Aaron van Dorn (00:07):

Welcome to AJP Audio for September 2022. I'm Aaron van Dorn. Today on the podcast I spoke with Dr. Lauren Lebois, Director of the Dissociative Disorders and Trauma Research program at McLean Hospital, and an Assistant Professor of Psychiatry at Harvard Medical School. Dr. Lebois and fellow researchers looked at persistent association following trauma exposure, and whether it can be predictive of later psychiatric outcomes in at-risk populations. Later I'll speak with AJP Editor in Chief, Dr. Ned Kalin about what else is in the September issue of the American Journal of Psychiatry and how it all fits together. Dr. Lebois, your paper defines disassociation as a disruption or discontinuity in the typical integration of psychological functioning in the aftermath of a traumatic event. Your paper looks at what persistent dissociation can teach us about outcomes after trauma exposure. What can you tell us about disassociation? How does it appear and what purpose does it serve?

Dr. Lauren Lebois (00:52):

Thank you so much for asking that, Aaron, and also, thank you so much for having me. I'm delighted to be in conversation with you and your listeners, especially about dissociation since it's so understudied and often misunderstood. Yes, that definition is a mouthful. Actually, I really like a definition from a former colleague of mine, Dr. Nina Lewis Schroeder. I like this definition that she uses that for dissociation, that it's anytime your mind is not where your body is, and that covers a broad spectrum of different types of experiences. I think the best way to really understand and feel what that means is actually if I could walk you through a prototypical adult case that I've encountered several times in a research context, and I won't be breaking any confidentiality. This is actually a conglomerate of a lot of people I've talked to.

Aaron van Dorn (01:49):

Yeah, that sounds great.

Dr. Lauren Lebois (01:51):

I'll call her Diana. When we were talking in these research clinical interviews, Diana actually had a lot of PTSD symptoms going on. She was telling me about how she had terrible nightmares, really restless sleep. She startled a lot to the point where her coworkers would notice this at work and comment on it. She talked a lot about really trying to avoid any thoughts or feelings about her childhood, especially about her father, who I later learned, as we talked, that he was one of her main abusers growing up. She also kind of alluded to this general sense that she felt that she deserved to be hurt, but she didn't really have any understanding of why she felt that way about herself.

Dr. Lauren Lebois (02:33):

With that backdrop of PTSD, she also had a lot of dissociative symptoms going on at top of that. She talked about gaps in her memory. She couldn't remember visits to her father's house growing up when she was a child after her parents got divorced. She sometimes felt unreal. She talked about how she felt like she existed only from the neck up and her body didn't feel like it was there at all a lot of the time. She often felt puzzled about what was real and what was unreal in her surroundings, so things kind of felt strange and unfamiliar, and she even likened it to feeling like she was in a movie and not in her actual life. In talking Diana, I myself would start to feel a little ungrounded and spacey. I think just picking up on maybe some of the dissociative experiences she was having, even in the moment talking to me, although to look at Diana, she seemed very calm and sometimes almost flat as we were talking.

Dr. Lauren Lebois (03:34):

As our interview went on and I probed a little bit deeper, she told me, despite looking on the outside calm and flat, inside her mind felt very busy to her. Specifically when I was asking about her trauma history, she started talking about some sexual abuse she had experienced at the hands of her father. She told me that when she was talking about that, she actually felt like an observer while someone else from inside was speaking. She knew that wasn't actually physically possible. It just felt that way to her somehow. She has intact reality testing. This isn't psychosis. It's actually a trauma related dissociative response.

Dr. Lauren Lebois (04:18):

At the end of the interview, I determined that Diana had the dissociative subtype of post-traumatic stress disorder, and on top of that, a complex dissociative disorder called dissociative identity disorder. We hope this case illustrates a lot of different ways that dissociation can show up for someone after trauma, and I think it's important to understand that these experiences can happen right in the moment when someone's experiencing a traumatic event and also in its direct aftermath, but it's when they persist beyond that. That's when we get into the land of PTSD and complex dissociative disorders.

