An Interview with Henry A. Nasrallah, MD

Dr. Henry Nasrallah received his BS and MD degrees at the American University of Beirut. Following his psychiatric residency at the University of Rochester and neuroscience fellowship at the National Institute of Mental Health (NIMH), he then served as faculty at the University of California, San Diego and the University of Iowa before serving as Professor and Chairman of the Ohio State University Department of Psychiatry for twelve years. At Ohio State, he increased the department's annual research funding by one hundred fold, and he also received the Distinguished Scholar Award, the highest research honor given by the University. He successfully lobbied the University to fund a new 120,000 square foot building for the Department of Psychiatry teaching, research and patient care. In 2003, he joined the University of Cincinnati College of Medicine as Associate Dean and Professor of Psychiatry and Neuroscience.

Dr. Nasrallah's research focuses on the neurobiology and psychopharmacology of schizophrenia and related disorders. He has published over 350 scientific articles, as well as ten books. He is Editor-in-Chief of two journals (*Schizophrenia Research* and *Current Psychiatry*) and recently co-founded the Schizophrenia International Research Society (SIRS), which now has 1,000 members worldwide. He is board certified in both adult and geriatric psychiatry. He is a Fellow of the American College of Neuropsychopharmacology, Fellow of the American College of Psychiatrists, Distinguished Fellow of the American Psychiatric Association, President of the Cincinnati Psychiatric Society and President of the Ohio Psychiatric Association Education and Research Foundation. He has twice received the NAMI Exemplary Psychiatrist Award and was voted in 2005 as the National Teacher of the Year by *Psychiatric Times*. He has received over seventy-five research grants and is listed in several editions of the book *Best Doctors in America*.

***CS*: Why did you choose a career in psychiatry?**

HN: I believe it was both nature and nurture, as is the case in most of the decisions we make in our life. My mother was a schoolteacher, my father a minister. I grew up watching them educate and counsel others, and thus I think my genes and my environment led me to be an academic psychiatrist. Other factors included my fascination with psychology and, especially, Freud's books, which I read before high school, because my parents did not want to have a television in our home, so I spent all my free time reading books in the library. By the tenth grade in high school, I had decided to become a psychiatrist and did quite a bit of counseling to my classmates about relationships and drug abuse, etc.

***CS*: What were key decision points in your career, and how have these ultimately led you to your present position?**

HN: The first key decision for me was to go to psychiatry training at the University of Rochester, where John Romano and George Engel shaped me as a competent clinician. However, because I was intensely interested in research especially in pharmacology, I sought the mentorship of Louis Lasagna, Chair of Pharmacology at Rochester, who helped me design and conduct three trials about chlorpromazine plasma levels and clinical response in schizophrenia. I was the only member of my residency cohort to present a paper at the American Psychiatric Association during residency training.

My second key decision was to pursue a research fellowship at NIMH after residency, and specifically in the neurobiology and neuropharmacology of schizophrenia. My research mentors at NIMH were Richard Wyatt and Chris Gillen. I published twenty papers during my research fellowship and that launched my academic career, starting as assistant professor at the University of California, San Diego.

The next major decision I did was to accept the invitation of George Winokur (the preeminent researcher whose publications I avidly read during medical school) to join his department at the University of Iowa as Associate Professor and Chief of Psychiatry at the strongly affiliated VA Medical Center. My loyal wife, Amelia, agreed to leave beautiful San Diego to raise our two young children in Iowa City, surrounded by cornfields. At age thirty-two, I became the youngest VA Chief of Psychiatry in the country. My research career blossomed in Iowa, thanks to the unmatched research culture in George Winokur's department. I mentored numerous psychiatric residents in research and many of them

published papers with me and later pursued academic careers.

The next major decision I made was to accept the offer to become the Chair of the Department of Psychiatry at Ohio State University at age thirty-eight and to move to Columbus, Ohio. I recruited dozens of faculty and increased the research funding at the department by one hundred fold! Shortly after I became Chair, I made a decision to start a journal for new data on schizophrenia, and I was able to convince Nello Spiteri of Elsevier, which had published my five-volume *Handbook of Schizophrenia*, to launch it. Shortly after Elsevier agreed to publish the new journal that I named *Schizophrenia Research*, I invited Lynn DeLisi to serve as my co-editor, and she enthusiastically accepted. (I was Lynn's psychopharmacology teacher when she was a resident and I was at NIMH, and she later pursued a research fellowship at NIMH as well.) We have continued to work together for twenty years, during which *Schizophrenia Research* became the premier journal for new data on schizophrenia.

My other major decisions included intense lobbying to replace the large but aging facility of my department at Ohio State, which I successfully did within a few years after I became Chairman, having significantly grown the department's faculty and research funding. Despite the hundreds of hours of planning, I enjoyed designing the 120,000 square foot building room-by-room with the architects, combining patient care, teaching, and research in one facility. Three years after the building was opened, my next major decision was that serving as department Chair for three terms (twelve years) was enough, and I took a sabbatical for the first time in my life after twenty years in academia. My major achievement during that extended sabbatical was to co-found the MIRECC (Center grant) that trained and mentored about fifty investigators in six medical schools and ten VA Medical Centers in the south. In January 2003, I decided to accept the position of Associate Dean for Faculty Mentorship and Development at the University of Cincinnati (UC), where I currently work.

