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Scientific Autobiography of a Professional Student and a Lifelong Learner

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PROLOGUE

It is surreal and humbling that someone born in a small town (Pimpalgaon) thousands of miles away in India, who did not begin to learn English until the seventh grade, would be invited one day to write a scientific autobiography for the premier journal in geriatric psychiatry. I feel that all I have done in my life is to learn and continue learning new things. I consider myself a lifelong professional student—what I do is not “work.” As Tommy Lasorda said, “If you love your job, you haven’t worked a day in your life.” I feel blessed that my “job” has been to learn from so many talented teachers: senior scientists, peers, trainees, patients, and research participants. While my learning has focused mainly on research in geriatric psychiatry, it has also included clinical work, teaching, administrative responsibilities, organizational involvement, and community relationships.

JOURNEY FROM PIMPALGAON, INDIA, TO SAN DIEGO

Growing Up in India

I grew up in India as a nerdy, albeit stubborn, bookworm. I became deeply interested in the mind and brain after reading, as a teenager, Sigmund Freud’s popular books on the interpretation of dreams and the psychopathology reflected in everyday errors of life. I was fascinated by how Freud, a neuropsychiatrist, sought to understand a person’s mind by

studying his or her dreams and slips of tongue. Freud believed that psychology rode on the back of physiology. I was intrigued by the mystery of the mind as a function of the brain, and joined medical school with the goal of becoming a psychiatrist—considered by many an odd choice, raising doubts about my sanity. For me, it felt like a calling. I have never lost that urge to learn more about the mind and the brain.

My medical school in Pune did not have a research program in psychiatry, so I moved to Mumbai for residency training, which I completed under the mentorship of two pioneers of academic psychiatry in India: (late) N.S. Vahia and D.R. Doongaji. I learned the basics of clinical research methodology. We diagnosed and treated several hundred patients every month. Not surprisingly, the papers we wrote had large sample sizes, but the data were mostly sociodemographic and phenomenological. From a therapeutic perspective, my knowledge was restricted mainly to psychopharmacology, including drug trials and electroconvulsive therapy (ECT). I longed for in-depth, biologically based research. I decided to head to the mecca of psychiatric research: the National Institute of Mental Health (NIMH).

Moving to the United States

I found out that the United States did not recognize residency training in India. I applied to a few U.S. programs and chose the New Jersey College of Medicine and Dentistry. I immigrated with limited financial resources but with three partners: my wife Sonali, my passion for psychiatry, and my Indian accent. To date, none of them has left me!

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The first year in Newark, New Jersey, was challenging. Our studio apartment was burglarized three times, although there was little to steal. It was a culture shock. I soon realized that this program was not the place for my growth. I applied for and was accepted into Cornell residency. George Alexopoulos and I trained together in New Jersey and Cornell. We became lifelong friends, though neither of us had anticipated becoming a geriatric psychiatrist.

At Cornell, clinical training was psychoanalytically oriented. I sought to gain experience in biological research. I heard about the Bourne Research Laboratory directed by Gerald (Jerry) Smith, who had a great reputation as a scientist and mentor. The only problem was that it was an animal lab. I decided to try it out despite my total lack of experience. Jerry was very supportive. We studied the effects of dopaminergic drugs in rats following stereotactic surgery.¹ This experience served to demystify animal research and helped me understand its strengths (e.g., tightly controlled experiments) as well as its limitations (e.g., issues translating findings to humans). Although most of my subsequent research has been clinical, I have supplemented it with animal studies from time to time.

Joining NIMH

Following my residency, I began a research fellowship at NIMH, which was a dream come true. My primary mentor there was (late) Richard Wyatt, chief of the neuropsychiatry branch, which focused on the biology and psychopharmacology of schizophrenia. These have remained my main areas of research ever since, although in recent years I have become more interested in successful aging and positive psychiatry. After my fellowship, I became chief of the unit on movement disorders. Thanks to Richard's efforts, I, along with two of my colleagues, Danny Weinberger and Joel Kleinman, was able to combine my research with formal residency training in neurology at George Washington University.

