agent as the first-line treatment for agitation, we need to have a complete picture of the patient and any factors that may have precipitated the agitation.

“For example,” says Dr. Kotbi, “someone with Lewy body dementia will have an exquisite sensitivity to an antipsychotic. Or perhaps a patient with Alzheimer’s has a specific nurse who comes at particular times. That is what anchors them. Then suddenly, that nurse is gone. The loss of that anchor could have caused the individual to become agitated. In these cases an antipsychotic medication will not address the real issue. Is this the failure of the antipsychotic or is it a failure to understand that patient’s baseline – a medical problem, environmental trigger, poor sleep, delirium, or depression?”

“The idea that antipsychotics are always the first-line treatment is not necessarily true,” continues Dr. Kotbi. “A National Institute of Mental Health study in 2002 looking at the efficacy of an antipsychotic compared to SSRIs to treat agitation in patients with dementia showed no difference and, in fact, the researchers found that the SSRIs might work better.”

According to Dr. Kotbi, despite this finding, antidepressants received limited attention in the treatment of agitation of dementia. A more recent study showed that the SSRI citalopram had equal efficacy to risperidone in the treatment of demented patients who required psychiatric inpatient care because of agitation. In a case report published in the *Journal of Neuropsychiatry and Clinical Neuroscience*, Dr. Kotbi and his colleagues reviewed the use of citalopram to treat two non-depressed patients with dementia presenting with agitation and delusions who had failed several trials of antipsychotics.

Case Study 1: An 84-year-old woman with Alzheimer’s/vascular dementia was acutely hospitalized because of physical aggression and somatic delusion. Trials of risperidone, haloperidol, and quetiapine led to equivalent response, while lorazepam worsened her agitation. Risperidone was replaced with citalopram 10 mg twice daily and increased to 15 mg twice daily. Within 72 hours, the agitation diminished dramatically, and the patient was discharged soon thereafter. On follow-up several weeks later she remained in good behavioral control.

Case Study 2: An 80-year-old woman with Alzheimer’s dementia presented with violent behavior and paranoia. She had failed trials of atypical and typical antipsychotics. She was initially treated with risperidone but showed no improvement. She was switched to citalopram 10 mg twice daily, which was later increased to



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15 mg twice daily. Her agitation and paranoia improved four days after starting citalopram and she remained agitation free throughout the hospitalization and several weeks after discharge.

“Combined with earlier studies,” says Dr. Kotbi, “this suggests that citalopram, which does not share the adverse side effects of antipsychotic agents, may be a reasonable treatment option for these patients.”

A PATH to Better Treatment

In elderly patients with major depressive disorder further complicated by cognitive impairment up to the level of moderate dementia, treatment with antidepressants has had limited success and psychosocial interventions have not been adequately

explored. Researchers at NewYork-Presbyterian/Westchester investigated Problem Adaptation Therapy (PATH), a novel psychotherapy delivered in the home designed to decrease depression in adults with this combination of disorders. “Our study sought to determine the effect of this approach on regulating emotions and reducing the negative impact brought on by behavioral and functional limitations as compared to supportive therapy for cognitively impaired patients,” says Dr. Kotbi. “PATH integrates problem-solving with compensatory strategies, changes in the patient’s environment, and participation by the caregiver and incorporates the distinguishing factor of the therapy taking place in the home over a 12-week period.”

The team hypothesized that PATH participants would have greater reduction in depression and disability than those receiving supportive therapy. They also compared remission rates, time to remission, and patient and caregiver satisfaction, as well as the effects of treatment on pharmacotherapy-resistant depression.

The researchers found that PATH reduced depression and disability more than supportive therapy and that pharmacotherapy has limited effectiveness. Reductions in depression and disability were both statistically and clinically significant. “This is the first randomized trial, to our knowledge, of a psychosocial intervention for older adults living in the community with major depressive disorder and cognitive impairment, of which more than half had dementia,” says Dr. Kotbi. “The study strongly indicates that PATH may provide significant relief to this underserved population and their families.”

