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Undergraduate

MOMENTS OF MANIA: EMOTION-RELATED IMPULSIVITY AND BIPOLAR DISORDER

Interview with Professor Sheri Johnson

BY SHEVYA AWASTHI, MATTHEW COLBERT, DOYEL DAS, MELANIE RUSSO, KAELA SEIERSEN, AND ELENA SLOBODYANYUK



Professor Sheri Johnson.



► **Figure 1:** One of Vincent van Gogh's most famous paintings, *The Starry Night*. Psychiatrists Hemphill and Blumer suggested that van Gogh had bipolar disorder.^{1,2}

Sheri Johnson is a Professor of Psychology and Director of the Cal Mania (CALM) Program at the University of California, Berkeley. She is also an affiliated faculty member at UCSF's Depression Center. Professor Johnson's research centers on understanding the triggers of mania and depression within bipolar disorder, and on emotion-related impulsivity more generally. In this interview, we discuss the study of emotion-related impulsivity in individuals with bipolar disorder as well as the development of new treatments for bipolar disorder.



their usual self. The human challenge of living a life like that was fascinating to me. A couple months into my internship, one of my clients said, “I don’t get it. You’re doing all this work on depression and we don’t even know what triggers episodes of BD. Isn’t that the kind of question you want as a scientist?” And for the next 20 years that became my driving question: why do people move into these episodes of mania?

BSJ: How heritable is BD?

SJ: BD is among the most heritable of disorders. The estimates of heritability of mania are 0.85 and above. These estimates are based on careful community-based twin studies, so there isn’t a biased sample. There’s a huge genetic component. One thing I want to say very clearly is that just because something’s heritable, that doesn’t mean you’re stuck forever in the same state. It’s still treatable, and we can still make a difference.

BSJ: Several of your studies focus on adolescents with BD. What is the significance of studying this age cohort?

SJ: BD often seems to come on during adolescence. Over time, those episodes have a pretty important role in somebody’s life. They can interfere with relationships and work. If you catch people early on, you may get closer to understanding the risk factors as opposed to their aftermath. Throughout our studies, we take a two-pronged approach. One is to conduct longitudinal studies on people who have already been diagnosed. We wait until they are well, compare their psychological traits to those unaffected, and then see how those traits predict the onset of episodes. This can get tangled up because the individual is already going through the disorder. Our other approach is to take people who haven’t had a full-blown episode but have signals that they are at risk. If you follow those people over the next 10 years, a group of them is likely to develop BD. When we see a psychological correlate in the at-risk group, we feel like the trait is not just entangled with the aftermath of a serious episode, and so we feel more confident that we are onto something.

BSJ: In one of your studies you investigated the connection between sleep disruption and impulsivity.³ Why did you decide to focus on this relationship?

SJ: Sleep helps your prefrontal cortex function better, it helps you self-regulate, and it helps you control your emotions. It has been shown that if you deprive somebody of sleep, they are going to be more impulsive. Impulsivity and sleep problems are two of the key features you see in BD. They have always been treated as two separate features, but we thought maybe they are not so separate.

BSJ: How did you get involved in the field of psychology and specifically in studying bipolar disorder (BD)?

SJ: I began college as a music major, and that was really demanding with low potential for full-time employment. I thought psychology classes were interesting and provided a more secure career path. I didn’t get interested in BD until the last year of graduate school. I thought I was going to be a depression researcher, and I wanted to do a one-year internship at Brown University because their program focuses on mood disorders. When I got there, I was assigned to work with people who had BD, and I was hooked. Imagine a group of people who are a little bit more energetic and sparkly than the typical population. Within a matter of hours, they can go through an episode that renders them startlingly different from

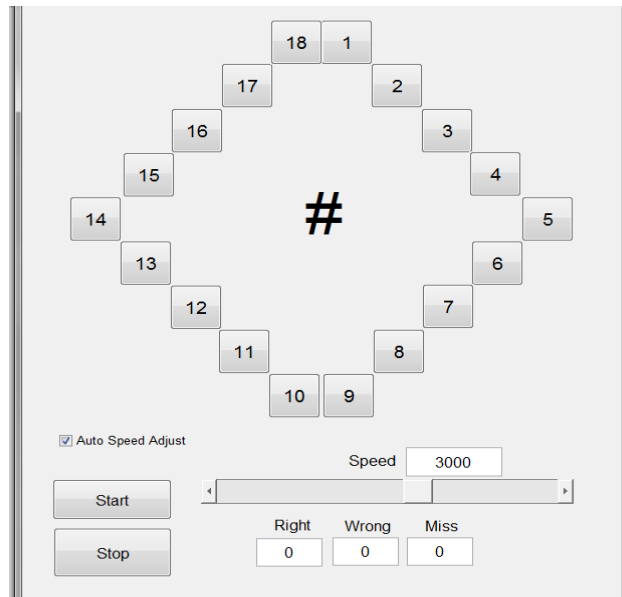


Figure 2: Example of the Paced Auditory Serial Addition Test (PASAT), a working memory task. Participants listen to numbers presented every 3 seconds one at a time and must add each number to the previous number. The participant's answer is entered by clicking the corresponding number on the screen.