At NIMH, I chose to work with both basic and clinical researchers. My main basic science colleague was David Stoff, with whom I studied behavioral pharmacology in rats, including the pharmacogenetics of agents acting on dopaminergic systems.²

On the clinical side, my colleagues and I studied psychopathology, cognition, and brain imaging in

schizophrenia. Our paper "Ex uno multi: subtyping the schizophrenic syndrome" won the A.E. Bennett Research Award from the Society of Biological Psychiatry.³ We argued that there were no fixed subgroups of patients with schizophrenia. Instead, each patient could be classified differently according to specific dimensions, such as cognitive impairment, negative symptoms, brain ventricular enlargement, and treatment response.

I also spent several months working in the famous Yakovlev brain collection at the Armed Forces Institute of Pathology. These brains came from people with schizophrenia who had died decades before the introduction of antipsychotics into psychiatry. One could, therefore, evaluate the neuropathology of schizophrenia—especially the hippocampus—without the confound of antipsychotics.⁴

In psychopharmacology, I was fascinated by antipsychotic-induced tardive dyskinesia (TD), a unique, potentially irreversible movement disorder caused by therapeutic agents that had no parallel in medicine. I spent a year combing through the literature on TD and published a book, *Understanding and Treating Tardive Dyskinesia*, with Dr. Richard Wyatt.⁵ A number of myths related to TD became apparent as I reviewed the literature and conducted studies. For example, we found that the almost universal recommendation for frequent neuroleptic-free periods for preventing TD was counterproductive, and that intermittent treatment was actually associated with an increased risk of persistent TD. We also showed limitations of the prevalent dopaminergic supersensitivity hypothesis of TD and proposed alternatives.

Settling Down at UC San Diego

After spending several years at NIMH, I felt it was time for me to strike out on my own in the "real world" of academic medicine. I visited several universities, but just one visit to the University of California, San Diego (UCSD), convinced me that it was THE place for me. It was not primarily the weather—great as it is, especially for someone who hates cold weather—but rather the culture of outstanding research combined with wonderful collegiality.

At UCSD and the San Diego VA, I was originally set to head a program in schizophrenia. However, just before my move, UCSD received VA funding to start a new clinical/research fellowship in geriatric

psychiatry. The department chair, Lew is Judd, asked me if I would head that program. I agreed despite having no expertise or focused interest in geriatric psychiatry. My first fellow was Jacqueline Harris, a brilliant physician with superb clinical and interpersonal skills and a long-standing interest in geriatrics but not in a research career—quite different from my own interests; yet, we worked together exceptionally well. We built the geriatric psychiatry program at UCSD from scratch. This program has been my professional home ever since.

Although I got into geriatric psychiatry serendipitously, I stayed in this field because of its incredibly collegial nature. One of the principal architects of the growth of geriatric psychiatry research in the United States was Barry Lebowitz, NIMH geriatric psychiatry branch chief.⁶ He was instrumental in creating, maintaining, and nurturing a growing number of researchers—both senior and junior—in geriatric psychiatry. Two main catalysts for this growth were NIMH-funded clinical research centers and the Summer Research Institute (SRI).⁷ Since Barry's retirement from NIMH, George Niederehe and Jovier Evans have been spearheading federal support for geriatric psychiatry research, researchers, and trainees. Along with Dan Blazer, Chip Reynolds, and George Alexopoulos, several others including Steve Bartels, Dev Devanand, Sandy Finkel, Gary Gottlieb, Anand Kumar, Helen Lavretsky, Henry Nasrallah, Ruth O'Hara, Gary Small, and Jürgen Unützer have been among my close friends and colleagues for decades.

RESEARCH AT UC SAN DIEGO

Schizophrenia and Aging

At UCSD, Jacqueline Harris and I focused on schizophrenia and aging, beginning with studies of late-onset schizophrenia (LOS). It was a highly controversial entity then, with the *Diagnostic and Statistical Manual of Mental Disorders, Third Edition*, having excluded a diagnosis of schizophrenia if the onset of symptoms was after age 45. When we wrote a grant proposal on LOS, NIMH reviewers questioned whether we actually had patients with true LOS, and conducted a site visit. The grant was funded. Shortly thereafter, we got funded for another research project grant for studying the incidence of and risk factors for TD in older patients. In

1992, we received funding for a clinical research center focusing on psychosis in older people.

