Student Driven Publication 2016

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Diego A. Pizzagalli, Ph.D.

McLean Hospital, Harvard Medical School

Nancy Lundin, Indiana University Bloomington
Tanya Tran, Queen's University
Shereen Khoo, University of Notre Dame
Joshua Mervis, University of Minnesota Twin Cities

It was a pleasure to speak with Dr. Diego A. Pizzagalli about his research trajectory and insights at the 2016 SRP meeting. He received his master's and doctoral degrees from the University of Zurich, Switzerland, where he began his research in ethology and then transitioned to neurophysiology. Dr. Pizzagalli's research is currently focused on the mechanisms of anhedonia, a treatment-resistant symptom that is linked to impaired functioning in mood and anxiety disorders. Specifically, his lab employs rigorous translational work to understand how environmental factors, such as early childhood sexual abuse and other forms of early adversity, can affect hedonic processing in reward learning systems of the brain such as the mesolimbic system. Aspects of Dr. Pizzagalli's research have been recently guided by principles of the National Institute of Mental Health (NIMH) Research Domain Criteria (RDoC) initiative. He views studying fundamental dimensions of behavior as clinically meaningful, and as an important complement to categorical classifications of mental illness. By branching out from a sole focus on the psychopathology of individual diagnoses, his work has delved into the transdiagnostic construct of reward sensitivity as a continuum.

Recent research in Dr. Pizzagalli's lab focuses on neurobiological and cognitive predictors of psychopathology in treatment-seeking patients at mood disorders clinics. These patients perform a probabilistic reward learning task (developed by Dr. Pizzagalli's research team) and undergo a battery of neuroimaging assessments at baseline and one-year follow-up.

"He is finding that regardless of diagnosis, these patients fall on a continuum of reward sensitivity, a measure that might help untangle their diathesis better than clinical presentation."

To illustrate this concept, he gave the example of two patients

receiving the diagnosis of depression from a clinic. On behavioral and neuroimaging assessments of reward learning, one patient may demonstrate a hyperactive reward system while the other demonstrates blunted reward learning. He adds that these dimensional measures across units of analysis can aid us in predicting whether these patients will develop hypomanic, impulsive, anhedonic, or unipolar depressive tendencies over the next year. Such predictions could provide critical clinical foresight and opportunities for novel interventions.

When asked about the clinical implications of his research, Dr. Pizzagalli explained that he sees his research applying to a patient's day-to-day experience of depression, in line with today's emphasis on personalized healthcare. While his research is what many might classify as basic human neuroscience, the drive to improve people's lives motivates this work, as through his lab's efforts to find biomarkers of treatment response. For example, basic neuroscientific findings might inform a clinician as to whether an individual client would respond best to a particular psychotherapeutic intervention, a certain medication regimen, or both.

Dr. Pizzagalli is optimistic about the future of translational neuroscience, noting that it is challenging work, but has potential for important findings. For example, "personalized treatments that really push the envelope" are critical targets of downstream translational work. He noted at his talk during this year's SRP meeting that it often seems that regardless of the particular intervention to treat depression, the response rate is about 50-55%. Dr. Pizzagalli laments that we as a field are still using the same type of antidepressants we used 40 years ago. He therefore called for greater progress in pharmacological mechanisms, seeking to use smarter ways to guide patient-specific treatment, noting that this problem is not unique to depression research. He hopes for new progress via genetic work or development of new compounds, especially fast-acting compounds, such as ketamine, or an agent with similar properties.

Dr. Pizzagalli expressed motivation to collaborate with preclinical researchers to accelerate the process of finding new treatment mechanisms. He reflected on the academic temptation to spend a career focused within one's own lab on just one construct, but notes that progress is best achieved through collaboration with scientists of many kinds who offer unique perspectives. Beyond collaboration with preclinical teams, Dr. Pizzagalli sees an important opportunity for experimental psychopathologists to join forces in tackling difficult clinical research questions. He explains, "The field of neuroimaging has great potential to benefit from those in engineering who use machine learning

and other sophisticated algorithms that

could assist in subtyping patients". In conjunction with the large genome-wide association studies using brute force with large sample sizes, Dr. Pizzagalli explains that experimental psychopathologists could play a unique, synergistic role by incorporating multi-faceted consideration of the phenotype in a coordinated parallel to the genotype.

