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INNOVATORS & IDEAS: RESEARCH LEADER

Harriet de Wit: What can we learn about behavior and brain processes by studying psychoactive drugs in humans? How can we harmonize behavioral research in humans and nonhuman species?

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Professor Harriet de Wit, a pioneering researcher in psychoactive drugs at the University of Chicago, shares her remarkable 45-year scientific journey in this illuminating Genomic Press Interview. As Director of the Human Behavioral Pharmacology Laboratory and recipient of prestigious honors including the 2019 European Behavioral Pharmacology Society Distinguished Investigator Award, Dr. de Wit has revolutionized our understanding of how drugs like MDMA and LSD affect human behavior and consciousness. Her groundbreaking research, continuously funded by the National Institutes of Health for over 42 years—an extraordinary achievement in scientific excellence—has revealed crucial insights into the therapeutic potential of psychedelics and their effects on social connection, empathy, and neural function. Most recently, her laboratory demonstrated that MDMA enhances feelings of social connectedness during interpersonal interactions, findings that have profound implications for PTSD treatment and psychotherapy. As the expert consulted by renowned authors like Michael Pollan to understand psychedelic neuroscience, Dr. de Wit bridges the critical gap between animal research and human studies, using pioneering methodologies to translate behavioral observations across species. Her innovative work on microdosing, place preference procedures, and drug-induced neural actions has established new paradigms in addiction science and psychiatric treatment. She served as Field Editor for *Psychopharmacology* and Deputy Editor for *Alcoholism: Clinical and Experimental Research* for many years. Throughout her career, Dr. de Wit mentored numerous post-doctoral fellows and graduate students. Her life's work has been defined by curiosity, patience, and scientific rigor, first acquired as a graduate student from her advisor, Jane Stewart, at Concordia University. From her roots in Canada, Dr. de Wit went on to become one of the world's foremost authorities on psychopharmacology.

Figure 1. Harriet de Wit, PhD, University of Chicago, USA.

Part 1: Harriet de Wit – Life and Career

Where were you born, and where do you live now?
I was born in Ottawa, Ontario, Canada, and I now live in Chicago, Illinois, USA.

Could you give us a glimpse into your personal history, emphasizing the pivotal moments that first kindled your passion for science?
After completing my BA at the University of Calgary, my hometown, I was not drawn to an academic career, and did not plan to attend graduate school. I did like traveling, however, and I found myself living in Oxford, England, working as a research assistant in the laboratory of Jeffrey Gray, a renowned British psychologist. My position in his dynamic and exciting group, among imaginative and creative behavioral scientists, sparked my interest in pursuing my career in experimental psychology. In Oxford, I met my future graduate advisor, Jane Stewart, who was on sabbatical with her husband, Dalbir Bindra. When she heard that I was considering graduate school, she directed me to Concordia University, where she was Chair of the Psychology Department. I followed her advice, and first completed my MA with Roy Wise, and then my PhD with Dr Stewart. The faculty in the Psychology Department created an exceptional training environment for graduate students: We had intense scholarly seminars, rigorous training in laboratory methods, and a lively atmosphere of curiosity and directed inquiry. In my graduate research there, studying

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cocaine self-administration in rats, I was fascinated by the commonalities (and differences) between drug-taking behaviors in humans and laboratory animals. After completing my PhD, I transitioned from animal research to research with humans, which opened the door to investigating self-reported states induced by drugs, as well as objective behavioral measures. The challenge of translating behavioral observations across species has continued to be a central theme in my research for the past 45 years.

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

From early on in my research career, I have been drawn to the challenge of bridging knowledge obtained across species and different levels of analysis. I love to think about the similarities and the differences in the factors that control human behavior, compared to the behavior of other mammals. Do the same variables lead to drug-taking, or to the resumption of drug-taking after abstinence, in humans and rodents? How does the capacity for language influence behavior in humans, relative to non-speaking animals? As a new graduate student, I was impressed by the fact that laboratory animals readily self-administer many of the same drugs that are used and abused by humans, including stimulants and opioid drugs. However, I was also curious about the drugs that humans take that animals do not, such as cannabis and psychedelic drugs. What are the fundamental commonalities and differences in the determinants of drug-seeking behavior across drugs and species, and can we determine their biological basis? Although my focus after graduate school has been on studying drug-related behaviors in humans, I have always kept in mind the possible counterparts of these behaviors in nonverbal animals.

