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INNOVATORS & IDEAS: RISING STAR

Nicolas Garel: Combining psychoactive molecules and psychotherapy for patients suffering from mood and substance use disorders: a new therapeutic paradigm

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Dr Nicolas Garel is an Assistant Professor in the Department of Psychiatry and Addictology at the University of Montreal and a junior investigator at the Research Center of the Centre Hospitalier de l'Université de Montréal. Dr Garel did his psychiatry residency at McGill University before completing the Clinician-Investigator Program and a Master's degree at McGill University, studying the potential role of ketamine in the discontinuation of benzodiazepines and related drugs. Dr Garel then completed a clinical fellowship in Addiction Medicine at Stanford University. His research program focuses on the integration of psychoactive molecules in conjunction with psychotherapy as a unique potential treatment approach for patients with comorbid mood and alcohol/sedative use disorders. In this "Innovators & Ideas" section, we are excited to feature Dr Garel in our latest Genomic Press Interview. We are thrilled he took the time to answer our questions and share his valuable insights with our readers.

Part 1: Nicolas Garel - Life and Career

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

Both my parents have been physicians deeply involved in academia

Both my parents have been physicians deeply involved in academia throughout their careers. My father has already retired, and my mother is set to retire this year. Witnessing their passion and fulfilment in their work has had a profound influence on me. My father was a paediatric interventional radiologist and my mother is a child psychiatrist, who naturally sparked my fascination for psychiatry from a very early age. Despite this longitudinal interest, I needed help to choose between internal medicine and psychiatry. I was accepted in both programs and ultimately decided to pursue psychiatry the evening before the deadline for declaring our medical specialty choices. During my undergraduate studies in psychology before starting medical school, I became particularly interested in the field of psychedelics and the notion that a single experience could profoundly and meaningfully mark and change a human being. It intrigued me how difficult it was for people to accept this idea, even though we readily accept that a single traumatic experience can negatively change someone's life forever.

We would like to know more about your career trajectory leading up to your current role. What defining moments channelled you toward this opportunity?

Initially, I began my research journey in an autism laboratory. However, the experience did not meet my expectations, and I found myself lost and disinterested in research. This changed when my colleague and close friend, Dr Kyle Greenway, who was a resident in psychiatry with me at McGill University, knowing my keen interest in psychedelics and ketamine, invited me to join him in developing the first ketamine clinic within the McGill University Hospitals network for treatment-resistant depression. I accepted the invitation as a second-year resident in psychiatry, and I



Figure 1. Nicolas Garel, MD, MSc, FRCPC, University of Montreal, Canada.

have been dedicated to studying ketamine and psychedelics ever since. I eventually entered the Clinician-Investigator Program at McGill University and pursued a Master of Science degree focusing on the potential role of ketamine in discontinuing benzodiazepine and related drugs. During this time, I also co-led a successful multisite randomized controlled trial, administering over 180 ketamine treatments in a psychedelic model to patients with treatment-resistant depression. This pivotal study, recently published, solidified my decision to pursue a career as a clinician scientist.

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

In addition to refractory mood disorders, addiction psychiatry has emerged as the discipline that I find the most interesting. This led me to complete a postdoctoral fellowship in addiction medicine at Stanford University in 2023. My interest in addiction psychiatry has shaped my goals and ambitions as a clinician, a scholar, a teacher, and an active citizen of my society. The interactions between this patient's population complexity with significant clinical and social dilemmas and a team-based work environment have both challenged me on an intellectual and humanistic basis and built my motivations for an academic career in addiction. Patients' decision to seek help and the interventions that we can propose serve as a unique window of opportunity to address crucial modifiable risk factors and improve long-term physical and mental health outcomes. The various clinical presentations combined with patients' self-motivated behaviours create fascinating patient-physician interactions. I am fulfilled when I see patients succeeding in becoming their health advocates and bravely taking on the challenges that come from confronting their deleterious

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substance use behaviours. Each encounter with a patient suffering from addiction requires reflection to provide optimal care to an underserved population. Addiction psychiatry appears to be in the process of an impressive ferment of ideas, giving rise to social advances and great scientific and humanistic understandings.

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

The current treatment gap in individuals with mood disorders and comorbid substance use disorders (SUD) emphasizes the need for new, innovative, and more effective interventions. The co-occurrence of these disorders significantly compounds the burden on individuals, their families, and society. These individuals often experience exacerbated symptoms, increased risk of relapse, reduced treatment response, and higher rates of morbidity compared to those with either condition alone. By developing and studying novel interventions targeting this specific population, we can bridge this treatment gap and provide much-needed support to clinicians and patients often overlooked.

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

My research program will focus on the integration of psychoactive molecules, initially ketamine, in conjunction with psychotherapy as a unique potential treatment approach for patients with comorbid mood and alcohol/sedative use disorders. The primary objectives are to evaluate ketamine-assisted psychotherapy's safety, feasibility, and, ultimately, efficacy on key clinical outcomes, examine changes in functional outcomes and quality of life, and explore the underlying neurobiological mechanisms involved in this treatment approach.

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

Throughout my academic studies and postdoctoral experiences, I deeply value creating a warm and welcoming environment within my lab. I believe fostering a culture where people support and help each other is crucial. A positive and secure atmosphere, combined with a strong sense of collaboration and team spirit over personal gains, significantly enhances creativity and generates better ideas and research outcomes. This collaborative ethos not only promotes individual growth but also drives the collective success of our research endeavours.