Dr. Pizzagalli has led an ambitious research career and attributes his successful line of work to the early days of following small ideas. Reflecting on a favorite moment of discovery, Dr. Pizzagalli noted an early prospective study looking at the effect of childhood maltreatment in females twenty years later. He found that even those who were not symptomatic had very blunted reward system activation, specifically in the striatum. This finding was one of the first to show that childhood maltreatment can influence longstanding neurobiological changes to brain reward pathways and increase the risk of these individuals developing psychopathology, higher rates of smoking and stimulant use, and maladaptive coping behaviors. In addition to a focus on risk, he is currently studying resilience factors that may protect victims of childhood maltreatment from developing psychopathology. In the future, his team is looking forward to continuing these lines of work and focusing on sex-specific differences in the manifestation of depressive symptoms from both behavioral and neurobiological perspectives.

When we asked Dr. Pizzagalli for advice that he would give students pursuing academia, he told us to prepare ourselves to experience setbacks. Persevere in the pursuit of a topic you are passionate about, for you will be rewarded later on regardless of whether others warn you that the line of research is not promising. He advised us that it is helpful not to be too rejection-sensitive, given that we are in a field in which we are constantly evaluated. Lastly, he encouraged us to read broadly outside of our immediate field; reading literature and connecting with colleagues in other areas can uncover the best insights. We were grateful that Dr. Pizzagalli took the time out of his busy schedule to chat with us, and we look forward to following his future research pursuits!

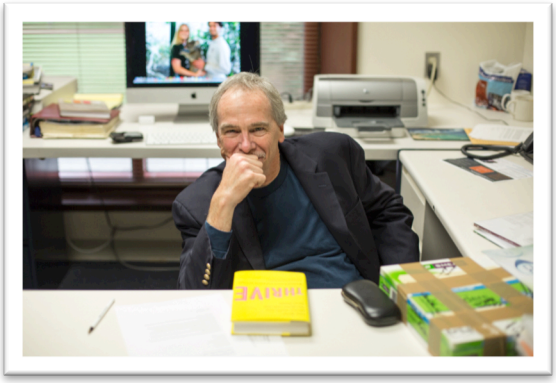
Steve Hollon, Ph.D.

Zubin Award Winner

Vanderbilt University

Chloe Hudson, Queen's University
Simone Cunningham, Queen's University
Lisa Bartolomeo, Indiana University
Ema Tanovic, Yale University
Docia Demmin, Rutgers University

Dr. Steve Hollon was this year's winner of the Joseph Zubin Award for his lifetime contribution to research on the etiology and treatment of depression. Dr. Hollon has made an enormous contribution to the field, with 250 publications–his favorites being the long-term follow-ups of treatment for depression. We had the pleasure to speak with Dr. Hollon to discuss the trajectory of his career and advice he has for current and prospective scientist-practitioners.



Dr. Hollon reported that he ended up in psychology "by accident." Dr. Hollon began his training with aspirations of becoming a lawyer, but quickly realized that he was more interested in psychology. Dr. Hollon attended Florida State University for his graduate training, which he admitted was partially to avoid the snow. Like many first year students entering graduate school, Dr. Hollon initially was plagued with doubts about his chosen path. Despite always being interested in depression, he was met with the struggle of integrating his own interests with those of his professors. It was not until his advisor shared a preprint of a book chapter on the psychology of depression written by Dr. Martin Seligman that he felt confident and motivated in his pursuits. These ambitions were further amplified upon meeting his beloved wife and fellow depression-crusader, Dr. Judy Garber.

Coincidentally, Dr. Garber planned to move to Philadelphia to work with Dr. Seligman, while Dr. Hollon aspired to work with Dr. Beck

and others recognized as pioneers in the field of depression research, like Lyn Abramson, Lauren Alloy, Harold Sackeim, Myer Mendelson, and Joe Mendel. Among these brilliant minds and exposure to different aspects of depression, Dr. Hollon had an epiphany that shaped his current approach to treating depression, which emphasizes long term, enduring effects:

"It is not enough to get someone better, we have to keep them better."

After completing his internship in Philadelphia, Dr. Hollon accepted a faculty position in Minnesota, while his wife, Dr. Garber, completed her graduate training focused on studying depression in adolescents. Home to both a pediatric and adult psychology department, the power couple happily found themselves at Vanderbilt next, where they remain today.