Dr. Lauren Lebois (04:54):

I really like what you asked, Aaron, about why do people experience this? What's the purpose? What's the function? I think dissociation is actually somewhat paradoxical. It's both incredibly adaptive and it can also interfere. It can become a disorder. The way it's adaptive is that it provides this psychological space, this distance between you and what's happening, so you're not hit with the full psychological impact of the traumatic things that are happening to you. It allows you to escape these inescapable traumas. I really like this example that a colleague in the field, Sachi Nakajima uses. She's a nonprofit founder, an author, lecturer, and she has some lived experience herself, but Aaron, do you like riding roller coasters?

Aaron van Dorn (05:45):

Yeah. Love rollercoasters. I haven't been on one in a long time though.

Dr. Lauren Lebois (05:48):

Yeah. Imagine you actually hated roller coasters, but you were forced to ride on one, and it was one of those really old ones that's rickety. You can hear it clacking as you're going up in this roller coaster. It's one of those ones that it has that huge dip right at the start, and you're about to go over and you can hear people starting to scream around you, anticipating that drop in your stomach. What if right before that happens, you could mentally pause and make it feel in your mind as if you were standing on the ground, safely on the ground, just watching yourself about to take that drop in the rollercoaster? That's exactly what can happen in dissociation. It gives someone somewhere else to be, somewhere safe to be in their mind while traumatic things are happening, and it feels like there's a separation there and a detachment there.

Dr. Lauren Lebois (06:42):

I think the adaptedness of this becomes even more salient when we're talking about the case of childhood trauma. If a child is being abused or hurt by a caregiver, they need that caregiver to survive. They can't go off and live on their own. If they can make it feel like what this person is doing to them is unreal or far away from them, they're separate from it, somehow that allows them to still attach to this

caregiver, to go to school the next day, to have friends, to live their life. I think that's, in particular, a space where this can be incredibly adaptive, but again, returning to the paradox, it also can get in the way. As people grow up, it can interfere with their day to day functioning. They've become so good at dissociating and detaching from things that they can't always control when it's happening for them. Even when they might want to stay present, they're unable to do so. In that way, again, we can enter the land of disorders like PTSD and complex dissociative disorders.

Aaron van Dorn (07:49):

Your comparison of disassociation to rollercoasters, I'm just wondering, when people have persistent dissociation, is it because they're being triggered by events in their life, or is it something that becomes kind of a self-fulfilling prophecy and it just becomes a thing that happens to them because it keeps on triggering itself? Does that make sense?

Dr. Lauren Lebois (08:04):

It does, yeah. I think it can span all those types of situations that you just described. It could be that someone starts to feel some of these dissociative symptoms when they're feeling triggered. There's something that reminded them of something that happened to them that was traumatic in the past. There's some resonance there and their body and mind go to this coping mechanism that they've, like I said, become so adept at using and has worked very well for them in the past. I think it can also happen without a specific trigger, so it doesn't need to be just in a situation of current life stress. It could also happen outside those contexts as well.

Aaron van Dorn (08:44):

Your study examined participants after traumatic events, both through self-reported means and in a subset through MRI scans. Why did you choose to differentiate the methods of assessment, and did the outcomes differ between the groups?

Dr. Lauren Lebois (08:55):

The goal of our study was really to understand the neurobiology and the long term impact of dissociation by following people longitudinally after a traumatic event. We recruited people from emergency departments all across the country, and like I said, followed them longitudinally up to six months later. We had over 1,000 people in this particular analysis who'd reported on their self-report surveys of dissociative experiences, among many other things. Then a subset of them, 145 people, completed, in addition to all these self-reports, neuroimaging brain scan. The socio-demographics across these two different groups, or rather bigger group with a subset of people who did some additional stuff, was very similar. Most of them were female. Our largest racial group self-identified as black, followed by folks who identified as white. Then most of the sample had received some college education and most of the people came to the emergency department because they had just been in a motor vehicle accident.