Within a year after joining UC, Lynn Delisi and I decided to form a non-profit international society for schizophrenia researchers, which we incorporated in 2005, wrote the bylaws for, formed a Board of Directors and held elections of officers. The Society had a highly successful first meeting in Venice in June 2008 with over 1,500 schizophrenia researchers from around the world. It was quite gratifying to see the Schizophrenia Research International Society (SIRS) gain wide acceptance in our field and to have such a remarkable inaugural meeting.

***CS*: You teach, conduct research, see patients, run two highly successful journals, publish a lot yourself, and are involved in university administration. How do you balance your life to achieve all of these things?**

HN: It's true, I do a lot, but it comes at a price that I have accepted, and that is to lead an unbalanced life, something often necessary to excel in many walks of life. I was inspired to do that since I was in high school when, as an Olympic games aficionado, I quickly realized that to become a world champion, an athlete has to make huge personal sacrifices and to practice ten hours a day for many years to become the best in any sport. So I have done that by working at least eighty hours per week for the past thirty years and learned to be content with simple and small pleasures in life outside academics. But I love scientific discovery, am passionate about teaching and mentoring and get great satisfaction from treating difficult and challenging psychiatric patients, so I really enjoy everything I do, and I feel fortunate to have the physical and mental energy for that. I also am blessed with a highly competent and loving psychologist wife who, in addition to being my partner in research and editing, manages everything in our household (sparing me all household chores) and has raised our high-achieving son and daughter who have recently given us four adorable grandchildren (soon to be five). I truly feel blessed.

***CS*: What advice would you give to residents considering a career in academic psychiatry today?**

HN: Recruiting and mentoring residents for an academic career in psychiatry is one of my highest priorities. Our field is desperately in need of future investigators and teachers. A few years ago, I served as a consultant to the Institute of Medicine, which was conducting a project examining the challenges facing departments of psychiatry in recruiting trainees to research careers. I believe it is impossible for a resident to choose an academic path unless he or she is in a department which has a thriving research culture, where the Chair is an established investigator and role model, and where the faculty comprises a research culture that celebrates the generation of new knowledge and its dissemination. So my advice is choose a research-oriented department, participate in research throughout residency (and good departments readily provide mentors to facilitate that), get involved in studies about a topic or disease of real interest to you, and most importantly, pursue a post-residency research fellowship where you formally learn research methodology and design, biostatistics and grant writing skills. Ideally, the research fellowship would culminate in the submission of an NIMH K-Award that would provide salary support for the fellow for three to five years when he or she joins a department as a junior faculty. Otherwise, the harsh reality is that

clinical service demands to generate salary can be so intense that a young investigator will wither on the vine if not protected. Only a department with a Chair who protects and supports young investigators to ensure their successful academic trajectory can become a breeding ground for future investigators.

***CS*: What changes do you consider are needed in psychiatric training to prepare and train tomorrow's psychiatrists?**

HN: To produce top-notch psychiatrists for the future, the training form and content must reflect both the needs of our patients and the trends of knowledge in our field. Follow the example of medical schools who are questioning the perpetuation of "sacred cows" in the curriculum, such as gross anatomy, when medical knowledge has increased by over fifty fold in so many other areas over the past few decades. Psychiatric residency training programs must emphasize the medical foundation of psychiatry as a clinical neuroscience, to train its residents in the biological, psychosocial etiologies, and treatment of psychiatric brain disorders. While psychotherapy skills are vital, only evidence-based modalities should be emphasized, and psychiatrists should retain a solid medical and neurological identity and not be transformed into counselors because there are countless other competent counselors and psychotherapists from other mental health disciplines, such as psychologists and social workers. The rate of expansion of neuroscience knowledge in psychiatry is so great that we would do an injustice to future psychiatrists practicing well into the twenty-first century by training them with last century's knowledge and approaches. Finally, and most importantly, the training program *must* teach its residents the habits of life-long learning by reading journals every day or every week to keep up with the deluge of new knowledge. The best way to do that is to involve all residents in research during residency, require that they publish a minimum of two papers in a peer-reviewed journal, and to present their data at a national meeting, so they can appreciate what goes into publishing a scientific article and to develop a critical eye for the literature. I would emphasize journal clubs for more than is currently done in most departments, and I would continuously teach the residents how to critique scientific articles and decide if the findings are valid and reliable for use in clinical practice.

***CS*: What did you learn early in your career that turned out to be important or helpful to you?**

HN: The important principles that I learned early in my career that are still relevant to me are:

1) Mentorship is vital, seek it and also provide it.
2) Set specific goals and pursue them relentlessly.
3) Ignore the clock and disregard the archaic notion of a 40-hour week. Follow your passion 24/7.
4) Do not get too attached to your favorite hypotheses or beliefs. Always seek and welcome critical views of what you are doing, because that refines your thinking and make you a better researcher and clinician, too.
5) The success of a mentee can be just as vicariously thrilling as your own success. It's no different from the pride in your children's achievements. So, I am keenly generative towards students, residents and junior colleagues.

