

Martin Alda: Deciphering heterogeneity: The key to personalized psychiatry

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Professor Martin Alda stands as a transformative figure in bipolar disorder research, revolutionizing personalized psychiatry through groundbreaking genetic discoveries that have reshaped treatment approaches worldwide. As the prestigious Killam Chair in Mood Disorders at Dalhousie University and a senior scientist at the Czech Republic's National Institute of Mental Health, Dr. Alda has published over 420 influential papers, developing the internationally acclaimed "Alda scale," now the gold standard for measuring lithium treatment response in patients with bipolar disorder globally. His pioneering research validated lithium-responsive bipolar disorder as a genetically distinct condition, fundamentally changing how clinicians approach treatment selection and sparking major international pharmacogenetic initiatives, including the ConLiGen consortium. This Genomic Press Interview explores the remarkable career of a scientist whose work bridges molecular genetics with compassionate clinical care, from his early days in Czechoslovakia to receiving the field's highest honors including the Colvin Prize from the Brain and Behavior Research Foundation, the Heinz Lehmann Award from the Canadian College of Neuropsychopharmacology, and the prestigious Mogens Schou Award for Research from the International Society for Bipolar Disorders. Through founding the Maritime Bipolar Registry and Halifax's Mood Disorders Program, Dr. Alda has created lasting infrastructure supporting innovative research into at-risk populations, metabolic dysregulation, and suicide prevention. His unique ability to identify connections across disparate research domains while maintaining deep clinical engagement exemplifies the future of precision psychiatry, where genetic insights translate directly into improved patient outcomes.

Part 1: Martin Alda – Life and Career

Where were you born, and where do you live now?

I was born in Liberec, Czechoslovakia, and trained in Prague before moving to Ottawa, Canada. At present, I divide my time between Halifax on the Atlantic coast of Canada and Prague, the Czech Republic.

Could you give us a glimpse into your personal history, emphasizing the pivotal moments that first kindled your passion for science?

My father was a scientist and mathematician, and my mother worked at the computer center of Charles University. In fact, she had hoped to study theology and become a minister, but in the 1950s, Czechoslovakia did not allow this. Many friends of our family were mathematicians and computer scientists, so, from early on, a career in mathematics seemed like a natural path for me as well. However, towards the end of high school, I became interested in neuroscience, and psychiatry seemed like a unique way to approach the question of the brain versus the mind.



Figure 1. Martin Alda, MD, FRCPC, Dalhousie University, Canada.

Please share with us what initially piqued your interest in your favorite research or professional focus area.

During my university years, I worked as a research assistant in molecular genetics, pathology, and psychiatry. When I began training as a psychiatrist, I sought an area where I could combine psychiatry with mathematical applications. A senior colleague was writing a textbook on psychiatric genetics and asked me to help with a chapter on statistics. At the same time, I was also working in psychopharmacological research, and all these interests converged into research that has guided my work ever since. In fact, my first three papers, published while I was still in Czechoslovakia, were on pharmacogenetics (effects of diazepam in twins), pharmacokinetics of lithium, and a family study of schizophrenia.

We would like to know more about your career trajectory leading up to your most relevant leadership role. What defining moments channeled you toward that leadership responsibility?

Administrative leadership has never been my greatest ambition. I took on more responsibilities gradually when I was developing the mood disorders





program in Halifax. On the other hand, in research, I have consistently enjoyed my involvement in consortia, where I have led specific projects, such as the IGSli (International Group for the Study of Lithium-Treated Patients) and ConLiGen (The International Consortium on Lithium Genetics), among others.

What is a decision or choice that seemed like a mistake at the time but ended up being valuable or transformative for your career or life?

Sometimes I worry that I have been spreading myself too thin. Ultimately, though, it helped me see the connections between different domains.

What habits and values did you develop during your academic studies or subsequent postdoctoral experiences that you uphold within your research environment?

Combining basic research with clinical observations has always been important, and to this day, I ensure that students spend time in the clinic. I have also been fortunate to have several exceptional mentors who were generous with their time and support. I also try to maintain and pass it on to the next generation.

Please tell us more about your current scholarly focal points within your chosen field of science.

My research focuses on optimizing the long-term treatment of bipolar disorder, lithium in particular – why it works so well for some people and not at all for others. It is evident that to succeed, we need to understand better how lithium works in the brain on the one hand and solve the problem of heterogeneity that plagues not only bipolar disorder, but practically all psychiatric conditions, on the other hand.

What impact do you hope to achieve in your field by focusing on specific research topics?

Ultimately, it is to improve the lives of people with mental illness. The work on lithium is exceptional in this respect; it serves as an example of how effective psychiatric treatment can be. However, we need to find equally applicable alternatives for those for whom lithium does not help.

What do you most enjoy in your capacity as an academic or research leader?

I enjoy the mix – seeing patients, supervising trainees and the research staff, and analyzing the data – when I have the time. Not to forget friendships with so many innovative and creative people – an important privilege of academic life!

At Genomic Press, we prioritize fostering research endeavors based solely on their inherent merit, uninfluenced by geography or the researchers' personal or demographic traits. Are there particular cultural facets within the scientific community that warrant transformative scrutiny, or is there a cause within science that you feel strongly devoted to?

