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Scientific Autobiography

Scientific Autobiography of a Spiritual Seeker in the Year of Hindsight's 20/20

“Was I deceived, or did a sable cloud Turn forth her silver lining on the night?” John Milton “Comus” (1634)

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I am honored to follow in the Journal's wisdom tradition and share my scientific autobiography, ironically, written in the year of hindsight's 20/20, when my research activities are suspended indefinitely, and I have plenty of time to reflect upon the meaning of life. We are living during unprecedented and difficult times when the entire world is asked to find its spiritual center and resilience in order to find collective solutions to its many problems. The surreal nature of the COVID-19

pandemic and the global lockdown makes each of us look back and ask “how did I get here?” followed by “and how do I move forward?” Reflections upon our life choices that resulted in the situation at hand can be very revealing and can help define our next chapter. Perhaps, we have been caught in the preprogrammed game of rules and expectation, and we can use this imposed pause to create a new game with the new rules. For the first time we are asked to consciously

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consider our choices that define our daily lives and determine our survival that is a truly global existential crisis. The COVID-19 pandemic pushed us to “go within” and to take personal responsibility for our existence. However, unfolding events have made us also more hopeful in our ability to create the new order that will support our lives in a new way. We are already witnessing high-paced scientific and technological innovation¹ that will require united transdisciplinary efforts to meet the demands of the world’s mental health post-COVID-19 that are described in our upcoming book co-edited with Harris Eyre, Michael Berk and Charles Reynolds “*Convergence Mental Health: A Roadmap Towards Transdisciplinary Innovation and Entrepreneurship*” that will be published later this year.² My “scientific activities” have been a big part of my spiritual journey focused on seeking to understand the true nature of human mental and emotional suffering and resilience, where all life events are assumed to provide valuable lessons and “silver linings” that ensure individual and collective evolution of consciousness. I look forward to this unprecedented opportunity for reinvention of ourselves, our world, our science, and the global evolution of consciousness as a result of our collective search for peace and alleviation of suffering.

EARLY FORMATIVE YEARS WERE “A PREP”

I grew up in Moscow, Russia. I often say that I was born to become a psychiatrist, in part, because, my mother was (and still is) a psychiatrist and my father was a neurologist and I had an easy access to the large library that introduced me to the workings of the mind and brain. Before I turned 10, I read books about cerebral palsy and Down syndrome and was strangely attracted to the pictures of young children who were clearly suffering. A natural empathy, I wanted to help the suffering. My first “patient” was my little friend, a three year old boy who was completely mute. I was able to understand his wishes intuitively and translated them to the adults. Although later, I went through decades of medical and psychiatric training, the essence of what I do for patients is not different: empathically understanding their suffering, translating it to the world, and helping in alleviating suffering by empowering them to change their lives.

During high school, I developed an interest in psychiatric research, and my first summer job was in a psychiatric hospital’ pharmacy. I watched patients who wandered in the beautiful gardens of the psychiatric hospital where they worked in the green houses as a part of their vocational rehabilitation program (the main staple of psychiatry in Russia) and tried to imagine what was going on in their minds. For high school science projects, I chose to perform hypnosis on my classmates, as was described in the book on hypnosis, using a pendulum, and described and classified their responses. The following year, after reading an old French phrenology book, I examined their skulls and made phrenological descriptions of their personality based on the skull topography, which gained me some popularity among my schoolmates and was a precursor of my current interest in mind-body interventions and brain biomarkers.

After I entered the Moscow Medical Institute in 1979, I joined a medical student research interest group in the Psychiatry Department and performed my first official research study of psychiatric symptoms in women with gynecological cancers that won an award at the Medical Student Research conference in Moscow and became my first published paper. During that time, I learned about research methods and mood and anxiety symptoms in women facing terminal cancer, as well as my own reaction to their suffering. The process of intellectual inquiry and discovery was fascinating to me, and I spent nearly every weekend working on this project. After graduating from the Moscow Medical Institute, I started my psychiatry residency at the Moscow Center of Mental Health of the Academy of Medical Sciences, where I became interested in geriatric psychiatry and the brain-behavior relationship in patients with melancholic depression and poststroke depression. I left Russia shortly after completing psychiatry residency and relocated to Los Angeles as a part of the third wave of the Russian Jewish immigration that just preceded the Fall of the Soviet Union.

