

Research the Resonates
Villanova CLAS Podcast
Episode 2 Transcription
Genetics: Nature vs. Nurture and Alcohol Abuse

HOST: Chelsea Gerrard

Guest 1(ED): Elisabeth Dimitratos '21 CLAS

Guest 2 (LW): Leah Waltrip '20 CLAS

Guest 3 (BS): Benjamin Sachs, PhD

Intro Sound: *Emergency vehicle sirens.*

ED: I'm an EMT and definitely a large majority of calls that Villanova and Radnor ambulance services receive are related to alcohol intoxication.

HOST: That's Elisabeth Dimitratos. She just graduated from Villanova University with a major in Cognitive and Behavioral Neuroscience with a minor in Classical Studies.

ED: Obviously, many people engage in drinking socially or in general but not everybody develops an alcohol use disorder so understanding the causes that go into that transition from being a casual social drinker to developing a problem like an alcohol use disorder is definitely important.

HOST: You're listening to Research that Resonates, the podcast from Villanova University's College of Liberal Arts and Sciences, that takes you inside the labs and classrooms to learn from our distinguished faculty and students. I'm your host, Chelsea Gerrard.

In this miniseries, we're talking to research teams who study genetics. I sat down with Dr. Benjamin Sachs and two of his student researchers to talk about the correlation between gender, stress and alcohol use.

BS: I'm Ben Sachs. I'm an assistant professor in Psychological and Brain Sciences.

ED: I'm Elisabeth Dimitratos.

LW: And I'm Leah Waltrip.

HOST: Elisabeth has been working in Dr. Sach's lab since her first year at Villanova and Leah joined his research team in her junior year. She graduated in 2020 with a double major in Cognitive and Behavioral Science and Peace and Justice.

There used to be different diagnoses between alcoholism and alcohol abuse, but the American Psychiatric Association has replaced these different types of disorders with one umbrella term: alcohol use disorders or AUD.

We know there is a genetic component to AUDs, but we also know there are environmental factors. Here's Leah.

LW: Alcohol use disorders exhibit heritability in some way, so we know that if it's heritable it means that there's a genetic component to it. What that genetic component is necessarily, we're not entirely sure. We know that stress and sex are both involved, but we still don't know exactly what these factors are.

We also know that not everyone whose parents had an AUD, develops an AUD, so there has to be environmental factors that are also impacting this which is where I think the stress comes in and is a big component of most developments of alcohol use disorder.

HOST: Elisabeth's research looked at those environmental factors, specifically stress. She found some really interesting data both about the type of stress—chronic versus acute—and the differences between males and females.

ED: One of the most major findings from what I've been working on is that it's only a period of chronic stress that will give you an increase in ethanol consumption in these mice whereas acute stress—so, stress for only a four-day period—does not show any significant increase in ethanol consumption. So, it's definitely a chronic effect that we're looking at in terms of stress and binge drinking.

HOST: Her other key finding was related to gender. When put under chronic stress, the female mice that indulged in binge drinking released more endorphins than the males.

You are probably familiar with endorphins, or have at least heard of them, but here's Dr. Sachs to explain a bit more about what the term means.

BS: Endorphin comes from “endogenous morphine,” so morphine being an opioid drug is very rewarding. Endorphins play a role in endogenous reward. If you eat something yummy and feel good about it, that’s probably partially endorphin mediated. For those of us lucky enough to get runner’s high, where you run really far but instead of being in pain, you feel good, that’s also thought to be endorphin mediated. There’s a lot of evidence now that endorphins play a role in how we respond to drug use. So, part of why a drug we might take makes us feel good and we want to take it again is because it can stimulate release of endorphins.

One of the major treatments for alcoholism or alcohol use disorders is an endorphin blocker or an opioid receptor blocker. So, we think that the endorphin system is involved in the rewarding effects of alcohol and other drugs, so the fact that there are these sex differences in how much endorphins or receptors there are could partially be explained why there’s differences between the sexes in drinking behaviors.

HOST: Elisabeth’s research helps inform the rest of the work that the lab is doing with the specific gene called TPH2.

BS: The main gene that we’re interested in is TPH2 which is the gene that makes serotonin. There was a group of researchers at Duke who found a mutation in this gene in a group of depressed patients. Then they went on to see if that mutation in the gene actually messes up the genes function, and they found that it did.

Then they made a mouse that expresses the mutant form of the gene, not the normal form of the gene. So, mice that have that mutation only make about a third as much serotonin as a normal mouse would. Presumably, people that would have that mutation would also only have about a third of the serotonin.

HOST: There is research that serotonin deficiency plays a role in alcohol use disorders, but the evidence for that is lagging. In his lab, Dr. Sachs is trying to build a pretty strong case that the mutated TPH2 which causes serotonin deficiency does play a role in AUDs.

Leah looked at male and female mice with this TPH2 mutation. Here she is.

LW: I researched male mice but compared it to data that we had previously on female mice. We found that brain serotonin deficiencies, so the mice

that we were using in the lab that had reduced serotonin—the TPH2 mice—confer susceptibility to stress-induced binge drinking behavior in females, but not the male mice. Basically, the females were more susceptible to this binge drinking following stress if they had the brain serotonin deficiency.

HOST: So, the females with the genetic mutation, and thus, serotonin deficiency, were more susceptible to binge drinking. As for the males, they will need to conduct further research, Dr. Sachs explains.

BS: We're stilling trying to figure out whether males also have increased susceptibility, but we would have to increase the stress duration or intensity for that because right now, none of the males are increasing their drinking after stress regardless of their gene type.

HOST: What could this research mean for AUD treatment? There are a few existing treatments for alcoholism, but not many that are very effective.

BS: There are a number of drugs that people try for alcohol use disorders, none of them are that effective. There are several that beat placebo, but usually they don't really help a large percentage of people.

I've talked a little bit about Naltrexone, which is this anti-opioid drug, also called Vivitrol. That one got approved so it does better than a sugar pill, but I think it's something like 17% effectiveness. So, there's huge room for improvement there.

It might be that if we can find subpopulations with genetic predispositions or genetic factors that make them more or less responsive, we might be able to select one medication over another.

HOST: So, in theory, if Dr. Sach's research team is able to better identify what is happening on a molecular level in the brain preceding, during, or after binge drinking episodes, we can develop pharmacological treatments that specifically target the problem. Here's Leah.

LW: Basically, if we're able to figure out what the molecular underpinnings are that explain why we're seeing these effects in the mice, we're much more likely to be able to develop a pharmacological target that could help people. Mice, at first, would be tested in but also help people long term.

If you're able to figure out if this is an individual who is under frequent stresses, then relapsing more often, you're able to help the people who are not responding to current interventions.

HOST: As college students, this research could hit close to home as drinking is often an outlet for stressed students.

LW: I think I see more frequently my alarm bells go off when I see students drink when they say that they're really stressed. I think for me personally that is something that I'm more like "maybe don't do that, maybe find a better stress coping mechanism." But the reality is that a lot of people do that, so I think that has made me more hyperaware of how I try to interact with friends when I see that they're stressed and what capacity I can support them in that's not just "let's go out," but rather, "let's find a way to take care of you."

CG: Thanks for listening to Research that Resonates. We've produced two other miniseries: one on sustainability and one on the intersection of youth and identity. You can check those out on Apple podcasts, Google Play, and Spotify.