

Nathaniel G. Harnett: Identifying the neurobiological mechanisms of susceptibility to trauma and stress-related disorders

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Dr. Nathaniel Harnett is Director of the Neurobiology of Affective and Traumatic Experiences Laboratory at McLean Hospital and Assistant Professor of Psychiatry at Harvard Medical School. His research investigates the neural substrates that mediate individual variability in susceptibility to trauma and stress-related disorders using a multidimensional approach that incorporates human brain imaging, psychophysiology, psychometrics, and behavior. Further, his laboratory examines how pre-, peri-, and posttraumatic environmental factors may modulate the efficacy of neural signatures of posttraumatic stress disorder (PTSD). Ultimately, the goal of his research is to advance our understanding of how we identify useful, effective, and generalizable neural predictors of PTSD to facilitate precision medicine approaches that might mitigate the social and emotional burdens of trauma and stress-related disorders. We are delighted that Dr. Harnett engaged in the Genomic Press Interview, enriching our readership with perspectives on his life journey and professional trajectory.

Part 1: Nathaniel Harnett – Life and Career

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

I originally never wanted to be a scientist. I was convinced I would become, and originally applied to school to be, a classical musician. However, I was worried about marketability and thought a dual major in psychology would be a smart move for my career options. It turned out to be a great choice, though, as early on in "PSYC 101," we had our module on behavioral neuroscience, and I was hooked. The understanding that the entirety of our experiences – what we have been through and what we will go through – are all processed by a squishy organ in our skulls was fascinating. I fully committed to studying psychology and neuroscience, and did some undergraduate research at my alma mater (Ithaca College) and the University of Maryland. My undergraduate research was focused on emotional memory processing and behavior in humans. I think those early experiences helped introduce me to the joy of doing research – of knowing something for a brief period that no one else does and being able to share it with the world. I then applied to graduate programs and made it into the Behavioral Neuroscience program at the University of Alabama at Birmingham (UAB).

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

Most of the defining moments of my career were when my mentors took a chance on me. I applied to graduate school with some research experience. However, I needed training in magnetic resonance imaging, coding, or other technical skills that would have been helpful in the lab I joined. Still, my graduate mentor – David Knight at UAB – took a chance and accepted me into his laboratory. Dave and his lab were highly supportive of



Figure 1. Nathaniel Harnett, PhD, McLean Hospital and Harvard Medical School, USA.

me, and there were many opportunities to learn the fundamentals of MRI research, ranging from recruitment, collection, analysis, and interpretation. With the work we were doing and the skills I was learning, I was fortunate enough to get some independent funding and start a dissertation project that I was passionate about. I also managed to get an award that would cover my time as a postdoc. So, when it was time to complete post-doctoral training, I reached out to Kerry Ressler at McLean Hospital, and by coincidence, the project he was working on was tightly linked to my dissertation. Kerry is a phenomenal mentor and has also been great at helping me understand the "hidden curricula" in science, enabling me to navigate the field. From there, the vast network of collaborations and experiences helped accelerate and expand my work. I managed to move to assistant professor and establish my laboratory at McLean Hospital, where I get to ask the questions I am most passionate about: trauma, stress, and psychiatric disorder susceptibility.

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

For whatever reason, I was always profoundly fascinated with personal accounts of how people dealt with highly stressful experiences. In high school, I would sit in the library and read personal accounts from Vietnam War soldiers (e.g., "Nam: The Vietnam War in the Words of the Men and Women Who Fought There" by Mark Baker), trying to understand more about how their ideas of the world and themselves changed after traumatic experiences. I think that aspect – of the dramatic shift in people



after stress – stuck with me and pushed me to think more about how traumatic stress and the brain are interlinked.

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

There is a lot to learn about how we can use brain imaging to understand who is most in need of resources after a traumatic event to help mitigate potential long-term psychiatric effects. Ideally, I would like my lab to contribute to novel ways to incorporate brain imaging into precision medicine or provide insight into why some neural signatures might be more predictive for some people compared to others.

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

My laboratory tries to leverage multiple ways of looking at the brain to understand two questions. First, how do we combine different modalities of brain imaging to come up with predictive neural models of transition to PTSD after trauma? That part of the research often involves using MRI to look at the brains of recent trauma survivors and see if there are particular neural systems or multivariate patterns that are associated with future PTSD development. The second question is: How do inequities in pre-traumatic exposures impact the generalizability of neuroimaging findings? We know that there is a wide range of systemic or structural issues (e.g., racism, sexism) that impact how people respond to later events, and we think delving into how these may have a longitudinal impact on the brain and relevant biology can help understand disparities in psychiatric disease.

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

Curiosity and an openness to explore have always been the most significant thing. MRI research often generates a good amount of data, and we are constantly learning new ways to analyze and look at it. I think a willingness and interest to ask new and different questions and push yourself out of your comfort zone to analyze data in a new way – while also digging into the fundamentals about *why* we might look at the data a certain way – helps with growth as a scientist.

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 deeply stirs your passions?

It is a complex question, but I think it is worth making sure we define what we mean by "merit." Not to completely endorse standpoint epistemology, but considering *who* defines metrics and *why* we define them that way is important for advancing science forward in an unbiased way. Much of the issue (around bias) is structural or systemic, and I am interested in how we might change the structure of science to break down barriers that might dissuade particular people or important research approaches.

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

It is still the flexibility of how I get to weave through my career and the rest of my life. I only sometimes strike the right balance, but being able to have the option is nice.

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?

There is a good mix of things to keep my mind off science. I usually find something to do between gaming, music practice, aerials training, or nature walks.

Part 2: Nathaniel Harnett – Selected questions from the Proust Questionnaire¹

What is your idea of perfect happiness?

Retirement.

What is your greatest fear?

Failing to live up to my potential.

What is your greatest extravagance?

Entertainment tech. I own far too many screens.

What are you most proud of?

My trainees.

What is your greatest regret?

Not starting a hobby for fear of looking stupid.

What is the quality you most admire in people?

Understanding.

What is the trait you most dislike in people?

Arrogance.

What do you consider the most overrated virtue?

Faith.

What is your favorite occupation (or activity)?

My favorite activity is probably gaming.

Where would you most like to live?

Someplace with actual seasons.

What is your most treasured possession?

My data.

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

Wow, this is a tough one. My mom recently moved to a farm upstate (an actual farm), and I got to spend a few days on the property. It was one of the most peaceful and serene times I have had away from everyone with loved ones.

What is your current state of mind?

At the intersection of stressed, content, and focused.

What is your most marked characteristic?

My height.

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.



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

What do you consider your greatest achievement?
Managing to make it to assistant professor.

If you could change one thing about yourself, what would it be?
I would not change anything at this point.

What do you most value in your friends?
Their honesty.

Who is your favorite writer?
Brian Jacques.

Who is your hero of fiction?
Spiderman.

Who is your hero in real life?
My mother, hands down.

What aphorism or motto best encapsulates your life philosophy?
I think Calvin from Calvin and Hobbes (Bill Watterson) said it best in response to "Life could be worse:" "Life could be a lot *better*, too!"

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