MOVE TO THE UNITED STATES AND PSYCHIATRIC TRAINING

Interestingly, the move itself, no matter how dramatic, did not change my professional trajectory. For the first time in my life, I felt at home. The “melting

pot" that Los Angeles is known to be was more accepting of me than Russia ever was. Shortly after arrival, I discovered the UCLA campus, the marvelous biomedical library, and the UCLA botanical gardens where I spent a lot of time while preparing for the medical board examinations. I liked the place and felt like I belonged here. The sense of belonging was reinforced after I found the book in the library that was written by my great-uncle, Alexander Shmaryan, who served as the Chief psychiatrist of Russia shortly after the World War II and was responsible for the development of neuropsychiatry based on his work on the war-related brain injuries. His book was forbidden in Russia and taken out of the libraries after Joseph Stalin's purges of Jewish physicians and scientists that also included other luminaries such as Alexander Luria, a prominent neuropsychologist who contributed greatly to the knowledge of brain-behavior relationship. After passing the board exams, I matched to the UCLA San Fernando Valley residency program in psychiatry that was receptive to my inclinations to pursue a research career. I loved the people, the Veterans Administration hospital's vast green gardens, and could relate to a familiar "socialized" model of medicine.

The psychiatric training differed from my Russian experience, especially the intense medical internship in the first year, and subsequent training in the psychodynamic techniques. I was dedicated to learning all I could, whether it was the theories of psychodynamic psychotherapy or group therapy with the World War II veterans from whom I learned the American interpretation of the war history. The Chair of the Psychiatry Department, Dr. Arthur Kling, recognized my drive to pursue psychiatric research during my residency and invited me to take part in a research project that resulted in my first research paper in the United States that was devoted to positron emission tomography neuroimaging in patients with behavioral and cognitive deficits following mild traumatic brain injury. This experience made me realize that my passion and focus in directing my efforts could transcend any obstacles in pursuing a much desired research career in neuropsychiatry.

By the end of my residency training, I felt that my initial interest in studying brain-behavior relationship should be the path to follow in the two fellowship training programs in geriatric psychiatry and neurosciences, both performed at UCLA. I was guided by a

group of superb mentors to whom I am indebted for providing the opportunity and willingness to tolerate my intensity in pursuit of knowledge and success. Among those are Ira Lesser, Bruce Miller, David Sultzer, Lissy Jarvik, and Gary Small, with whom I worked on several projects dedicated to neuroimaging of late life depression and cognitive decline and to the treatment of agitation in dementia. One other important person was Dilip Jeste, whom I met at that time because of my interest in the neurobiology of late life psychosis, and we have continued collaborating ever since with a parallel evolution of our research interests into the area of wellbeing and positive psychiatry. At that time, he suggested that I write a paper on the Russian concept of schizophrenia because nothing was known about it in the United States.³ This paper was published in the *Schizophrenia Bulletin*, and also served as a cathartic 9-month-long journey that helped release all of the "Soviet" experiences. In the process of working on it, I discovered my passion for academic writing. This was the only paper of to-date that received a single line review "A magnificent contribution." This was more of a "passion project" that one of my supervisors called "avocational," but I highly recommend this type of experience to learn about moving beyond your comfort zone and pushing your own limits. Later, I also learned that merging personal interests (e.g., in yoga) with professional activities can eradicate burnout and lead to the ultimate job satisfaction.

ALL YOU ALWAYS WANTED TO KNOW ABOUT "ACADEMIC LADDER," BUT WERE AFRAID TO ASK

Despite a relatively "smooth sailing" through the academic system, the intricate details and secrets of academic success were still elusive, and the road was rather "bumpy." I attended workshops put together by the American Psychiatric Association appropriately entitled "Swimming with sharks" explaining unwritten and untold "rules of engagement" and the relational hierarchy that seemed intentionally complex and biased. In the 1990s, there were very few women mentors and role models to share their wisdom and the "operating manual." I used to say that I was well prepared to be "a woman in academia" because I had been "a Jew in Russia," and after I had

read that women in Academia had 0.75 children, I felt that I was a close match with my 1.0 son. Many academic institutions and scientific societies have recently recognized that the implicit biases that we all harbor can be barriers to fairness and progress and have since provided greater resources and training. Also, the landscape of academic medicine and psychiatry has been rapidly changing and becoming more diverse, with over 50% of the psychiatry residents being women and minorities and 30% foreign medical graduates. These difficult experiences at the early stages of my professional journey have made me more sensitive to the implicit and explicit biases within academic medicine, and I now use the knowledge and skills I gained in mentoring others.

