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Randy J. Nelson: Disruption of circadian rhythms on brain function and health

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Randy Nelson studies sleep and circadian rhythms in health and illness. For the past 15 years, his lab has focused on the role of disrupted circadian rhythms on physiology and behavior. He studies the effects of these disrupted circadian rhythms on several parameters including immune function, neuroinflammation, metabolism, sleep, and mood. He has published nearly 500 papers and more than 12 books during his career describing studies in biological rhythms, behavioral neuroendocrinology, stress, immune function, and aggressive behavior. He has been elected to Fellow status in several scientific societies. Nelson earned his AB and MA degrees in Psychology at the University of California, Berkeley. He earned a PhD in Psychology, as well as a second PhD in Endocrinology, both from UC Berkeley; he was the first in the US to simultaneously earn two PhDs. Dr. Nelson then completed a postdoctoral fellowship at the University of Texas, Austin, after which he joined the faculty at The Johns Hopkins University, where he became professor of Psychology, Neuroscience, Biochemistry, and Molecular Biology. He then served on the faculty at The Ohio State University from 2000–2018, during which time he served as Distinguished University Professor and Chair of Neuroscience, as well as the co-director of the Neurological Institute. Dr. Nelson was recruited to WVU in 2018 to serve as professor and inaugural chair for the new Department of Neuroscience. In addition to his NIH funding, he is Co-I of the NSF Track 1 award, 'West Virginia Network for Functional Neuroscience and Transcriptomics'. He has directly mentored 25 PhD and 16 postdoctoral colleagues. In this Genomic Press Interview Dr. Nelson shares insights into his personal and professional trajectories.

Figure 1. Randy J. Nelson, PhD, West Virginia University, USA.

Part 1: Randy J. Nelson – Life and Career

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

I was born in Detroit, Michigan USA, and I currently live in Morgantown, West Virginia.

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

My path to academia is typical in the sense that it is not 'typical'. I grew up working on a farm in Northeast Ohio. During my last two years of high school, I worked in a turkey processing plant every night. I first attended a small college, Hiram College, that was 3 miles from my house, but I quit after a year. During college, I continued to work nights, typically a 3:00 pm to 3:00 am shift at the abattoir, a schedule that turned out to be incompatible with success in college. Instead of college, I took a job as an autopsy diener at the St. Lukes/Cleveland Clinic, where I learned a lot about anatomy. I worked there for about 18 months and conducted about 100 postmortem exams. After a particularly disturbing case, I took a vacation to San Diego. Like everyone else, I was enchanted with the place. I did all the touristy things, including going to the zoo on my last day. I decided that I should be living in San Diego and went to their HR to inquire about jobs. I was told there were no entry-level jobs available and indeed the only job posting they had was for someone to help conduct autopsies on the animals that died in the zoo. After giving my notice, I showed up 3 weeks later and the curious HR person asked me whether I had received their letter—I said no. She told me that they had re-organized the position and now it was a work-study position for a student at UCSD. Being the naïve 20-year-old that I was, I asked, "what is a UCSD". They explained it was the newish shining academic light on the La Jolla mesa, so I applied to attend UCSD. Unfortunately, my income over the previous 2 years put me out of the running to receive work-study financial aid, so I never got the San Diego Zoo gig, but found myself enrolled at UCSD.

While working as a rat runner/lab assistant with Professor Tony Deutsch in studies of cholinergic mechanisms in learning and memory, I read an article assigned in my comparative psychology course written by Frank Beach at Yale entitled, "The Snark was a Boojum." This 1950 article bemoaned the fact that American comparative psychology was not particularly comparative in terms of species (70% of published studies were on rats) or approach (the vast majority of studies were on conditioning/learning paradigms). I discussed with Dr. Deutsch this paper, given his research animals were rats and his approach was definitely learning and memory. He knew Beach and said he could arrange for me to transfer to Berkeley to work with him. I did not know that Beach had moved to UC Berkeley from Yale several years previously, and in those days it was relatively easy to transfer among the UC schools, so I did. I transferred and ultimately worked in Beach's beagle lab doing work with a postdoc on maternal hormonal effects on social behavior during my last two years as an undergrad. I also worked for a grad student in Irv Zucker's lab where I did

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my senior honors project (Zucker's group discovered the primary role of the suprachiasmatic nuclei in circadian rhythms). During my last term as an undergrad, I took a graduate seminar that Beach and Zucker led on hormones and behavior. Beach offered me a graduate fellowship to work in his lab and I did so for about a year, but eventually I transferred to the Zucker lab where I finished my dissertation work. I currently work on how light at night disrupts circadian rhythms and how that affects physiology and function, as well as how brain, behavior, and other processes vary across the day.

