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INNOVATORS & IDEAS: RESEARCH LEADER

Carrie Bearden: What causes the onset of psychosis in adolescence, and how can we predict (and ultimately prevent) it?

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Dr. Carrie E. Bearden is a Professor of Psychiatry and Biobehavioral Sciences and Psychology at the University of California, Los Angeles (UCLA). Dr. Bearden received her Ph.D. in Clinical Psychology from the University of Pennsylvania and completed her clinical training at UC San Diego. She joined the UCLA faculty in 2003. Her work aims to understand neurobiological risk factors for the development of severe mental illness in youth, both in clinically defined high-risk cohorts and in highly penetrant genetic conditions. She is particularly known for her research taking a 'genetics first' approach to studying brain mechanisms underlying the development of severe mental illness. Dr. Bearden is the Director of the UCLA Center for Assessment and Prevention of Prodromal States (CAPPS), a clinical research program for youth at high risk for psychosis and Co-director of UCLA's Neurogenetics Training Program. She has over 350 peer-reviewed publications and is among the world's most highly cited scientists, according to Clarivate, Web of Science. Currently, she serves as Deputy (Reviews) Editor for the journal *Biological Psychiatry*, as Chair of the DSM-V Serious Mental Disorders Committee and is President-Elect of the Society of Biological Psychiatry. She has received numerous awards and honors, both for her research achievements and for teaching and mentorship, including the Joel Elkes Research Award (ACNP), the A.E. Bennett Neuropsychiatric Research Award (Society of Biological Psychiatry), and an NIH Method to Extend Research in Time (MERIT) award. Professor Bearden is delighted to engage in the Genomic Press Interview, sharing insights about her personal and professional journey with our readers.

Figure 1. Carrie E. Bearden, PhD, University of California, Los Angeles, USA.

Part 1: Carrie E Bearden – 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 mostly grew up in Hawaii, on the island of O'ahu. It was a great place to grow up to truly appreciate nature, particularly the power of the ocean and the incredible range of marine life it supports. I also loved mysteries as a child- first the Nancy Drew series, then Agatha Christie. I loved solving puzzles and envisioned a career as either a marine biologist or a glamorous private detective. In high school, my love of literature took over, and I started college at the University of California (UC) Berkeley as an English and Theater major. However, the light bulb went on when I took a Biological Psychology course in my sophomore year. What could be a better mystery to focus on than the human brain?

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?

As a graduate student at the University of Pennsylvania in Ty Cannon's lab, I started working on very large epidemiological datasets, linking prenatal and early childhood history information to psychiatric hospital records to investigate the earliest precursors of schizophrenia. This led to some quite interesting discoveries. As early as you look, there are indicators of subtle developmental delay or differences. This was when we as a field began re-conceptualizing schizophrenia as a neurodevelopmental disorder, recognizing that the onset of full-blown psychotic symptoms represents a late stage of the illness. So this was incredibly interesting, but I also yearned to have more direct contact with patients and involvement in hands-on data collection rather than only working with large databases. Serendipitously, I began a neuropsychology placement at the Children's Hospital of Philadelphia, where through their multidisciplinary Center, I started seeing a large number of children with 22q11.2 deletions.

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I noticed that the vast majority had a characteristic cognitive and neurobehavioral phenotype. At CHOP, cutting-edge research was ongoing on the genetics and other medical aspects of the disorder, but there was no active research program at the time focused on the brain and behavioral phenotype. So I was given pretty free rein to start collecting data; retrospectively, it was an incredible opportunity for a graduate student. This was how my research interests were born and raised; with this background, when the opportunity arose to get involved in a new research program at UCLA focused on early intervention for psychosis risk, I jumped at the chance. Building this program from the ground up was quite challenging, but I am really proud of the program we have built, which is now well known for providing free access to high quality assessment and early intervention for severe mental illness.

However, regarding leadership, I did not seek it out. The process was more analogous to a twig getting caught up in a fast-flowing current. I took on leadership roles at UCLA when more senior people stepped down from those positions, and initially, it was incredibly stressful. Nevertheless, I have become much more comfortable in these roles over time. From a scientific perspective, I have enjoyed having leadership roles in major international multisite projects, where you can collaborate with people worldwide. I began to appreciate how important it is for more junior folks in an organization to see kind, compassionate leadership. And from that vantage point, I realized that if I really care about changing structures I need to forge the path. I cannot just keep my head down and focus on my own work, no matter how attractive that often seems.

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

Two courses at UC Berkeley – Biological Psychology and Developmental Psychopathology, taught by Steve Hinshaw- really brought things into focus for me. I wanted to understand the developing brain and what might cause that development to go awry; I was able to do a senior Honors project at UC Berkeley in the context of an advanced seminar focused on sleep. Therefore, I decided to focus my paper on nightmares and psychopathology. This got me diving into the stacks at the Biomedical Library, furiously digging up research articles and scribbling notes everywhere. Marrying my interests in detective work and science was a dream come true. And then, in graduate school, it was pure serendipity that I had the opportunity to combine my clinical and research interests, working with a youth population with a rare genetic disorder at high risk for psychosis.