At Genomic Press, we prioritize fostering research endeavours 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 deeply stirs your passions?

What deeply stirs my passion is the drive to help patients and find ways to improve the lives of those who suffer. My primary motivation lies in alleviating the burden of mental illness and providing effective treatments for individuals battling severe conditions like treatment-resistant depression and alcohol use disorder. The goal of my research is to bring hope and tangible improvements to the quality of life for patients who struggle daily with debilitating mental health issues.

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

One aspect I most enjoy as an academic and researcher is the opportunity to work alongside brilliant individuals who constantly inspire and challenge me. Every day, I am intellectually stimulated by engaging in innovative projects. Having the unwavering support of mentors and colleagues has been invaluable. Their guidance and encouragement have helped me grow professionally and enhanced my creativity and scientific achievements. This dynamic and supportive atmosphere makes my work so fulfilling and exciting.



Figure 2. The Garel Kaminski family during Nicolas Garel's postdoctoral fellowship at Stanford University, California, USA.

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?

I am a man of family and friends and live my best moments surrounded by the people I love. Sharing time with them brings me immense joy and fulfilment. Additionally, I am passionate about traveling and backpacking. I have had the incredible opportunity to explore diverse regions, including Central and South America, Western and Eastern Europe, the Middle East, and Asia, often for extended periods. These adventures have broadened my horizons and enriched my life with unforgettable experiences and memories. Given the choice, I would always choose to spend my leisure time with loved ones or discover new places and cultures.

Part 2: Nicolas Garel – Selected questions from the Proust Questionnaire¹

What is your idea of perfect happiness?

Happiness is a transient state, flowing and ebbing through our lives. Perfect happiness, therefore, arises from the awareness of its presence in the first place. We often take for granted our blessings, forgetting the fragility of life and how everything can change instantly. Thus, perfect happiness is the mindful state of contentment, where one fully appreciates the present moment and the beauty of life. It is about recognizing and cherishing those fleeting moments of joy and peace and understanding their impermanence.

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 35question Proust Questionnaire became famous after Marcel Proust's answers to $these \ questions \ were \ found \ and \ published \ posthumously. \ Proust \ answered \ the \ questions$ tions 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.

What is your greatest fear?

My greatest fear is that we might reach a point of no return regarding climate change, ultimately losing the Earth as we have known it. The prospect of reaching a stage where there is no hope of reversing the damage we are causing is deeply unsettling.

Which living person do you most admire?

I admire my parents most. They immigrated to Canada and raised five children without the support of any extended family. They worked tirelessly throughout their lives to provide us with the most optimal environment possible. Balancing their professional and personal responsibilities, they never complained about anything. To this day, they remain a steadfast presence in my siblings' lives, supporting us through every challenge we face. Their resilience, dedication, and unwavering support are my constant source of inspiration.

What is your greatest extravagance?

A good bottle of Japanese whisky.

What are you most proud of?

I am most proud of balancing my personal and professional life. Achieving this equilibrium allows me to enjoy my career while nurturing meaningful relationships and personal fulfilment.

What is your greatest regret?

Not to have been 20 years old during the 1960s.

What is the quality you most admire in people?

The quality I most admire in people is their ability to think about others and show genuine care. This selflessness and empathy reflect a depth of character and compassion that I genuinely admire.

What is the trait you most dislike in people? Fanaticism.

What do you consider the most overrated virtue?

True virtue, by definition, is not overrated.

What is your favourite occupation (or activity)?

There are too many activities I enjoyed to list them all, with outdoor activities being at the top of the list.

Where would you most like to live?

In my city, Montreal, or in San Francisco.

What is your most treasured possession?

My most treasured possession is a painting by Parisian artist Micha Tauber, which I received during one of the most difficult periods of my life. This artwork holds significant sentimental value and serves as a reminder of resilience and hope.

When and where were you happiest? And why were you so happy then? I have learned to find joy in little things, but let us be honest: a week off without e-mails, deadlines, and duty does help!

What is your current state of mind?

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Multicentred, including my family, my profession, and the state of the world.

What is your most marked characteristic?

My most marked characteristic is probably my deep interest in others and the time I spend connecting with them.

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

One of my key talents that gives me a competitive edge is my ability to strategize effectively.

What do you consider your greatest achievement? My education.

If you could change one thing about yourself, what would it be? To be a better sleeper.

What do you most value in your friends?

Generosity and sense of humour.

Who are your favourite writers?

Boris Vian, Romain Gary, Naguib Mahfouz, and Stefan Zweig.

Who are your heroes of fiction?

I have many, but Hector from the Iliad² has always been a great hero to me since I was a child.

Who are your heroes in real life?

My heroes in real life are my grandparents. They fought against the Nazis during World War II and lost many family members and friends. They were members of the French resistance and created a network, "le reseau Garel," that saved thousands of children. Their courage and resilience in the face of immense danger and hardship have always been a profound source of inspiration for me.

What aphorism or motto best encapsulates your life philosophy?

"Logic will get you from A to B. Imagination will take you everywhere." Albert Einstein.

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²In Greek mythology, Hector was the firstborn child of King Priam and Queen Hecuba,