Dr. Lauren Lebois (10:03):

All the procedures that everyone did were the same, except for the group who did the scan. They obviously had the MRI scan about two weeks after their emergency department visit. As part of that scan, they did something called a resting state scan. In this type of scan, we don't ask the participant to do anything in particular. They're just asked to kind of lie there and think about nothing in particular, not given an explicit task. Then we also gave them an explicit task that was kind of emotionally provocative.

We showed them these fearful looking faces, and that can be, like I said, kind of emotionally activating for folks. I think the benefit of using both these methodologies, the self reports and the neuroimaging scan, was that we could reach a lot more people with the self reports. It's logistically easier to do widespread research like that, but then we could pair it with a cohort of people who also had the brain scan and have this objective biological marker of what someone's subjectively reporting on their surveys.

Aaron van Dorn (11:11):

How was the imaging cohort chosen? Were they picked at random or were they picked for a particular set of purposes?

Dr. Lauren Lebois (11:16):

Yeah. It was a little bit of a convenience sample in the sense that we had four sites around the country who had access to an MRI scan and a number of emergency department feeder sites. If you happened to live in that city and go to that emergency department and then you were willing to then participate in an MRI scan and you met all the eligibility criteria for safety, then you got to participate in the imaging portion of the study.

Aaron van Dorn (11:47):

Speaking of the imaging portion, your study was looking at potential biomarkers associated with disassociation and later psychiatric outcomes. What did you find?

Dr. Lauren Lebois (11:54):

We had two key findings, Aaron. One of them had to do, just like you said, with the dissociation biomarkers, and a key brain region that came out in these analyses was the ventromedial prefrontal cortex. This is a region in the brain involved in a lot of different functions, but a shorthand we can use in this conversation is that it's involved in helping us to regulate our physical and emotional reactions. If you experience something threatening or activating, like we were doing in our study with the fearful faces, once that threat has passed, the task is done or you're out of the traumatic experience, this region puts the breaks on your emotional and physical reactivity, so kind of helps you calm down afterwards. The threat is no longer present. You don't need to be all amped up, ready to deal with it.

Dr. Lauren Lebois (12:46):

What we found with folks in our study who had more dissociation on board, they actually had more ventromedial prefrontal cortex activity during the fearful faces task. It was as if the breaks for them were too good or too tightly bound up, and I think this is really interesting because we often actually talk about the opposite, especially in the context of post-traumatic stress disorder, where the breaks are off. People are feeling hyper-aroused and reactive, emotionally flooded, and we see that in their brain activity, but here we're seeing the opposite. The brain activity is showing that the breaks are too good. People are reporting that they're feeling numb and detached, so we wanted to delve a little bit further into this ventromedial prefrontal cortex region and see how it communicated with other regions of the brain.

Dr. Lauren Lebois (13:39):

We went ahead and also looked at our resting state data and the functional connectivity there. This is a measure of whether different brain regions are active at the same time or not. The idea is if they're

active at the same time, they're presumably involved in a similar function. What we saw was that if people had more dissociative symptoms, their ventromedial prefrontal cortex actually had decreased connectivity with two other regions of the brain, orbital frontal cortex and right lobule 8A in the cerebellum. If we extrapolate a little bit from there, this might mean that the ventromedial prefrontal cortex is communicating less with these regions of the brain, and maybe that's underlying some of these feelings that people get when they're dissociative of the perceptional and effective distortions that they experience.

Dr. Lauren Lebois (14:31):

That was our first major finding. Then secondly, we showed that dissociation was linked with more severe later psychiatric outcomes three months after these folks had experienced their traumatic event. In both the self-report surveys of dissociation and in the ventromedial prefrontal cortex activity, if people had more of either of those, it predicted more severe PTSD symptoms at three months, and this was distinct from someone's baseline level of post-traumatic stress and also their trauma history.

Aaron van Dorn (15:06):

Are there clinical treatment implications for those biomarkers?