I can give two examples of this translational theme in my research with humans. About 20 years ago, we came across a report of an intriguing finding in laboratory animals, known as 'incubation'. Yavin Shaham at NIDA reported that rats that had been trained to self-administer a drug and then removed from the context showed a *stronger* motivation to resume taking the drug after more extended periods of abstinence. This was interesting because it seemed counterintuitive and did not fit with the apparent experience of decreased craving in drug users. We decided to test this idea in human cigarette smokers. We found that, as in the animals, craving for cigarettes increased, rather than decreasing, after longer periods of smoking abstinence over about a month. This result was important because of its parallel to rodent behavior, and because of its clinical relevance to drug users who are attempting to abstain. In another example, we showed that humans develop a preference for a place where they had received a rewarding drug, just like laboratory animals. Place preference procedures have been used in laboratory animals for nearly 50 years to assess the rewarding effects of drugs, but they have never been used with humans. In the animal studies, researchers often infer from the behavior that the animals 'like' a drug that induces the place preference, but this cannot be measured without self-report measures of internal states. In humans, we can measure both the behavioral preference and the participants' ratings of how much they like the drug. We showed that humans, like rats, prefer the place where they experienced a rewarding drug, and importantly, their preference was related to how much they liked the drug. Thus, we demonstrated generalizability across species and also supported an important inference in the procedure. So, an ongoing theme in my research has been the presence and limitations of cross-species comparisons.

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?

My progression through the academic ranks at the University of Chicago was slow, due in part to the constraints of being a PhD researcher in a clinical department. However, I am patient, and despite the job insecurity, I was fully engaged in conducting my research as long as it was funded. My current 'leadership' role is mainly due to my longevity as a scientist; over time and in a range of professional roles, I have acquired expertise and perspective in the field. I have not pursued leadership roles with administrative responsibilities or major leadership responsibilities. However, instead, I have been fully occupied and satisfied as a scientist in the fascinating field of drugs and behavior.

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 have not made significant mistakes in my career choices. I made the best choices I could at each crossroad, and then moved on to follow that path. Someone else, with a different vision or disposition, would have made other choices, but I never regretted mine.

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

I had to learn to be patient and to pay meticulous attention to detail.

I needed patience because the studies, especially with human participants, often take months or years, and involve numerous unforeseen (and uninteresting) setbacks. I also needed patience in obtaining funding, suffering many disappointments along the way. I needed attention to detail to ensure that the studies were correctly designed, executed, and analyzed. Without precision, the data are useless. Other values that are essential in the work are curiosity, honesty, flexibility, and creativity.

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

In the last 15 years, I have begun to study so-called 'mind-altering' drugs, or drugs that produce novel psychological states. Drugs such as MDMA (ecstasy) and low doses of LSD produce unusual alterations in self-reported internal states, such as feelings of empathy, awe, and oneness with the environment, states that cannot readily be assessed in nonverbal animals. Do these altered states change overt behavior? Do they make people more generous, insightful, or egalitarian? Do the feelings of empathy and connectedness, or meaningfulness and loss of boundaries, change subsequent behavior, or change users' perspectives on their lives? If so, how does this happen? This exciting new avenue of research has the potential to offer new insights for understanding the brain and human behavior. At the same time, it may also be an insoluble challenge to my interest in cross-species comparisons: The attractiveness of psychedelic drugs to some people is likely a uniquely human phenomenon, with no transparent counterpart in non-speaking animals.

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

I aim to demonstrate the importance of basic human experimental research with drugs, particularly studies that bridge the gap between preclinical research and clinical applications of psychopharmacology outside the laboratory, encompassing both recreational and therapeutic uses.

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

My greatest pleasure is talking about science and ideas with friends, colleagues, and trainees. Whether it is planning the next study, puzzling over unexpected results, or tossing around ideas and speculations over a glass of wine at a meeting, these conversations are among the most satisfying aspects of my academic career (see Figure 2). A close second is the pleasure of introducing my world of science to bright and enthusiastic students, and seeing the creative work they can do with the handful of tools we provide them with. It is a great pleasure to see them develop their own ideas and then their own careers. I love to see them succeed.

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?

I am concerned about the decline in respect for science, scholarship, and education. I want our society to invest in public education for everyone and at every level.