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

It was initially an *approach* to research, rather than a research focus, per se. Zucker's lab was laser focused on using strong inference a la John Platt in scientific endeavors, whereas Beach was a "I wonder what would happen if…" guy. I was strongly attracted to the strong inference approach and my focus became blended between circadian rhythms and behavioral endocrinology. I was interested in motivation—why individuals do what they do—with a temporal component—why do individuals do what they do when they do.

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?

I have now been a faculty member at three different universities, and counting joint appointments, six different departments. I started my academic career at Johns Hopkins in the Psychology Department with a joint appointment in Neuroscience (Medicine) and Reproductive Biology (Public Health). At the time Hopkins only gave tenure as a full professor, so I was fortunate to attain tenure. I had great colleagues and wonderful collaborations with Sol Snyder (Chair, Neuroscience), Pat Walsh (Chair, Urology), and Ed Wallach (Chair, OBGYN) among many others. While at Hopkins I also spent 2 years as a rotator program officer at the US National Science Foundation, which honed my scientific breadth and critical thinking. It also gave me a deep appreciation for the hard work these federal government workers expend—they find money savings wherever they can—I recall after a study section, my team leader going around the room collecting paper clips saying, 'more money for research.'

My leadership roles, like my educational choices, are mostly the result of serendipity, and not planned or plotted. My wife and I were recruited to Ohio State (OSU) and we spent 18 years there, first in psychology, then we moved to neuroscience where I was appointed as chair. Prior to taking on the chair position, I was co-director of the neuroscience graduate program for several years. I did not really want to be chair or be in a medical school, frankly, but they had a new dean from Hopkins who knew me. He said he was unhappy with the program and was going to shut it down unless I became chair. Many of my grad students and collaborators were in the neuroscience program, and during a time when neuroscience was expanding nationwide, it did not seem prudent to shut this program down. I therefore agreed to become the chair (of course, it turned out that he was bluffing). We added several outstanding faculty and trainees and worked with psychology to launch a new undergraduate neuroscience major which reached 1000 majors after just 3 years. The president of OSU moved to West Virginia University (WVU), and he recruited me to start a new neuroscience program, which I have done with several recruits of amazing young talented neuroscientists. In addition to my chair job, I also served as Director of the West Virginia Center for Foundational Neuroscience Research and Education. I have never actually wanted to be a chair and I have declined many dean level jobs; It takes a lot of convincing arguments for me to agree to become a chair. Currently, I am serving as the president of the Association of Medical School Neuroscience Department Chairs, and I am truly inspired by these chairs who try to move Heaven and Earth to support the faculty, trainees, and staff in their departments.

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?

I trained in Colleges of Arts and Science and felt most comfortable having colleagues who comprise behavioral scientists, zoologists, ecologists, and evolutionary biologists; I incorporate adaptive functional perspectives into our work. From this perspective, my trainee colleages and I wrote syntheses of Behavioral Endocrinology, Ecoimmunology, and Seasonality. I was concerned that moving to a College of Medicine would limit my ability to do integrative work. However, since moving to Neuroscience Departments in two Colleges of Medicine I have been able to translate some of our foundational science work on circadian rhythms to clinical medicine. I ve also been able to collaborate with many amazing scientists in the biomedical field.

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

I learned, almost as a reaction to some of my colleagues in grad school, that one does not sit on data. As I was lectured by a postdoc in the Zucker lab, taxpayers fund much of our work so I am keen to communicate the data that we obtain. My grad students are very productive. Not surprisingly, they are all very successful. The second experience that I 'absorbed' is that science is fun! We have tried to have a fun lab—bowling teams, happy hours, softball teams and so on. I am saddened that grad students and postdocs do not seem to have as much fun any more. I suppose it is all the pressure that they feel since COVID, but the signs of mental health pressures were starting to show prior to COVID. For the past 10 years or so, we have heard a lot about work-life balance. I do not think one must be at the expense of the other. I prefer to consider it work-life integration. We have always integrated our work into our lives. When we attended conferences, we always took our kids, especially to international conferences, and extended our visit so they could see new places and meet new people.

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

Our current research projects focus on three aspects of biological timing. Most of our foundational research examines the role of disrupted circadian rhythms using light at night on physiology and behavior. We have two clinical trials in which we are examining the role of blocking the disruptive effects of light at night on clinical outcomes after stroke and cardiac surgery in the intensive care units, as well as a clinical trial examining the use of bright blue light visors on resetting the circadian rhythms of night shift nurses to improve their sleep, cognitive performance, and mood. Finally, we are advocating the importance of time-of-day as a key biological variable that should be reported in all studies of brain and behavior.