Dr. Lauren Lebois (15:09):

Yes. I think the biggest one that I'd like to emphasize is to encourage clinicians and medical practitioners to screen for dissociative symptoms, to learn about how to assess for it, and if it's appropriate for their context, how to treat it. The lifetime prevalence of PTSD is close to 10% in the general adult population. If almost a third of those people will actually suffer from, as we've talked about, understudied, often misunderstood dissociative subtype of PTSD. Just looking in the context of the US alone, that's almost eight million people. Then even a subset below that are folks who have even more dissociative symptoms going on if you ask a few more questions, reaching levels of complex dissociative disorders. If we omit a conversation about dissociation from our practice, this leaves our patients and clients vulnerable to going down this more severe chronic psychiatric course. That's exactly what we showed in our study. Left untreated, people who have more dissociation after trauma. It's linked to those more severe PTSD symptoms later on.

Dr. Lauren Lebois (16:22):

We want to leave your listeners with a couple of assessment tools for probing dissociation. Two of these are self-report surveys that are freely available online. One is the Cambridge Depersonalization Scale by doctors Sierra and Barios, and also the Multidimensional Inventory of Dissociation by Dr. Paul Dell. If people want to go even more in depth, there's a structured clinical interview for dissociation and dissociative disorders by Marlene Steinberg.

Aaron van Dorn (16:55):

What were the limitations of your study?

Dr. Lauren Lebois (16:57):

Our study was part of the huge Aurora study, which had many different goals and assessed a ton of different symptoms that people could experience after a trauma, so we had a limited amount of time to ask people specifically about dissociation. All the different types of dissociation we talked about at the start with Diana, we couldn't get into all of that. We only got a small slice of what dissociative

experiences people could have after traumatic event. On top of that, we also excluded individuals in ongoing domestic violence situations and those with self-inflicted injuries that brought them to the emergency department, so we may actually have a restriction in the range of our dissociative symptoms because those types of experiences, domestic violence and self-inflicted injuries, are linked to higher levels of dissociation. Like I was saying, we may not have captured people at these higher, more severe levels of dissociation.

Aaron van Dorn (18:00):

What's next for your research?

Dr. Lauren Lebois (18:01):

There are lots of exciting things happening for the broader Aurora study, but specifically for our team at McLean, we are really interested in diving deeper into the full spectrum of trauma related dissociation that we didn't yet have the opportunity to look at in the Aurora study. I'm fascinated by how dissociation can impact someone's sense of self and identity. If you think back to our rollercoaster example at the start, what if in your mind you could not only feel like you were standing safely on the ground watching yourself on the roller coaster, but what if you could take it one step further and actually make it feel like it was someone else entirely riding that roller coaster?

Dr. Lauren Lebois (18:46):

That's exactly the type of dissociation that can occur in dissociative identity disorder, so I'd really like to understand what's happening in the brain that makes it feel like your own body, your thoughts and your feelings aren't yours, and that sometimes they feel like they belong to someone else, but at the same time, you maintain that intact reality testing. It's not psychosis. You're understanding that even though it feels that way, that's not physically possible. That's what we are hoping to look at on the horizon, and to find out what we discover, I encourage your listeners to check out our lab at the Dissociative Disorders and Trauma Research Program at McLean Hospital, and our website is www.ddtrp.com.

Aaron van Dorn (19:37):

Well, Dr. Lebois, thank you for taking the time to speak with us today.

Dr. Lauren Lebois (19:40):

Thank you so much for having me.

Aaron van Dorn (19:42):

Up next, Dr. Ned Kalin. Dr. Kalin, welcome back to AJP Audio for September 2022.

Dr. Ned Kalin (19:46):

Thank you. It's a pleasure to be with you.

Aaron van Dorn (19:48):

I spoke with Dr. Lauren Lebois earlier in this episode about the predictive effects of disassociation on long-term prognosis of those who have suffered a recent trauma. What can you tell us about the paper?