THE AAGP

The main source of professional support, collaborators, mentors and mentees, and simply, good friends, has been my membership in the American Association for Geriatric Psychiatry (AAGP). I remember my first meeting in 1995 in Cancun, Mexico, and it was magical with the warmth and receptivity of the colleagues; connection to other trainees who were struggling with the same career-related issues; excitement of hearing the latest scientific discoveries, accompanied by magnificent Cancun sunsets on the beach. I was immediately "sold." To paraphrase Woody Allen, this was exactly the "Professional Club" I wanted to be a part of that also fully accepted me as a member. I became an active participant in the organization. I devoted a lot of time to the AAGP by serving on various committees of the organization and the Board of Directors, as well as chairing the Research Committee. I have contributed to the various mentoring programs and developed the original "Neuroscience Teaching Day" program in 2006 that is still alive and well to date. Another contributing factor to my success was the excellent mentoring network that served as a source of a professional and personal support through close relationships with my peers and mentors. Generally, I admire the dedication of the membership to this professional organization and its wellbeing, and the concern for developing a robust "pipeline" of researchers, educators, and clinicians. Such dedication led to the development of many innovative programs over the years, including the

Summer Research Institute (SRI- currently Research Career Institute in the Mental Health of Aging (CIMA-R25 MH112484; PI: F. Gunning), and the Advanced Research Institute (ARI- R25 MH119050; PI: M Bruce) (<https://www.mentalhealthandagingresearch.org>).⁴

THE SRI AND THE ARI: PROGRESS REPORT

My career trajectory serves as an illustration of the success of the innovation offered by the SRI and ARI. The programs were conceived as collaborations between the talented and dedicated AAGP researchers (principal investigators - Dilip Jeste [SRI], Martha Bruce [ARI], George Alexopoulos and Faith Gunning [CIMA]) and the National Institute of Mental Health Aging Branch with its program chief's and officers in sequence (Barry Lebowitz, George Neiderehe, and Jovier Evans) with the vision of building a mentoring network to ensure the development and progress of geriatric mental health research. These programs were designed to help early career scientists to develop their ideas and shape their research proposals with the input from the field's best and brightest researchers. Over time, the research network has expanded to over 700 graduates from the SRI (starting in 1995), and 158 Scholars from the ARI (starting in 2004) with the amazing outcomes of 95% of participants reporting remaining in academia; 23% reported obtaining an Early Stage grant funding and 44% obtained an Early Career Development grant. These programs also became blueprints for other NIH training initiatives.

I participated in the second SRI (1996) and the first ARI (2004). I am the first alumna of the SRI and the ARI who has received the three existing research awards from the AAGP: the member-in-training (MIT - 1997); Junior Investigator Award (2001) and the Distinguished Investigator Award (2020) to-date. I am also the only one who received the three main awards for geriatric psychiatry from the AAGP, the American Psychiatric Association, and the American College of Psychiatrists in the single year of 2020. I called that the trifecta of 2020, the year of cancelled meetings, which took place in the virtual surreality of the COVID-19 pandemic. I am certainly hoping that

many more will be able to achieve these honors in years to come.

I am forever indebted to the numerous mentors I met through these programs who became my colleagues and friends, and later, close collaborators. Many former scholars like myself went on to become the SRI/CIMA/ARI mentors that also cemented cross-generational lines of the organizational wisdom transmission. This was also a good way to learn the “do’s and don’ts” of mentoring that helped in shaping up my own mentoring identity. Today, I learn as much from my mentees as they learn from me as a result of this training.