An exciting part of research is challenging existing theories in order to change what we preach and practice. Our studies revealed that several traditionally accepted "facts" were no more than myths. Thus, in contrast to Kraepelin's concept of dementia praecox, we found that the usual outcome of schizophrenia in later life was not dementia, but rather improvement in symptoms, and occasionally even remission.^{8,9} Yet, there was considerable resistance in the United States to accepting the possibility of sustained remission of schizophrenia—until the release of the movie "A Beautiful Mind," the true story of a Nobel laureate whose schizophrenia began to improve after age 50. Gradually, thanks to a growing movement led by the National Alliance on Mental Illness, recovery became accepted as a feasible outcome in schizophrenia.

Interventions

My original interest was in psychopharmacology. We conducted many trials of different antipsychotics—especially the newer atypical ones—in older people with psychosis, including that associated with dementia. The results were mixed, showing some improvement but also significant adverse effects. We studied the neuropathologic effects of antipsychotics in rats. We also developed treatment guidelines for older patients.

Growing increasingly disappointed with the unsatisfactory long-term efficacy and safety of the drugs, I moved toward psychosocial interventions. My psychologist colleagues Eric Granholm, Tom Patterson, Beth Twamley, and Colin Depp have developed effective interventions, such as cognitive behavioral social skills training, functional adaptation skills training, vocational rehabilitation, and, in recent years, technology-supported behavioral strategies, for older patients with schizophrenia. I have increasingly come to appreciate the critical value of psychosocial interventions for serious mental illnesses.

Successful Aging, Wisdom, and Positive Psychiatry

In 2004, I was appointed director of UCSD's Sam and Rose Stein Institute for Research on Aging. Previously, this institute had focused on research in aging-associated illnesses such as dementia and cancer. I

wanted to do the opposite, i.e., study successful aging. If people with schizophrenia can have improved mental function with aging despite worsening physical health, could the same thing also occur in the general population?

Successful Aging

We began the Successful Aging Evaluation study of 2,500 community-dwelling adults, aged 21–100 years, seeking to assess not only physical and cognitive aging but also psychosocial functioning, including positive constructs, such as happiness, resilience, optimism, and well-being.¹⁰ We found an increase in well-being with aging. Looking at the animal equivalent of successful cognitive aging, we published papers on the neurobiological correlates of preservation of cognitive function in old mice.¹¹

My interest progressively shifted to abilities that improve with aging. Growing up in India, I had always thought of older people as being wiser. But is there science of wisdom?

Wisdom

Our first task was to define the fuzzy construct of wisdom. We reviewed the empirical studies on wisdom that had begun in the 1970s. We also polled international experts in wisdom and conducted a mixed methods qualitative-quantitative study of wisdom in an Indian scripture—the Bhagavad Gita. Astonishingly, all these investigations seemed to arrive at similar conclusions. Wisdom is a complex human trait comprised of specific components: emotional regulation, prosocial behaviors (e.g., empathy and compassion), self-reflection, acceptance of diverse value systems, decisiveness, social decision-making, and spirituality. Wisdom is useful to both the individual and the society. Next, we sought to determine the putative neurocircuitry of wisdom by reviewing the literature on the neurobiology of each component of wisdom and by studying “experiments of nature,” i.e., case reports of persons who changed from being wise to unwise following localized brain trauma or disease.¹² All the evidence pointed to the prefrontal cortex and limbic striatum. Wisdom tends to improve with aging, and the neuroplasticity of late life helps this process. Wisdom of aging likely has evolutionary value for humans’ survival fitness. We recently developed

the San Diego Wisdom Scale.¹³ To study a component of wisdom in animals, we studied a mouse model of empathy.¹⁴ I feel that we will witness even more exciting wisdom research in the next decade.

Positive Psychiatry

I have developed a growing realization that psychiatry needs to broaden its field of work from illness to health—both physical and mental—and from treatment to prevention.¹⁵ My group has been studying the biology of positive traits, such as resilience and wisdom, along with interventions to enhance them in people with serious mental illnesses.