Dr. Ned Kalin (19:56):

Yeah. This is a really interesting and potentially important study that will be coming out in the September issue. Basically what these researchers are attempting to do is to identify behavioral, emotional and brain markers that may predict the likelihood of developing PTSD after an acute traumatic event. This study used a number of individuals. It was a multi-site study called the Aurora study that presented to emergency rooms after acute traumatic experience, then about two weeks later got an MRI in the patients to look at brain activation in relation to what they experienced. Also, they measured symptoms associated with the stress of being acutely traumatized, especially interested in dissociative symptoms and more specifically interested in derealization, which is a sense of being detached from the world type of feeling and experience.

Dr. Ned Kalin (20:53):

What they found was that as they follow these individuals longitudinally, they found that about 55% of the participants had persistent derealization symptoms that occurred during the first two weeks after their traumatic experience, and that these symptoms were also associated with increased activity in a brain region called the ventromedial prefrontal cortex when they looked at fearful faces. This is a part of the brain that has a lot to do with emotion related regulation and processing. There are some other alterations as well that they found in brain function using MRI or functional MRI, but what's most important is that the level of derealization that individuals had that was noted at two weeks was predictive of developing PTSD when individuals were assessed at three months post-trauma.

Dr. Ned Kalin (21:45):

This really suggests that persistent dissociative symptoms and people that have been acutely traumatized are a predictor of long-term outcomes from the standpoint of developing illness, i.e., PTSD. They also found that their brain alterations that they assessed at two weeks were also predictive of developing PTSD, so really important early paper with the idea that we can get better at predicting who's going to develop significant psychiatric disabilities and illness after trauma with the intent of intervening prior to that, with the hope that we could actually change that risk or that likelihood.

Aaron van Dorn (22:25):

Related to Lebois and colleagues, Gregerson and colleagues have an interesting paper looking at potential predictive effects of childhood psychotic experiences in early and middle childhood.

Dr. Ned Kalin (22:33):

This is an interesting paper and also gets at this idea of risk for the development of psychopathology. It's a different type of risk. In this particular study, risk is defined as being a child of a parent that either has schizophrenia or bipolar disorder. We know that this is a risk based on heritability and what we understand about the genetics of these illnesses. What these investigators were interested in was understanding what it meant for offspring of parents that either had schizophrenia or bipolar disorder to have a psychotic experience from the standpoint of its predictive value. First of all, I want to point out that psychotic experiences in childhood are relatively common. They occur more than sometimes we think about. What these researchers found was that children that are at high risk for schizophrenia were significantly more likely to report psychotic experiences compared to controlled children. This was actually in roughly 30% of the children reported psychotic experiences compared to roughly 18% in controlled children.

Dr. Ned Kalin (23:34):

This was not the case for bipolar offspring. That is to say that they did not differ from controlled children in the number of psychotic experiences, but regardless of what your parents suffered from, 30% of these kids reported that their psychotic experiences at seven years of age also persisted and occurred all the way up to 11 years of age. That's important because it turns out that those kids that had psychotic experiences during early childhood that were persistent were more likely to develop other types of psychopathology and meet Axis-1 criteria. I think that this study is important because it gets at risk for developing either schizophrenia or bipolar disorder, it looks at children that have psychotic experiences, and basically the results underscore the importance of persistent psychotic experiences in childhood being more common in schizophrenia at risk children compared to bipolar children, and also being related to the development of psychopathology, and actually the likelihood of developing psychopathology during childhood, if you had persistent psychotic experiences, was about fourfold greater than for controls.

Aaron van Dorn (24:48):

Another large longitudinal cohort study by Kendler and colleagues has a very interesting study design looking at anxiety disorders and major depressive disorder in offspring and parental groups in Sweden. What can you tell us about it?

Dr. Ned Kalin (24:58):

This study is one of numerous studies that Ken Kendler has been involved with, along with the use of the Swedish National Database, which affords an opportunity to look at lots of demographic issues related to psychopathology. In this particular case, the question that was being asked was around understanding more about the heritability, genetic and rearing influences on the intergenerational risk to developing anxiety disorders in comorbid depression. This used a database that contained over two million offspring, which is obviously an extremely large sample, and the design of this is to capitalize on adoption data. In this particular study, what the investigators did was that they looked at different configurations of families, ranging from intact families to families where mom or dad were not present, to families where there was a stepfather or stepmother, or to families that were completely adoptive by using these different parental configurations, one can estimate the relative influences of genes versus rearing on the intergenerational transmission of anxiety disorders in this particular case.