Figure 2. Attendees of the Harriet de Wit Festschrift, June 27, 2025. De Wit (center, back row) pictured with collaborators and former trainees who gathered for a day-long symposium celebrating her scientific contributions and mentorship. The program featured talks blending personal reflections on Chicago lab experiences with presentations of subsequent scientific accomplishments, embodying the intersection of social connection and scientific achievement that characterized de Wit's laboratory. The formal symposium was followed by an evening reception in the garden of an Italian restaurant.

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?
My non-work-related pleasures include spending time with good friends and family, including time spent in nature (hiking, biking) and at cultural events (theatre, symphony). I love to travel to remote corners of the globe to experience landscapes, cultures, and ways of being that are entirely new to me. Some highlights of my travels include Svalbard, Patagonia, Madagascar, Myanmar, Namibia, Shetland, and Galapagos. I also persist in taking drawing and watercolor classes, despite little visible progress.

Part 2: Harriet de Wit – Selected questions from the Proust Questionnaire[1]

What is your most marked characteristic?
I am low-key, agreeable, positive, and patient.

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

If you could change one thing about yourself, what would it be?
To be more dynamic as a public speaker.

What is your current state of mind?
Calm, peaceful, and grateful.

What is your idea of perfect happiness?
Good health, good friends, peace of mind, and being occupied with activities.

When and where were you happiest?
No single phase or event in my life stands out above the rest. However, there have been many happy occasions: hiking to a temple in Bhutan, snorkeling in Raja Ampat, celebrating a holiday with family and friends, receiving good news on a grant review, gardening, biking along the lakefront, playing with my dog; just too many to list.

What is your greatest fear?
Illness, infirmity, and loss of autonomy.

What is your greatest regret?
That I lacked confidence earlier in my life.

What are you most proud of?
My research accomplishments.

What do you consider your greatest achievement?
Keeping my primary NIH grant for 42 years.

What is your greatest passion?
To live life fully.

What is your favorite occupation (or activity)?
No single favorite. I like a mix of active (e.g., biking) and passive (eg, Netflix), art and science, social and solitary, being at home and being away.

What is your greatest extravagance?
Traveling to remote places in the world.

What is your most treasured possession?
I have a life-size, bronze sculpture of a cat cleaning itself. My artist aunt made it during the WWII occupation in Amsterdam. The Germans

[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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required Dutch citizens to give up their cash, but rather than hand over her penny collection, she melted down the coins to make this beautiful sculpture.

Where would you most like to live?
I am deeply divided between wanting to stay in my comfortable, long-time neighborhood in Hyde Park, Chicago, and wanting to be back in Canada, my country of origin.

What is the quality you most admire in people?
Warmth, generosity, humor

What is the trait you most dislike in people?
Right-wing beliefs. Greed, intolerance, and arrogance.

What do you consider the most overrated virtue?
Religiosity.

What do you most value in your friends?
Warmth, intelligence, reliability, and a sense of humor.

Which living person do you most admire?
I admire Jane Stewart, my one-time graduate advisor and now my friend. Jane had a highly successful career as a professor and research scientist in biological psychology. She was an exceptional mentor and a wonderful role model as a creative and well-informed scientist. Then, upon retiring from her job as a professor, Jane fearlessly embarked on a new career as a painter. She applied the same enthusiasm, creativity, and hard work to this new occupation as she did to the previous one, and she has become as successful in her art as she was in science. Jane still lives her life fully, at 91, entertaining her many friends, reading voraciously, cooking, painting, swimming, and staying attuned to news and events. She is my model for living a full and rich life.

Who are your heroes in real life?
Barack Obama, Bernie Sanders, and Leonard Cohen.

If you could have dinner with any historical figure, who would it be and why?
I would decline this dinner invitation because I would be frozen with fear.

Who are your favorite writers?
John Banville, Colm Tóibín, Graham Greene, William Boyd, Mary Oliver, E. M. Forster, and William Trevor.

Who are your heroes of fiction?
No fictional heroes stand out for me.

What aphorism or motto best encapsulates your life philosophy?
The phrase my trainees hear from me most often is “keep it simple!”.

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Harriet de Wit[1]
[1] *Department of Psychiatry and Behavioral Neuroscience, University of Chicago, 5841 S Maryland Ave, Chicago, IL 60637, USA*
✉ *e-mail: hdew@uchicago.edu*