When asked about his SRP presentation, Dr. Hollon emphasized that there is an abundance of research supporting the use of cognitive behavioral therapy (CBT) to treat depression. In particular, he emphasized that patients who are treated with CBT experience higher remission rates than patients who are left untreated and lower relapse rates than patients who are treated with medication. In his talk, he discussed how people often accept that both medication and CBT are useful in treating depression, so they assume that using them in conjunction is also likely to be helpful. However, Dr. Hollon's work suggests that this may not actually be the case for promoting the best long-term outcomes. Dr. Hollon presented a series of randomized control trials that suggest that: 1) CBT often has enduring effects that continue to prevent depressive episode relapses after treatment has ended, 2) that combining CBT with medication may undermine the enduring effects, and 3) that antidepressant medications may inhibit spontaneous remission and leave patients at increased risk for relapse when they discontinue medication.

When asked how the findings of his work could be implemented in the United States, Dr. Hollon responded: only with a single-payer healthcare system. The way that he sees it, the current healthcare system in the United States is not particularly effective and has a problematic incentive structure. "Why are we using meds to only treat, when we could cure using therapy?" he asked, "Because it's not affordable [to provide therapy]

and the system keeps it this way." He contrasted the American system with that of the United Kingdom, where there is a National Health Service that takes care of citizens' healthcare, "from the cradle to the grave." Because of this, he explained, the British government invests in training mental health providers on the most effective treatment techniques. Looking forward, Dr. Hollon expects that the future effectiveness of mental health care in the US will depend on whether the Affordable Care Act survives the presidential election; if so, he predicts that coordinated health insurance, like a single-payer system, is on the horizon. In his view, having a healthcare system that is conducive to the delivery of therapy is important. Dr. Hollon explained that he believes that most non-psychotic disorders can be treated as effectively, if not more effectively, with psychosocial interventions compared to medication. An avenue for future work that he is excited about is developing individualized treatments that are unique to each patient to maximize effectiveness.

Dr. Hollon's career path has not been without its challenges and he offer several pieces of advice to aspiring scientist-practitioners. Dr. Hollon says, "Do what you want, take chances, and let other people tell you no. Don't assume no." He notes this same philosophy is applied in the treatment of depression and we can learn from the parallel. "Don't handicap yourself," he says, "who knows what you're going to get, you'll never know until you try." Dr. Hollon recognizes that it may appear as though he and his colleagues had everything planned out, but in fact successful careers rarely happen in such a way. Like many young graduate students, Dr. Hollon reported that he felt like a fraud upon first entering the field. He admits that this feeling has never really changed, but suggests, "it doesn't need to." "You always stay just one step ahead of being found out, that's what it comes down to," he says. Early on, Dr. Hollon learned he could build a career from making mistakes and then correcting them in the next trial, and he advises young investigators to do the same. He challenges young people interested in pursuing graduate school in psychology to "do something interesting and hard" in the interim. It seems Hollon learned a great deal from his early hurdles, and it is these experiences that helped shape his career into what it is today.

Dr. Hollon believes that when you find what truly excites you, you can realize your true potential. "If it doesn't keep you up at night because you're interested in it, then it's not the right fit." Dr. Hollon advises. For Dr. Hollon, this passion

is evident in his lifelong research on the treatment of depression, and we are tremendously grateful for his dedication.

Richard Zinbarg, Ph.D.

Northwestern University, Department of Psychology

Mayan Castro, University of California Irvine
Alexandra Moussa-Tooks, Indiana University
John Purcell, Indiana University
Colin Stanton, Yale University

We were excited for opportunity to sit down with Northwestern professor Dr. Richard Zinbarg during the 2016 SRP meeting in Baltimore, Maryland to discuss the development of his research interests, previous experiences at SRP conferences, advice for younger researchers and foci of current research. Dr. Zinbarg's work investigates numerous topics including anxiety disorder psychotherapy, measurement, and development via the lens of personality traits. His work has exerted an immense impact on current understanding of the etiology and treatment of anxiety disorders.