Dr. Ned Kalin (26:18):

What the researchers found were a number of interesting things. First of all, maybe not surprisingly, the highest incidence of anxiety disorders, both in parents and offspring, was observed in families that did not have mothers, as well as in those with stepparents. The lowest incidence of anxiety disorders was found in intact families. Overall, the findings for anxiety disorders showed that there was a correlation between an anxiety disorder and a parent and a child. That is to say that if parents had an anxiety disorders, children were more likely to have them. By using this method of looking at the different levels of genetic relatedness and these family configurations, it was determined that 70% of the relatedness between parents and children was due to genetics, and it was estimated that 30% of this was due to rearing.

Dr. Ned Kalin (27:06):

This is also found for depression, as well as for comorbid depression and anxiety. This is a very interesting design, as you pointed out. It uses an extremely large sample and allows us to gain more insights into the factors that contribute to passing down the likelihood of developing anxiety or

depression, or the comorbidity through families, suggesting that the large part of this is related to genetics, roughly 70%, and 30% related to rearing.

Aaron van Dorn (27:39):

Moving away from the longitudinal studies we just discussed, Chand and colleagues have a paper looking at brain structure and the risk of developing schizophrenia in at risk youth, which used a machine learning approach. What can you tell us about it?

Dr. Ned Kalin (27:49):

Now, this is another interesting study that tries to get at risk, and also one of the longer term implications for this and the other studies we talked about is thinking about novel early interventions once risk is identified. In this particular study, a number of different databases were used to first understand the neural signatures that are associated with schizophrenia and to validate that from other work, and then in more population based samples, including a community sample, to take a look at the extent to which these different neuro-signatures that are associated with schizophrenia are found in these different samples, and also whether or not they're predictive of more serious problems. What these researchers found, and this is building on previous work that they identified using all of the structural alterations in white matter and gray matter, they identified two brain signatures. One was predominantly characterized by reductions in the volume of a number of brain regions, including the thalamus, the nucleus accumbens, prefrontal regions, temporal regions, and insular cortex.

Dr. Ned Kalin (29:04):

They found that roughly 58% of the individuals in the schizophrenia sample had that configuration, whereas 42% of the individuals had what they considered a type two or signature two, which was more specifically characterized by increases in the striatum and internal capsule volumes. After identifying these two different neuro-signatures, they went on to look in these other more population based samples the prevalence of these signatures. What they found was that in a population or a sample that included youth with psychosis spectrum symptoms, they found that the signature one pattern, where there was a more or less reduction across a variety of brain regions in volume, that 40% of youth with psychosis spectrum symptoms had that signature one pattern. That was significantly greater than what was found in the controls in that particular cohort, which was only 23%. Now showing that in this population based sample children with psychotic spectrum disorder or youth with psychotic spectrum disorder were more likely to have this signature one pattern than controls. Interestingly, the second pattern, the signature two pattern, did not differ between with psychosis spectrum and controls.

Dr. Ned Kalin (30:24):

They also then went on to look at a much larger sample from the UK Biobank, and this is now in adult's, not in youth. What they found in that sample, which is not selected for any particular psychiatric illness, is that the signature one pattern was present in 24% of the participants and the signature two pattern was present in 20% of participants, and roughly 45% of participants did not have either signature one or signature two. In both cohorts, these population cohorts, what was interesting is that the signature one pattern was associated with decreased cognitive performance. Also, in the UK Biobank sample, it was associated with higher polygenic risk scores for schizophrenia. I've said a lot here, but I think the bottom line is that these different neuro-signatures were identified to be associated with schizophrenia. The first one, signature one, which is more prevalent and is characterized by volumetric productions across the number of structures, was enriched in youth with psychotic symptoms that are at risk to develop

schizophrenia, and that this pattern also is associated with higher loading for genetic variants that are related to schizophrenia.