THE IMPORTANCE OF BEING EARNEST

The big discovery early in my career was the need to participate in the competitive peer-reviewed process of funding novel research ideas. However, this became increasingly difficult in the late 1990s due to reduced research funding. Programs like the SRI/ARI were invaluable in teaching me how to develop research ideas and prepare grant applications and the importance of these for your research career. The VA National Neuroscience fellowship was the first competitive grant that I received. It gave me the foundation for success in clinical research and brought me back to my original interest in brain-behavior relationships by funding several studies in older adults with microvascular disease and depression. Those funded programs led me to receiving another competitive grant from the NARSAD (now the Brain and Behavior Foundation), followed by three NIH research career awards, first Mentored (K23), and later Mentoring (K24) from the National Institute of Mental Health, and most recently, from the National Center for Complementary and Integrative Health. These NIH research career grant programs allow physician-scientists to dedicate up to 75% of time entirely to research and research mentoring. In early 2000s, I began mentoring junior colleagues in translational neuroscience of neuropsychiatric disorders and in the development of novel intervention for late life neuropsychiatric disorders. I find it extremely gratifying that after having received a lot of help, I am able to give back and assist others in developing their research and academic careers.

IT TAKES A “VILLAGE”

Modern research is highly complex and requires collaborative work to develop novel ideas and utilize individual talents and the cutting edge technologies in order to advance the field. Research community forms a “group-consciousness” that defines the direction of the field’s development and benefits from the advanced “laboratory” that is a research collaborative group. Recently, I was given an opportunity to work with like-minded collaborators (all are esteemed members of AAGP) who came together to form the collaborative five-site OPTIMUM study that has been funded by the Patient-Centered Outcomes Research Institute to develop novel pharmacological interventions for treatment-resistant depression (PI - Eric Lenze; other site PIs- Jordan Karp; Steven Roose; Benoit Mulsant; and with the important support from Charles Reynolds).⁵ This collaboration later received additional grant funding from the National Institute of Mental Health (NIMH) (PIs - Aristotle Voyneskos and Meryl Butters) to study biomarkers of depression and cognitive decline that has become an interesting laboratory for the development of new ideas for developing novel treatments of older adults with depression that was recently challenged by the COVID-19 pandemic. We have proceeded with collaborative problem-solving, learned from each other, and supported each other, making the challenges much easier to cope with. “A greater truth” about that nature of late life mood and cognitive disorders will emerge from this collaboration and will be the source for new research ideas for years to come.

GOT RESEARCH IDEAS?

Another bit of advice regarding developing research ideas and securing funding that I received was to have an idea that is novel “enough” but not too far “ahead of the curve” in order to be accepted as a “fundable idea.” The original impetus of studying brain-behavior relationships that I harbored since my early years fueled my initial research ideas focused on geriatric depression and cognitive decline, and the vascular hypothesis that served as the basis of my earlier grant submissions and received the AAGP Member in training (1996) and Junior Investigator Award

(2001). These projects would not be possible without my UCLA mentors who facilitated my original ideas (Ira Lesser and Bruce Miller and Lissy Jarvik).^{6,7}

In the later years, new research questions originated from my clinical experience. I wanted to answer clinically relevant questions on the behalf of the entire field. For example, the decades-old question of whether depression and cognition improve with the addition of methylphenidate has been of interest to many psychiatrists and primary care physicians. With the help of the R-01 grant funding, I conducted a study on methylphenidate augmentation of citalopram and the findings of this study put "a nail in the coffin of the decades-old question" proving that the addition of methylphenidate could accelerate and improve treatment response in older adults. Because of its high clinical relevance, this paper was named among the top 10 articles in Psychiatry by the New England Journal of Medicine in 2015.⁸ I also learned to use the intervention studies to understand brain mechanisms of treatment response, while developing novel pharmacological and behavioral interventions and mastering advanced research tools like neuroimaging, genetics, inflammatory markers.^{9–12} In the early stages of career-development, my traditional and "expected" neurobiological direction in academic psychiatry was easy to adopt and keep "ahead of the curve" to identify the next important question to answer.

At the stage of mid-to-senior career development, one is encouraged to take risks in order to move forward and retain a sense of purpose. It is important to re-invent oneself periodically to avoid repetition. My "dizzying" turn-around shift occurred when I encountered a Kundalini yoga practice that captured my imagination by its observed health benefits. It occurred during a very stressful time in my life, and I was looking for tools for stress reduction. Everything about this yoga practice seemed amazing: learning about mind-body connections via yogic body postures, breathing, chanting, community, gathering, and vegetarian food. I pursued yoga teacher training and certification followed by years of rigorous practice resulting in the complete makeover of my body, mind, immune system, and discovery of my own spirituality. My colleagues were amused by the transformation of my reductionistic "neurobiological self" into my newly discovered "spiritual self" that emerged, along with my desire to study the brain,