BSJ: In this study, you found that sleep disruption was associated with greater impulsivity in the BD group but not the control group. How can you explain this result?

SJ: One of the things with BD is that there is a greater vulnerability to certain kinds of challenges. If you have something that will change mood state, for most of us it might affect us only a little bit, but for individuals with BD it is likely to have more influence.

BSJ: A lot of your work centers on investigating emotion-related impulsivity (ERI). Can you define ERI and explain its importance in the context of psychopathology?

SJ: More than a decade ago, Whiteside and Lynam conducted a massive study to measure the different dimensions of impulsivity.⁴ There was a unique group of people who only became impulsive during states of high emotion, and during those states they would do and say things that they later really regretted. Whiteside and Lynam initially studied negative emotion, but of their protégés, Melissa Cyders, created a scale characterizing response to positive emotion states. It turns out that the negative and positive emotion scales are highly correlated; people with one tendency are very likely to have the other tendency. Furthermore, compared to any other self-rated form of impulsivity, ERI is much more predictive of psychopathology. The effects of ERI are stronger for conditions like aggression, depression, and anxiety. In our own work, we've

shown that ERI is very present for people with BD even after they remit. So it seems like ERI gives us much more predictive power in understanding psychopathology.

BSJ: In one study, you investigated neurocognitive mechanisms underlying ERI.⁵ What is response inhibition and how does it relate to ERI?

SJ: The basic idea of response inhibition is that you have to withhold the prepotent response. Why does that matter for emotion? Let's say you are driving down the road and somebody cuts you off. The impulse to go, "Ugh!" is prepotent. Not doing that, say if you were an Uber driver (who has to stay polite and serene), takes inhibiting your response. We know a lot about the neural circuitry involved in response inhibition, and it turns out to be the very same neural circuitry used when engaging in different forms of emotion regulation. It made sense to us to think that response inhibition could be one of the things going wrong for people with ERI. We and many other researchers have now shown that people with high levels of ERI show deficits in response inhibition.

BSJ: Why did you choose to focus on the effects of emotional arousal on response inhibition?

SJ: Most previous studies were just putting people into a standard response inhibition task. But where is emotion in that

“Compared to any other self-rated form of impulsivity, ERI is much more predictive of psychopathology.”

story? Clinically, people with ERI say that they are falling apart and can't constrain their behavior during states of high emotion. What do good and bad emotions—being euphoric and angry—have in common? High arousal. That was the next direction we went—looking at arousal and its influence on response inhibition for people with ERI. In two studies we did this through a mood induction. We brought people into the lab and showed them a scary or upbeat movie and then tested response inhibition. We could see that people with high levels of ERI were having problems with their response inhibition.

BSJ: Upon inducing a heightened emotional state in your participants, you measured arousal by pupil dilation. Why did you choose this over other measures such as heart rate?

SJ: One reason is that we frankly haven't had great effects with measuring heart rate. The other reason is that the pupil is pretty interesting. We know a lot about the circuitry guiding pupil dilation, and if you keep light levels constant, pupil dilation is directly influenced by noradrenergic systems in the brain (parts of the sympathetic nervous system that are highly involved in arousal), which have been really nicely traced out. Now you have this beautifully observable proxy for some of the noradrenergic spikes that might be happening in the brain.

BSJ: Finally, we read about your study evaluating a cognitive control training program for reducing ERI.⁶ Could you explain the cognitive training procedure, particularly the PASAT and Go/No-Go tasks?

SJ: Broadly, we've been trying to understand whether we can make a difference for ERI. There's a huge amount of literature out there that suggests that we might be able to strengthen some of these cognitive processes by practicing them. Andrew Peckham was the leader of this study, and he simply conducted six sessions of 15 minutes of practice of the Go/No-Go task and 15 minutes of the PASAT. The Go/No-Go task is a classic measure of response inhibition. We say to you, “Every time you see the letter X, we want you to press a button as quickly as you can. If you do that successfully, you are going to earn money.” We have you do that a lot of times so it becomes automatic. You see the X, boom!

You get very good at pressing the button. Then we say, “If you see a Y, don't press the button.” The PASAT is a working memory task where you have to attend to a sequence of stimuli that show up on the screen. It's very challenging, and people rate it as more unpleasant than a lumbar punch. That makes it seem like a terrible task to choose! On the other hand, if you wanted to look at your ability to use your prefrontal cortex during moments of distress, that's a perfect training task. You're catching people in a moment of frustration and asking them to get better at the skill. Andrew combined both of these tasks and saw that at the end of training, there was a lower score on ERI. He didn't see the same thing in the control group, and now he has five years to look more carefully at this training in a partial hospital program. We'll see how we do!