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

Circadian rhythms are a fundamental aspect of biology, and much is known from foundational science about them ranging from the genetic and molecular mechanisms to the functional regulatory mechanisms to the output effects of circadian rhythms on physiology and behavior. However, little of this foundational science has been translated to clinical medicine.

Similarly, circadian rhythms influence the outcome of experiments—that is, the answer to an experimental question may depend in part on the time-of-day when the question is asked. Yet, the time-of-day is rarely reported in scientific correspondence. It is a neglected, yet crucial, methodological variable in research on living systems. We have proposed that more explicit consideration of time-of-day information in experimental designs, analyses, and reporting will improve the rigor and reproducibility of scientific research.

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

The best part of my chair position is observing and enjoying my colleagues' successes. Also, the opportunity to help colleagues, especially early-stage colleagues, achieve their research and career goals is a great part of my job. Providing resources, advice, support, and sometimes a sympathetic ear seems helpful to others. Often relatively small time and resource investments can help early-stage faculty keep moving towards their goals. Without question, the most rewarding experience for me has

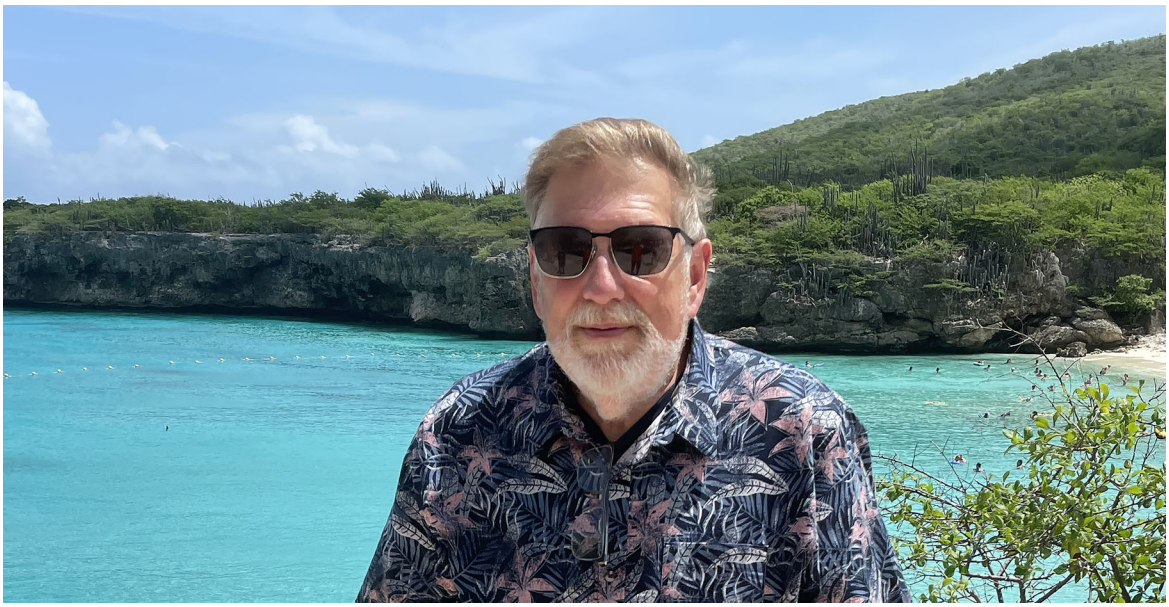

Figure 2. Randy Nelson, at the Playa Kenepa overlook in Curaçao in 2024.

been playing a small part in helping students and trainees achieve their goals and channeling my own love and excitement for the field. That seems to stoke excitement in our students. We attend the State Fair and provide demos about brain and nervous system functioning for small children and it is very rewarding to see the excitement spread from our grad students to elementary school students.

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?
One of the important reasons we moved to West Virginia was to help with recruitment of rural and first-generation college and graduate school students. As a first gen student myself, I experienced the transformative power of higher education. I appreciate that this deeply red state is highly suspicious of higher ed. We have started several outreach programs out of neuroscience to help bridge the gap between misconceptions and the reality of higher education. First, we sponsor a summer Brain Camp, a week-long experience for high school students to live on campus and to learn about the brain. They even watch a brain surgery via CCTV. We regularly get 12 or more students deciding to attend WVU and major in neuroscience or psychology after attending Brain Camp. Our Feed Our Brains program raises money by selling tee shirts and community contributions (restaurant donations of their proceeds every 3 months) to pay off overdue student lunch balances at elementary and middle schools in the surround counties. These schools are visited by a team of grad students and faculty who explain the importance of good nutrition for typical brain development and function. Then, they anonymously pay off lunch bills. By helping the underserved in a positive way, we hope to continue to build trust in higher ed and add additional first gen students at all levels of academia.