health, and consciousness effects of mind-body practices. I turned my attention to developing studies of yoga, Tai Chi and meditation in older adults and stressed dementia caregivers. The initial studies preceded "the curve" by 10–15 years and were some of the earliest studies of mood and brain effects accompanied by profound epigenetic changes, anti-inflammatory effects, and most importantly, direct neuroplastic effects and cognitive improvement.^{13–18} The findings were novel and well-received by the medical and research communities, and especially, by the yoga communities around the world. This was also an opportunity to turn a passion project into a professional, evidence-based one. A number of new collaborations outside of the comfort zone and the field now include mouse biologists, stress biologists, respiratory physiologists, anthropologists, and neuroscientists. Our goal is to develop a translational center dedicated to the study of mechanisms of breathing control of emotion regulation in the mouse and human models of anxiety and panic. Our hope is that this work will take the field of mind-body medicine even further in promoting understanding of how our breath can help regulate our emotions during stress or panic. This has become particularly relevant given the recent global distress emphasizing the importance of promoting personal wellbeing using ancient breath practices as the simplest and all-encompassing solution. In addition, after thirteen years of conducting mind-body research, we have started an Integrative Psychiatry clinic that uses mind-body, lifestyle, and spirituality-based approaches to help patients with neuropsychiatric symptoms. We hope to empower our patients to take control of their own health and learn resilience-building tools to allow for self-regulation during these difficult times and for stress-related psychiatric disorders. Now, more than ever before, the healthcare system is ready to endorse integrative medicine that has accumulated evidence of its low-cost effective therapies for stress-related disorders.

RESILIENCE AND AGING

Experimenting with mind-body research and with my own yoga immersion led me to shift from the medical disease models to the health-promotion and wellbeing models, with resilience being a mechanism of maintaining wellbeing.¹⁹ Antidepressants and

psychotherapy can improve resilience and prevent depression recurrence. However, providing patients with the ability to learn about their own strengths and utilize their lifestyle choices and spirituality to improve treatment outcomes is another powerful therapeutic and preventive approach to neuropsychiatric diseases of late life, such as depression, caregiver stress and dementia. During this pandemic, the entire world population can benefit from this knowledge and skills of stress reduction that may continue to be beneficial post-pandemic as well. As a clinician and a researcher, it is much more gratifying to understand patients from the point of their own strengths and to empower them to take charge of their health by learning and using the tools of self-regulation of their choice. These resilience-boosting techniques can be powerful additions to the traditional psychiatric practices.

The best way to master the subject is to write a book. Most of these ideas are expressed in two books: "Resilience and Aging: Research and Practice" (2014)²⁰ followed by the edited international textbook "Complementary and Integrative therapies for mental health and aging" (2016) that I coedited with my esteemed colleagues Martha Sajatovic and Charles Reynolds.²¹ Both books outline the bio-psycho-social definition of resilience and wellbeing and examine the use of complementary and integrative practices to improve mental health and aging-related outcomes.

This line of research also attracted a new generation of mentees ranging from high school students, undergraduate, graduate, medical, and postgraduate students and MD/PHD trainees who were interested in the translational neuroscience of mind-body medicine resulting in a large number of publications that they co-authored. I also found that younger generations of students and investigators were much more open to integrative medicine and were passionate about making it a part of their work life while seeking a greater life/work balance for themselves and their patients. I find this very promising for the world's ability to rebalance itself and for our future

TO BE CONTINUED

Over the past 25 years, I have been blessed by the good fortune of being a member of the AAGP and by close relationships with my collaborators and mentors, who have embraced and assisted my transformations, transitions, and progress. I am grateful to my "work-sisters" and colleagues, Drs. Linda Ercoli, Katherine Narr, and Prabha Siddarth, on whose professional opinion and personal support I have relied over the years. I also want to thank my post-doctoral trainees, especially Harris Eyre, Hongyu Yang, Kelsey Laird, Adrienne Grzenda, and Beatrix Krause-Sorio, who shared my scientific passions and co-authored many published papers that made writing them so much more fun. All successes and challenges proved to be useful lessons, silver linings and blessings in disguise that led to a greater wisdom and growth. I am certainly looking forward to the new adventures and progress in next 25 years.

AUTHOR CONTRIBUTION

Helen Lavretsky was the sole contributor to this manuscript.

DISCLOSURE

There are no conflicts of interest to declare.



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