Reference Articles

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Advancing Precision Medicine in Psychiatry

“There is a revolution underway in oncology and in other areas of medicine where a true precision medicine-based approach is being implemented to study and treat a wide range of medical conditions,” says **Sander Markx, MD**, a clinical psychiatrist at NewYork-Presbyterian/Columbia University Medical Center (NYP/CUMC), with extensive research expertise in genetics of neuropsychiatric disorders. Precision medicine is a model in which medical practice is customized to an individual’s physiological information, including their genetic, molecular, and cellular data. This paradigm is becoming well established in cancer, and there is a growing body of evidence for the potential of precision medicine in neuropsychiatric diseases. There are increasing examples of genetically targeted therapies in epilepsy and a range of other childhood genetic conditions, often with lifesaving outcomes. By developing individualized treatments that target the specific disease mechanism associated with the cause of a patient’s illness, researchers have been able to demonstrate dramatic improvements in outcomes across medicine. Given the rapid advances in genetic sequencing technology and innovations in areas such as human stem cell research, Dr. Markx notes that a precision medicine-based approach can play a significant role in understanding psychiatric disease and improving outcomes for patients. “Our approach to studying psychiatric illness is specifically inspired by these latest advances that make it possible to improve diagnosis, classification, and treatment of psychiatric disorders,” says Dr. Markx.

A New Diagnostic Clinic for Precision Neuropsychiatry

Recognizing the power of applying genomics to psychiatric diagnosis and treatment, **Jeffrey Lieberman, MD**, Chair of Psychiatry at CUMC, appointed Dr. Markx to develop a diagnostic clinic to bring this leading edge technology to patients. “The time has come for clinical psychiatry to move beyond traditional treatment approaches and innovate by bringing the precision medicine-based approach widely applied in cancer and other fields of medicine to mental disorders. The drugs available today for severe psychiatric disorders do not target the primary cause of the psychiatric disease and they come with many debilitating side effects,” explained Dr. Lieberman.

The last several years have marked a turning point in our understanding of the genetics of neuropsychiatric disorders. The current sophisticated genomic medicine approaches have enabled us to reliably map the genetic mutations that underlie debilitating psychiatric disorders of individual patients. Dr. Markx and his team are now positioned to follow up on these findings and efficiently study the biologic consequences of these mutations. This has allowed Dr. Markx to identify relevant disease mechanisms and screen for novel treatments for psychiatric disorders for which there are currently few viable treatment options available, such as schizophrenia, autism spectrum disorder, and mood disorders. Notably, when diagnostic sequencing has been performed in the case of other serious genetic diseases, a remarkably high diagnostic yield has been obtained. While the utility of this diagnostic sequencing paradigm is yet to be confirmed in the context of psychiatric disease, it is expected to be most effective among the most seriously affected patients. These are also the patients most likely to benefit from a precision medicine-based approach, as current treatment options are limited in their ability to improve quality of life.

The new diagnostic clinic for precision neuropsychiatry takes a



Dr. Sander Markx

pipeline approach, starting with extensive phenotypic characterization of patients suffering neuropsychiatric disorders, followed by a comprehensive assessment of the underlying genomic mutations. These genetic findings are then studied in different model systems (animal and stem cell models) to identify the disease mechanisms driving the disease phenotypes, along with developing appropriate clinical biomarkers. In collaboration with several specialized labs at CUMC, high-throughput tools will be utilized to screen drugs and their capacity to restore normal neuronal function by targeting these disease mechanisms. As promising drugs are identified, the clinic will conduct targeted clinical trials for the specific patients who carry a given genetic variant – indeed, the first of these trials is already underway.

The launch of the new diagnostic precision neuropsychiatry clinic comes just as the push for introducing precision medicine-based approaches is gaining broad traction. Last year, President Barack Obama highlighted this scientific strategy as revolutionizing modern health care in his State of the Union address and called on Congress to increase funding for the Precision Medicine Initiative. The diagnostic clinic for precision neuropsychiatry at CUMC includes a basic science laboratory led by Dr. Markx together with **Bin Xu, PhD**, and a clinical facility for performing clinical assessments, biomarker studies, and conducting clinical trials. The diagnostic clinic will be part of the larger, CUMC-wide Columbia Precision Medicine Initiative led by **Tom Maniatis, PhD**, and will be closely aligned with the Institute for Genomic Medicine at CUMC under the leadership of **David Goldstein, PhD**. Dr. Markx and his colleagues also call on the resources of the Irving Institute for Clinical and Translational Research, the academic home for the next generation of clinical and translational research at CUMC. These partnerships are key in complementing and strengthening this novel neuropsychiatric diagnostic clinic in its mission to improve the diagnosis and classification of neuropsychiatric disease and bring new and effective treatments to our patients.

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