Aaron van Dorn (31:41):

Finally, we have Jaffe and colleagues looking at gene expression in PTSD.

Dr. Ned Kalin (31:45):

Yeah. This is another really interesting study using postmortem brain tissue to characterize molecular alterations in specific circuits that we know to be involved with the pathophysiology of PTSD and depression. In particular, these investigators, that is Jaffe and colleagues, used RNA sequencing data to understand alterations in molecular regulation and prefrontal brain regions in the amygdala. The reason that's important is because prefrontal amygdala circuitry is thought to be altered in a variety of stress related disorders, including PTSD and depression. They went to their brain bank, they looked at postmortem brains from individuals that had major depression without comorbid PTSD, individuals that had PTSD with comorbid depression or bipolar disorder or substance use disorder. It's very common as you know, that there are many comorbid conditions with PTSD. They also had a cohort of control brains to compare to.

Dr. Ned Kalin (32:49):

The bottom line is what they found is that when they looked at these different brain regions and looked at messenger RNA, they found a number of alterations. I should say the reason that they looked at mRNA is because mRNA is a reflection of not only the genetic endowment that we inherit from our parents, the structural gene variation, but also mRNA is a product of the environmental interactions with our genome through epigenetics. mRNA measures, at least conceptually, are a reflection of both structural genetic variation and environmentally influenced genetic gene expression.

Dr. Ned Kalin (33:25):

Anyway, what they found was is that when they looked in these brain regions, that there are lots of shared abnormalities across both PTSD and depression, and there are some distinct abnormalities. Importantly, in relation to PTSD, in their analyses, they controlled for important variables, such as antidepressant usage, the presence of opioids in the blood, ways of controlling for, in a sense, these comorbid issues like comorbid [inaudible 00:33:55] or substance abuse. The expression of the genes that were found to be altered fell into interesting categories. One was immune function, another was microglial function, and finally inhibitory neurons, GABA inhibitory neurons. I think the bottom line is that this is data that is showing how within a critical circuit that's critical to both illnesses, depression and PTSD, we can identify alterations in the way genes are working, that there's a lot of shared alterations across these disorders, but there are some distinct ones as well. I would encourage our readership to take a look at this article in more detail if they're interested in the specific genes that were identified.

Aaron van Dorn (34:35):

What draws all these papers together in the September issue?

Dr. Ned Kalin (34:39):

This is, I think, a really interesting set of papers. It combines our traditional phenotype diagnostic measures at different levels of analysis, behavioral with neural circuit and molecular and genetic, so it

really goes all the way from diagnosis, to circuit, to molecules, to genes, to better understand what underlies the illnesses that we work with. It really brings together, I think, nicely and it underscores the importance of combining molecular and neuroimaging measures to better understand mechanisms related to psychopathology. Overall, I think it brings us to the point of thinking about how we get closer to having really sound scientific rationales for developing early intervention strategies that target specific circuits and underlying molecular substrates in ways that are novel and hopefully in ways that are earlier on in the progression of these illnesses, such that we can have a better shot, if you will, in thinking about how to reduce risk for individuals that are at risk.

Aaron van Dorn (35:48):

Well, Dr. Kalin, thanks once again for helping to put the issue into context for us.

Dr. Ned Kalin (35:51):

You're very welcome, and it's pleasure to be talking with you.

Aaron van Dorn (35:54):

That's all for this month's episode of AJP Audio, but the APA has other podcasts you can listen to. This month, Mentally Healthy Nation answers questions about the new number for the national suicide and crisis hotline, 9-8-8, as well as look at its future. Check out that and all the other podcasts offered by the APA at psychiatryonline.org/podcasts, or wherever you normally listen to podcasts. The views and opinions expressed in this podcast are those of the individual speakers only and do not necessarily represent those of the American Psychiatric Association. The content of this podcast is provided for general information purposes only, and does not offer medical or any other type of professional advice. If you're having a medical emergency, please contact your local emergency response number.