Other Areas

With colleagues, I am working to learn about bioethics (Barton Palmer), brain imaging (Lisa Eyler), sleep (Ellen Lee), and diversity (Maria Marquine). Recently, I was appointed codirector of the IBM-UCSD Center on Artificial Intelligence for Healthy Living. It is hard to believe that I get paid to learn all these things!

MENTORING

Mentoring is a powerful relationship for influencing behavior. Mentors provide vision, guidance, and inspiration to trainees.¹⁶ I have been fortunate to have had several outstanding mentors in my professional career. Now, training younger students, fellows, and junior faculty is my passion. We have had a successful T32 program for the past 25 years. While this training is mostly at an individual level, we also have developed several NIH-funded national-level summer research training programs in geriatric psychiatry for undergraduate, graduate, and medical students, as well as a local one for high school students.

SRI

During the mid-1990s, Barry Lebowitz, Ira Katz, Maureen Halpain, and I started the SRI in geriatric psychiatry, supported by a grant from NIMH.⁷ The first SRI was held at UCSD in July 1996. Chip

Reynolds, George Alexopoulos, and several others became integral parts of the SRI leadership. Subsequently, Martha Bruce—and more recently Faith Gunning—became the principal investigator. The SRI has proved to be an outstanding model for creating a research workforce in a new area. The joy of seeing the mentees become established independent investigators is similar to that of seeing one's children grow into successful adults.

ORGANIZATIONAL AND COMMUNITY WORK

I have been incredibly fortunate to have had several amazing opportunities for organizational involvement that have broadened my field of professional vision.

AAGP

I have been a member of the American Association for Geriatric Psychiatry (AAGP) since the late 1980s. My AAGP activities have helped me develop a deeper understanding of the field. In 1998, I was honored to become AAGP president. During my presidency, we laid out plans for the first general election by AAGP members for all offices, including the president's, and for initiating AAGP membership for nonpsychiatrists by creating a new associate membership category.

APA

As a geriatric psychiatrist, I felt that it was important to represent our subspecialty within the American Psychiatric Association (APA), the largest psychiatric organization in the world, with over 36,000 members. I have been involved in APA activities for many years. In 2012, I was privileged to be the first board-certified geriatric psychiatrist to be elected APA president. (I hope there will be many more in the years ahead.) An important task during my APA presidency was completion, approval, and publication of the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)*. There was unprecedented public and media scrutiny of DSM-5. The

work required coordination and collaboration among various groups that did not always agree. There were plenty of debates. I feel proud that we completed our work in a timely manner while at the same time ensuring quality. DSM-5 has several limitations, but it is the best clinical diagnostic manual for today's mental health system.

The theme I chose for the annual conference of APA was Pursuing Wellness Across the Lifespan, which highlighted positive psychiatry and successful aging.

Geriatric Psychiatry Journals

Journals are a vehicle not only for publishing research studies but also for informing clinician readers. I had the privilege of serving as the editor of *The American Journal of Geriatric Psychiatry (AJGP)* from 2001 through 2015. In 2001, AJGP was an 8-year-old quarterly with about 70 submissions per year; the entire process of submission, review, and decision took place through the Postal Service; and the Impact Factor was modest. A large team, including the editorial board, reviewers, and staff, worked together to take the journal to progressively higher levels. It became a monthly, the number of submissions grew several-fold, the Impact Factor became the highest among all geriatric journals, and AJGP was consistently rated number one in AAGP membership benefits in annual surveys. I was delighted that Chip Reynolds became the next editor, and he has been doing a superb job in that capacity.

I recently became the editor of *International Psychogeriatrics*, the journal of the International Psychogeriatric Association.¹⁷ Leading an international journal is a different challenge, as *International Psychogeriatrics* represents various countries with marked differences not only in language but also in the state of science, clinical practice, research support, and training programs. Personally, this is a wonderful opportunity for me to learn new perspectives and work with international geriatric mental health experts on global issues.

Other Organizations

Participating in various organizations is useful and rewarding but also time-consuming. Therefore, one needs to find the right balance between personal and

organizational commitments. For me, one of the most unexpected honors was being elected to the Institute of Medicine of the National Academy of Sciences, Engineering, and Medicine. It is a privilege to know major leaders in fields that are far away from what I do daily; their work is inspiring.