BSJ: Do you see these trainings becoming accessible to individuals beyond the study?

SJ: That's the great hope of cognitive remediation. One of the big controversies in the field right now is that when people were given access to a remediation program over the internet, it didn't seem to help. What happens there? Is it that when we shut down every other piece of stimulation in your life (like we can when you visit our lab), you rehearse more deeply? Is it that you work harder with the experimenter coming back to check how

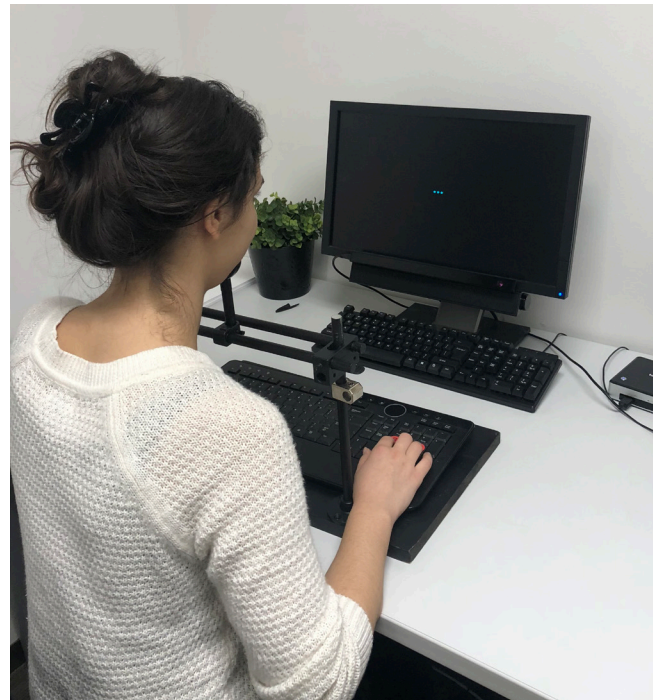


Figure 3: Participant completing the Go/No-Go task. The participant is instructed to press a button in response to a symbol (“Go”) and withhold responses to another symbol (“No-Go”), which appears much more frequently. The task is a measure of response inhibition.

you did? Or maybe when you push it out that broadly, you might not get the people you want to get? There's a lot of questions about what we need to do to disseminate. We've set up a web-based intervention on hyperarousal, but we're still keeping close tabs on it because we want to do a lot of interviews to evaluate how it works. Our hope is that it would be something very accessible for people to take from home, whether or not they feel like seeing a therapist.

BSJ: What are some limitations of self-report measures in your studies?

SJ: One limitation is that a lot of the items on ERI measures are about feeling regret about your activities. There may be people who show extremes of ERI but don't particularly regret it. There also may be people who are overly critical of themselves. They do something that's pretty modest, and they feel a deep sense of regret about it, even if it's exactly what most of us do during states of high emotion. One way researchers have gotten around that is to develop interviews from a parent's or friend's perspective, or to ask for observer ratings. The findings from those scales look very similar to the findings from the self-ratings. That's a good sign because it suggests that for the most part, people are pretty good informants about themselves on this front.

BSJ: How do different trainings for BD such as medication, cognitive training, and psychosocial training compare to each other?

SJ: At this point, every major treatment guideline worldwide would put medication first. We don't have anything that tops the effects of medication, so it's the first line of defense. Lithium is one of the first well-documented treatments for BD, and it's shown to be related to lower rates of suicidality. Most people are looking at the role of psychotherapies as adjuncts to medications. There's a lot of evidence that adding psychotherapy should be standard care—it helps people have a better quality of life, lowers the risk of relapse and hospitalization, and helps build back social and occupational roles. Unfortunately, psychotherapy is not always provided. We only have a couple studies of cognitive remediation for BD, and while there are some fascinating findings, I think we are in the earlier phases of understanding its effects for BD.

BSJ: What are the implications of your research in developing treatments for BD?

SJ: Much of my work for 20 years was focused on understanding reward systems in BD, and we have developed a pilot treatment that focuses on those facets. We need to test it more thoroughly, but we think that people can have a better sense of control by understanding that they may need to implement more emotion regulation strategies in situations with high rewards. We have not yet tested our treatments related to ERI and BD, but that's one of the next things we would love to do. We know that

“Our hope is that [cognitive remediation] would be something very accessible for people to take from home.”

this form of impulsivity is really important in BD; it predicts relapse, aggression, problems in functioning, lower quality of life, and greater risk of suicidality. If we could target ERI effectively, we might make a difference in some really important outcomes. I'm hoping that our work on ERI could be rapidly applied to BD and tested as an intervention.

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