***CS*: What has been the greatest disappointment in your career?**

HN: A major disappointment early in my career was that the development of antipsychotic drugs was halted completely just as I embarked on my research career in neuropsychopharmacology at NIMH. No new antipsychotics for schizophrenia were approved in the United States market for twenty years until the second-generation antipsychotics (SGAs) were introduced. But the silver lining for that gap was that, as a result, I pursued other emerging neuroscience areas, such as neuroimaging at a very early phase of that field of research, and published extensively about CT, MRI, and MRS findings in schizophrenia before refocusing on psychopharmacology when the SGAs were developed and returned to doing FDA and post-FDA studies of efficacy and safety of all atypical antipsychotics.

Another disappointment has been the large amount of data that my research team generated over the past twenty years, which have yet to be analyzed or written for various reasons. This is actually a common problem in academia where the analysis and writing of data often lag behind the generation of data. Some gems may be dormant and undiscovered in our old data.

My greatest disappointment, however, is watching the sad state of serious mental illness in our country throughout my career as a schizophrenia researcher: there are still no truly effective treatments, and our patients remain disabled, poor, stigmatized, homeless, incarcerated, victims of crime and drug use, and dying young due to high rates of obesity, diabetes, hypertension, dyslipidemia, coupled with an appalling lack of basic primary care. I am also very disappointed by the de-medicalization of the public sector mental health system, and the huge missed opportunities for research in that key sector, and the inexcusable neglect of the physical health of the seriously mentally ill in the United States.

***CS*: What has been the greatest joy in your career?**

HN: Apart from the fact that despite my heavy workload, my marriage of thirty-seven years to my college sweetheart continues to be strong and blessed with wonderful children and grandchildren, my greatest career joys are:

1) Watching many of my former residents, whom I mentored in research over the years, become nationally eminent academicians and researchers.
2) My feeling of pride and accomplishment about my important contributions to the field of psychosis research including many "firsts" most of which have been replicated by others, such as:

   a) The first study of dopamine synthesis inhibition in schizophrenia.
   b) The first CT neuroimaging study in subtypes of schizophrenia.
   c) The first neuroimaging study in bipolar mania.
   d) The first study of cortical sulcal widening in schizophrenia and bipolar disorder.
   e) The first longitudinal study of progressive ventricular enlargement (brain atrophy) in schizophrenia.
   f) The first MRS study showing a decrease in the neuronal marker NAA in the hippocampus in schizophrenia.
   g) The first study of cognitive deficits in bipolar disorder showing overlap with schizophrenia in several domains.
   h) The first study showing that bipolar disorder is more sensitive to the extrapyramidal side effects (EPS) compared to schizophrenia.
   i) The first study of apoptotic markers (caspases, Fas-APO1, bcl-2, etc.) in the CSF of schizophrenia.
   j) The first study showing higher mortality in geriatric patients receiving first-generation versus second-generation antipsychotics.
   k) The first study of low treatments of metabolic disorders among persons with schizophrenia in the United States.
   l) The first patent for using deep brain stimulation for the treatment of refractory auditory hallucinations in schizophrenia.
   m) The first patent for using olfactory neuroepithelium as a proxy to measure antipsychotic drug reduced neurogenesis in the brains of persons with schizophrenia.

***CS*: Among the information that we do know about schizophrenia, what in your opinion are the most salient and robust "facts" about the disease?**

HN: The answer to this question is so extensive that it would fill the entire issue of this journal! Let me refer you to a series of articles that I wrote with Rajiv Tandon and Matcheri Keshavan in *Schizophrenia Research* in 2008 and 2009 reviewing "what we know" about schizophrenia. Part 1 is an overview, part 2 is epidemiology and genetics, part 3 is neurobiology, part 4 is clinical features and part 5 is (in preparation) about treatments.

The conceptualization of schizophrenia is evolving from a psychotic to a cognitive disorder, and its biology is transforming from a neurochemical pathology to a neuroplastic brain disease with gray and white matter pathology, both cortical and subcortical. Future treatments should transcend dopamine D2 receptor blockade to a model of early neuroprotection and reversal psychosis-induced brain tissue loss. But until we leverage the genetic discoveries to specific pathophysiological lesions, it is difficult to develop comprehensively effective specific treatments that lead to complete recovery or effective prevention.

***CS*: What do you think are the major opportunities for schizophrenia research over, say, the next ten years?**

HN: In my opinion, there are enormously promising research opportunities in schizophrenia research between now and 2020. The hottest areas in etiology are molecular genetics and pathological neuroplasticity (developmental as well as progressive). The most promising treatment approaches are modulating glutamate and GABA pathways as well as deep brain stimulation. Finally, intensified early identification of at-risk individuals and novel neuroprotective interventions may become a promising avenue for prevention. I urge young investigators to choose schizophrenia as an area of research. I have done it for the past thirty years and I am more excited and optimistic today about major breakthroughs than ever before!