Media

For a number of years, I avoided the media because of the feeling that they distort scientists' perspectives and present a highly biased view to the public. In recent decades, however, I have come to realize the value of working with the media. They can be a conduit for educating the public. Working with knowledgeable science and health reporters is helpful in reaching out to the masses. Of course, caution is needed to avoid oversimplifying or overselling research results.

EPILOGUE

A long professional career is never a straight line; it will have unexpected and exciting opportunities mixed with unanticipated obstacles and losses. It involves taking calculated risks, and luck undoubtedly plays a role in how things turn out, but support from friends and colleagues is even more critical. For me, the riskiest decision was to

move to the United States, but my experience as an immigrant has taught me the value of resilience, openness to new ideas, and balancing focus with flexibility.

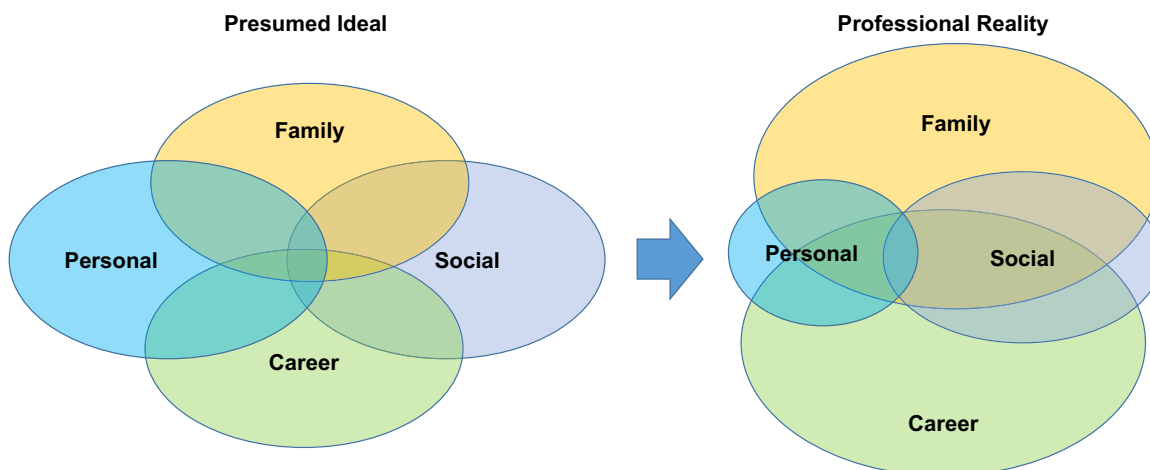
I have three families. My immediate family includes my wife Sonali and our daughters Shafali and Neelum. They are all highly accomplished physicians at different stages of their careers and, importantly, they are wonderful and caring human beings. My career would be nothing without them.

My second family which forms my professional home, includes the people I work with—faculty, trainees, and staff—who all share the same value system. I feel fortunate to have found and formed such a home at UCSD. I am especially proud of my mentees, including the 20+ research fellows who obtained NIH or VA career development awards. A majority of them have been women, and many now hold tenured faculty appointments in prestigious universities. I have special respect for women professionals. Our society is still sexist and expects more from, yet gives fewer rewards to, women professionals.

My third family includes a national and international network of colleagues who are also friends. Geriatric psychiatry is an inherently collaborative and collegial field.

In discussing career development, people often talk about career-family balance as if this were a zero-sum game in which more time for one means less time for the other. I consider this a false dichotomy. It

FIGURE 1. Venn diagrams of life balances: presumed ideal and professional reality.



is a Venn diagram with four, not two, overlapping circles: family, career, social life, and personal hobbies (Fig. 1). To me, family and career—in that order—have always been the prime considerations. As they grew, my social life and personal hobbies became merged into family and career. Thus, much of my social circle today is comprised of colleagues and families of our children's friends. Similarly, my personal hobbies, such as travel, sports, movies, and theater, now take place in the company of my family and friends. Everyone needs to find the right life balance for herself or himself.

I believe the future of geriatric psychiatry is bright. I have great faith in our trainees and younger colleagues. I feel proud to be a geriatric psychiatrist. I would not trade it for any other career!

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