Indeed. A scholarship should be about open discussion and the free exchange of ideas, not burdened by dogma and ideology. Having lived in a totalitarian system for part of my life, I am quite sensitive to this. Additionally, research and science are becoming an industry plagued by excessive regulation and bureaucracy. There are numerous low-quality papers, predatory journals, and unnecessary conferences, as if quantity mattered more than quality.

Outside professional confines, how do you prefer to allocate your leisure moments, or conversely, in what manner would you envision spending these moments given a choice?

Time is the most precious commodity ... Dividing it between Nova Scotia, with its fantastic hiking and beaches, and Prague, with its rich culture, looks excellent on paper, but I wish I could do these things more often. Travel and books are another passion.



Figure 2. Martin Alda in the Pirin Mountains, Bulgaria, in the summer of 1977, early in his career, when he was developing his research interests in pharmacogenetics and lithium treatment, while maintaining his passion for hiking, an activity he continues to treasure decades later.

Part 2: Martin Alda – Selected questions from the Proust Questionnaire¹

What is your most marked characteristic?

Curiosity. Moreover, one of my colleagues characterized me as overly optimistic.

Among your talents, which one(s) give(s) you a competitive edge?

Being able to see connections between disparate areas or link clinical insights with biological concepts.

If you could change one thing about yourself, what would it be?

I should learn to say no more often and not take on more than I can manage.

What is your current state of mind?

I plan to consolidate what I have learned and prepare for the next conceptual steps.

¹In the late nineteenth century, various questionnaires were a popular diversion designed to discover new things about old friends. What is now known as the 35-question Proust Questionnaire became famous after Marcel Proust's answers to these questions were found and published posthumously. Proust answered the questions twice, at ages 14 and 20. In 2003 Proust's handwritten answers were auctioned off for \$130,000. Multiple other historical and contemporary figures have answered the Proust Questionnaire, including among others Karl Marx, Oscar Wilde, Arthur Conan Doyle, Fernando Pessoa, Stéphane Mallarmé, Paul Cézanne, Vladimir Nabokov, Kazuo Ishiguro, Catherine Deneuve, Sophia Loren, Gina Lollobrigida, Gloria Steinem, Pelé, Valentino, Yoko Ono, Elton John, Martin Scorsese, Pedro Almodóvar, Richard Branson, Jimmy Carter, David Chang, Spike Lee, Hugh Jackman, and Zendaya. The Proust Questionnaire is often used to interview celebrities: the idea is that by answering these questions, an individual will reveal his or her true nature. We have condensed the Proust Questionnaire by reducing the number of questions and slightly rewording some. These curated questions provide insights into the individual's inner world, ranging from notions of happiness and fear to aspirations and inspirations.



Figure 3. Martin Alda enjoying cross-country skiing in Norway, March 2013, exemplifying the outdoor pursuits he values as essential counterpoints to his intensive research on bipolar disorder heterogeneity and personalized psychiatry.

What is your idea of perfect happiness?

A good dinner with family or friends, ideally after a long hike in the mountains.

When and where were you happiest? And why were so happy then?

On many occasions, usually in connection with my family. Any travels with my wife in particular.

What is your greatest fear?

Losing my independence.

What is your greatest regret?

I do not have any major regrets. Circumstances beyond my control constrained my choices at different points in time, and I had to accept that.

What are you most proud of?

Professionally? I have developed a productive clinical academic program at Dalhousie University and have mentored many exceptional people.

What do you consider your greatest achievement?

The genetic studies of lithium responders that Paul Grof and I initiated helped trigger renewed interest in this remarkable drug and led to significant international research efforts.

What is your favorite occupation (or activity)?

I enjoy the outdoors, including hiking, skiing, and cross-country skiing.

What is your greatest extravagance?

I am running out of room for books. Travel is another one.

What is your most treasured possession?

Memories of good times are more than anything material.

Where would you most like to live?

Currently, I divide my time between Halifax, Canada, and Prague, Czech Republic, and I am happy with the arrangement. It is an excellent mix of the outdoors and the ocean on the one hand, and history and culture on the other.

What is the quality you most admire in people?

Honesty and integrity.

What is the trait you most dislike in people?

Ambition not matched by substance.

What do you consider the most overrated virtue?

If it can be overrated, it may not be a virtue. Not all virtues are equally relevant in different environments and under different circumstances, however.

What do you most value in your friends?

Loyalty and tolerance.

If you could have dinner with any historical figure, who would it be and why?

Aristotle or John von Neumann. They both had a great breadth and depth of knowledge. I would have so many questions to ask.

Who are your favorite writers?

Too many to list. However, to promote Czech literature, I will list Karel Čapek and Josef Škvorecký.

Who are your heroes of fiction?

I would have to say Danny Smířický. He did not take himself too seriously, and life experiences made him wise, not jaded. As background, Danny Smířický is the protagonist of Josef Škvorecký's novel *The Engineer of Human Souls*. He is portrayed as a semi-autobiographical character: a Czech émigré, former WWII survivor, and now Canadian English professor who reflects on his experiences under Nazi occupation and Communist repression in Czechoslovakia, as well as his life in exile in Canada.

What aphorism or motto best encapsulates your life philosophy?

"Dii facientes adiuvant."

Gods help those who help themselves.

—Marcus Terentius Varro, Roman scholar

De re rustica (On Agriculture), 37 BCE



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