When Dr. Zinbarg began his PhD at Northwestern University, he was primarily interested in disrupted behavioral inhibition systems (BIS) in psychopathy. However, he soon became fascinated by the ways that an overactive BIS might manifest in anxiety disorders. Finding this area of research more akin to his own experience, Dr. Zinbarg began moving toward research of anxiety-related problems with a primary focus on the psychopathology of anxiety disorders though also conducting some research on interventions for anxiety. Presently, Dr. Zinbarg describes his research as falling into two major domains. The first lies at the intersection of personality and psychopathology, taking into account variation in general factors (akin to general intelligence) and group factors (akin to verbal and spatial ability) to better characterize vulnerability to the development of anxiety disorders and depression. His second line of work concerns psychometrics, and, in particular, internal scale consistency. In this domain, Dr. Zinbarg focuses on the tendency for researchers to utilize Cronbach's alpha as a "measure of oneness", when alternatives such as

Revelle's β or McDonald's ω_h may provide a better conceptualization of reliability.

To provide further insight into his development as a researcher, Dr. Zinbarg cited some of his key influences. Dr. Zinbarg expressed his admiration for the research of the late Dr. Jeffrey Gray, and especially for his conceptualization of the BIS. Dr. Zinbarg noted that he admires the strong neural component of this model and has incorporated this concept into his own research. Additionally, he spoke highly of Dr. Lorna Benjamin, describing her as an "expert on the treatment of Borderline Personality Disorder." Dr. Zinbarg praised her as both "one of the most gifted clinicians" and one of the most "psychometrically sophisticated" individuals in the field. Finally, he recognized the contributions that Dr. David Barlow, his post-doctoral mentor, has made towards the integration of science and practice and the understanding that "human behavior is complexly determined." Dr. Zinbarg esteemed Dr. Barlow as a "pioneer" for his work on applying single-case experimental designs to the study of individual psychological treatment.

Dr. Zinbarg also spoke about changes to the SRP conference over the course of his career. When he first started attending SRP as a post-doctoral researcher in 1992, there was little representation of research on anxiety disorders; the conference was dominated by schizophrenia and bipolar research. Over time, research presentations diversified to include more anxiety research. Furthermore, Dr. Zinbarg asserted:

"Designs and statistical approaches have become more refined over time, such that researchers are now focusing on manipulating variables such as information processing biases rather than passively measuring them. These changes have aided in the diversity of ideas and improved the development of impactful interventions."

Yet, some important aspects of SRP have not changed over the years, including the intimate and highly interactive atmosphere and "crowd of curious attendees that ask thoughtful and respectful questions." Dr. Zinbarg praised these elements that make SRP the "amazing, unique" conference that it is.

When asked about advice for younger researchers, Dr. Zinbarg responded that "the best research comes from passion." He suggested that in order to stay productive and energized, students should: "lead a happy life by living in the moment," and "do good research by identifying questions

that excite you." Dr. Zinbarg also stressed the importance of "struggling through" early anxieties that can arise when young researchers formulate research questions. This struggle helps students learn to independently conceptualize research projects. Dr. Zinbarg's final word of advice was to encourage students to work on research outside of what is handed to them by their mentors, when funding allows. This independence allows student to invest in unique research questions and propagate new and exciting lines of research.

Our conversation with Dr. Zinbarg left a lasting impact, as has his research on the field of anxiety disorders. We are grateful for his time and immense contributions to psychology and SRP.

Sunny Dutra

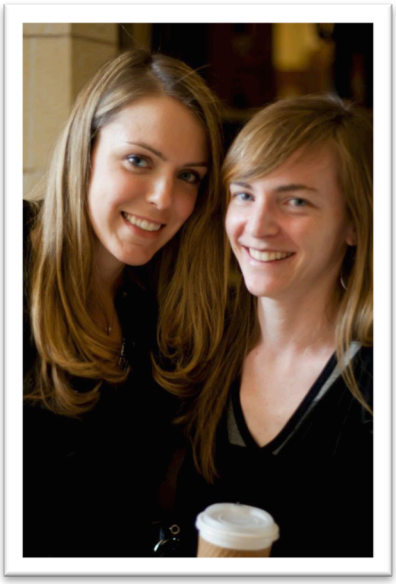
Yale University

Mentor: June Gruber

Smadar Levin Award Recipient

Shaynna Herrera, Yeshiva University
Susan Kuo, University of Pittsburgh
Keira O'Donovan, University of Massachusetts, Boston

Sunny Dutra, a recent graduate of Yale University, is the winner of the 2016 Smadar Levin Award. Members of the newsletter committee had the great pleasure of interviewing Sunny on her career path, research program development and future plans.