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 love to travel when I have large blocks of time: we are heading to Eastern Europe during summer 2025. More commonly, I enjoy biking and walking the trails in the surrounding areas of my house. I also like to garden during the warmer months.

Part 2: Randy J. Nelson – Selected questions from the Proust Questionnaire[1]

What is your most marked characteristic?
I am [brutally] honest.

Among your talents, which one(s) give(s) you a competitive edge?
Two talents: (1) I am a very hard worker and (2) I enjoy writing.

If you could change one thing about yourself, what would it be?
Aging has already changed this thing about me a lot; i.e., being quick to respond. My former students often remark how 'easy-going' I am now, in contrast to what they refer as "Johns Hopkins Randy," reflecting to a time when everything for me was about the moment.

What is your current state of mind?
At peace, which is remarkable to me given the current events.

What is your idea of perfect happiness?
Being at the beach with my adult sons and wife.

When and where were you happiest? And why were so happy then?
I can think of several answers to this question. Considered together, I think I was happiest during my sabbatical leave in the South of France. I was

[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.

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writing the first edition of a textbook, *An Introduction to Behavioral Endocrinology*. We had just been married before setting off to France and a year focused on each other was an ideal way to start out our lives together. We rented a small house in a hillside village (Cabris) and every morning I would write while overlooking Cannes with Nice to the left and St. Tropez to the right and the Mediterranean in front of me. Inspiring.

What is your greatest fear?
I worry that my biological kids and recent trainees will not have the opportunities that I had in academia, or biomedical research generally.

What is your greatest regret?
I feel like Scottie P in the comedy "We're the Millers" who insisted that he had no regrets, even when questioned about a large tattoo across his chest that said "NO RAGRETS," which was his credo. I really don't have any regrets that I can recall (or tattoos).

What are you most proud of?
Easy—my sons. Without any input from me, our oldest son attended UCSD and majored in neuroscience and our youngest son attended Berkeley and majored in Biochemistry. Both attended grad school on the East Coast.

What do you consider your greatest achievement?
This was the toughest question to answer. I usually think that my sons are my greatest achievement, but I do not think that is the kind of answer that is being sought. Academically, I think my record of training graduate students and postdoctoral fellows stands out. I have been remarkably fortunate to have had such talented and motivated individuals in our lab. Folks who populate the faculty at places like Duke, Johns Hopkins, Chicago, Berkeley, UC Davis, Indiana, Wisconsin, Ohio State, and West Virginia University.

What or who is your greatest passion?
Family.

What is your favorite occupation (or activity)?
I love to **t**ravel. I like gardening and writing. I also like to eat out in restaurants. Indeed, during my postdoc in Texas, I wrote and published a restaurant guide, *101 Great Places to Eat in Austin*.

What is your greatest extravagance?
A water view from my home.

What is your most treasured possession?
Our ski boat. Great memories of dragging along our kids, their friends, and cousins on rafts and skis, or sometimes just cruising the lake, or anchored and fishing.

Where would you most like to live?
Southern California or Guanacaste Province, Costa Rica.

What is the quality you most admire in people?
Kindness.

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

What do you consider the most overrated virtue?
Being busy (but not productive).

What do you most value in your friends?
Reliability.

Which living person do you most admire?
Until recently, Jimmy Carter. Now it is Barack Obama.

Who are your heroes in real life?
My wife, Courtney DeVries, a remarkable human being.

If you could have dinner with any historical figure, who would it be and why?
Charles Darwin—I visited his Down House in Kent where he conceived his theory of natural selection through evolution and could really feel his presence there. I also followed the route of the HMMS Beagle throughout the Galapagos Islands. I have come to really admire him for seeking of the truth despite the remarkable resistance at the time and even today.

Who are your favorite writers?
Richard Dawkins, Robert Sapolski, Joan Didion, Jonathan Franzen, Kurt Vonnegut, Jared Diamond, and Ernest Hemingway.

Who are your heroes of fiction?
Ignatius J Reilly, Kilgore Trout, Atticus Finch, and Sherlock Holmes.

What aphorism or motto best encapsulates your life philosophy?
Be present and be grateful.

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