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

I was very naïve when I started in this field, thinking that by focusing on a highly penetrant genetic variant with a well-understood genetic etiology, we would be able to 'solve' schizophrenia in short order. Of course, nothing is that simple, but it is astonishing when we look at how far we have come in psychiatric genetics in the past 20 years or so. That progress, combined with considerable advances in neuroimaging technology, stem cell biology, big data, and artificial intelligence (AI)– my work has become increasingly interdisciplinary. I enjoy a highly translational approach, working with big teams with diverse expertise. I firmly believe that the investigation of pre-onset or prodromal clinical risk syndromes to psychosis offers hope of overcoming reliance on a post-hoc perspective of disease causation. Further, our two-pronged strategy – that is, taking both a behaviorally defined and genetically defined approach to the problem – holds promise for understanding points of convergence along the risk pathway(s). For example, I am excited by the opportunity that we now have to connect cellular and molecular phenotypes in neurons derived from 22q11.2 deletion carriers to neurobehavioral phenotypes from the same individuals. My vision is to continue to expand this work into the development of specific molecular targets for novel preventive treatments.

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

I find the dynamic changes in the brain and accompanying behavioral shifts that occur in adolescence- and the corresponding risk for neuropsychiatric disorders – to present both an incredibly scientifically interesting and clinically important area. As a period of rapid development of social competence and increased plasticity in social-affective neural networks, adolescence provides a unique opportunity to understand how abnormalities arise in the structure and function of these brain networks, as well as an opportunity to define biomarkers for the development of treatments to improve outcomes. Interestingly, I have recently returned to my interest in sleep, sparked as an undergraduate. Sleep is still poorly understood, but it is essential for health and well-being, changing dramatically in adolescence. So, I think it holds much promise as a modifiable treatment target. A graduate student in the lab convinced me that we should venture into it in the next phase of our prospective longitudinal study; new wearable technology has made this feasible to do in kids with neurodevelopmental disorders, which was not possible before. I am now excited to see these results.

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

Stubborn determination has been valuable, as has learning how to work as part of a multidisciplinary team with people who may be very different from me. The importance of kindness, compassion, and empathy cannot be overstated. I am proud of the inclusive environment we have built in our lab, aimed at making people feel supported and welcome.

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?

I am really concerned about academic silos and 'ivory towers', and the lack of trust in science and medicine in many communities. It is critical that we are able to make science accessible to everyone.

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

I absolutely love mentoring trainees and seeing them get excited about a discovery, or something they are working on.

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?

On a steep rocky hiking trail with beautiful views. And after that, a delicious plant-based dinner.

Part 2: Carrie E Bearden – Selected questions from the Proust Questionnaire[1]

What is your idea of perfect happiness?

Sitting on a beach watching the sunset with my family. Including our dogs! And eating ice cream.

[1]In 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 2. Carrie Bearden hiking in the Santa Monica mountains (Westridge Trail) with her two rescue dogs Loona (female lab/bulldog mix, age 8) and Otis (male jindo mix, age 5) against the backdrop of the Los Angeles cityscape.

What is your greatest fear?
For me personally, cognitive decline. More broadly, an unlivable planet.

Which living person do you most admire?
Jane Goodall; also Greta Thunberg. They are just incredibly brave, fearless women.

What is your greatest extravagance?
Korean spa days.

What are you most proud of?
My two kids. They are both incredible human beings.

What is your greatest regret?
Not wearing sunscreen as a kid.

What is the quality you most admire in people?
Standing up for what you believe in and not giving up.

What is the trait you most dislike in people?
Hypocrisy and being a bully.

What do you consider the most overrated virtue?
Patience.

What is your favorite occupation (or activity)?
The one that I've got!

Where would you most like to live?
Right here in Los Angeles. I do occasionally fantasize about moving to the mountains, though.

What is your most treasured possession?
Photo albums of my family

When and where were you happiest? And why were so happy then?
I am pretty happy right now. But I am happiest when my whole family is together.

What is your current state of mind?
Unsettled. There is a lot to do.

What is your most marked characteristic?
My family would say that I do not compromise. I don't know if that's good or bad from their perspective!

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

What do you consider your greatest achievement?
In addition to my children, all of the trainees who have gone on to flourish in their own careers. It brings me joy to see that.

If you could change one thing about yourself, what would it be?
I am an absolutely awful singer. It would be really cool to have a beautiful singing voice.

What do you most value in your friends?
Love and support. They are there for me for the good, the bad, and the ugly!

Who are your favorite writers?
Haruki Murakami, Elena Ferrante, and Annie Proulx. I am drawn to Murakami's blend of the everyday with the surreal, particularly in novels

like *The Wind-Up Bird Chronicle*. Ferrante's Neapolitan novels captivated me with their raw honesty about female friendship, and Proulx's ability to create such vivid characters and landscapes, especially in works like *Brokeback Mountain*, is remarkable.

Who are your heroes of fiction?
When I was a kid, probably Jane Marple (Agatha Christie). Also, Uncle Iroh from Avatar: The Last Airbender.

Who are your heroes in real life?
Jane Goodall, Michelle Obama.

What aphorism or motto best encapsulates your life philosophy?
Keep calm and carry on (at least I try).

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