Sunny's journey began as an undergraduate at the University of California, Santa Barbara. It was there that she completed her honor's thesis in the Center for Evolutionary Psychology (CEP) under the mentorship of Leda Cosmides, PhD. While in the CEP one day, a researcher told Sunny that a career in science can afford one the unique opportunity to create new knowledge, knowledge that has never existed before in the world. She wondered, "What could ever be more meaningful, or more important, than creating new knowledge?", and now remembers this as the moment she decided to pursue a career in research.

Sunny noted that she has always been fascinated by mood disorders and the ways they can alter an individual's fundamental experience of the world. This curiosity led her to her lab manager position under Dr. Diego Pizzagalli at Harvard University after graduating college. There, she began to learn about neuroimaging, anhedonia and depression, eventually honing in on the neuroscience of reward processing. Sunny expressed gratitude to Dr. Pizzagalli for the many opportunities in his laboratory that helped to build the foundation for her research interests moving forward.

When she entered graduate school, Sunny reconnected with Dr. June Gruber (picture above with Sunny). She and Dr. Gruber had originally met when Dr. Gruber was a graduate student at UC Berkeley and Sunny was a summer research assistant with Dr. Gruber. They maintained their connection and had

very similar research interests in the ways that reward and positive emotion can go awry and contribute to psychopathology. Even before Sunny entered graduate school, they began designing a large research project from which Sunny's dissertation data were collected. Sunny stated that one of Dr. Gruber's strengths is her ability to organize all of the necessary resources and personnel to smoothly and efficiently coordinate all aspects of a large research study. Sunny is grateful for Dr. Gruber's mentorship, guidance, and generosity throughout graduate school that allowed her to successfully complete her dissertation.

Sunny's dissertation focused on the neural underpinnings of reward related dysfunction in bipolar disorder. At the trait level, people with bipolar disorder show elevated sensitivity to rewards and persistent positive emotion. Sunny wanted to understand the neural underpinnings of this process in terms of regional activation and functional connectivity. To do this, she used a modified version of a Monetary Incentive Delay task developed by Dr. Brian Knutson and colleagues. However, they also wanted to understand the processing of social rewards, so they designed a parallel task in which participants earned social praise as a reward. Sunny noted that a great deal of research uses money as a reward, but as reward vary, so it is important to capture this diversity. Results indicated that both monetary and social reward elicited greater striatal activation. They also found that when participants with bipolar disorder expected to receive a reward but didn't, there was a reduction in frontostriatal functional connectivity. This suggests a failure to "put on the brakes" in reward pursuit, despite signals to slow down and reevaluate.

Regarding her future, Sunny has just finished her internship at the Boston VA and is staying to complete a T32 postdoctoral fellowship at Boston University/VA Boston under the mentorship of Dr. Brian Marx. She plans to study individual differences in reward processing under stress, addressing questions regarding similarities and differences in anhedonia between depression and PTSD. She is also interested in examining whether we can better predict suicide in veterans by improving our understanding of alterations in reward processing in anhedonia. Ten years from now, Sunny envisions herself continuing to conduct research on reward processing dysfunctions and their contributions to psychopathology.

Not Pictured: Keira O'Donovan

Sunny described her mentoring relationship with Dr. Gruber as being an invaluable learning experience because of Dr. Gruber's fresh perspective and openness to developing new ideas. In particular, she appreciates learning from Dr. Gruber about ways to shape big ideas into reality, coordinating large teams of undergraduate and graduate trainees to work on large-scale studies. Furthermore, being Dr. Gruber's first graduate student allowed her to be involved in key decisions in the development of a research lab from its beginning stages and provided her with the unique opportunity to think about the long-term future of the lab together.

When asked about advice for up and coming researchers, Sunny particularly appreciates that Dr. Gruber encouraged her to think from early on about developing an independent research program. Sunny attributes much of her success in research and clinical work to thinking about an overarching framework of the larger questions she is interested in addressing, rather than approaching her work as a compilation of individual projects. She says that having a continuous dialogue about focusing her interests guided her in figuring out projects she wanted to be involved in and allowed her to maximize her investment in projects that build upon each other.