JOURNAL OF GAMBLING ISSUES

session

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Session I: Critical issues in the etiology of problem gambling

The neurobiology of pathological gambling

Presenter: Jon Grant

(Introduction.) **Alex Blaszczynski**: The first speaker is Jon Grant. Jon Grant received his JD, which I presume is not juvenile delinquency, from Cornell University in 1992 before going on to get his MPH in public health from Harvard University and his MD from Brown University Medical School in 1999. He's currently a very enthusiastic worker. He's the editor-in-chief of the *Journal of Gambling Studies* and assistant professor of psychiatry and human behavior. I'm not sure whether we separate out psychiatry from human behavior or whether they're the same, but it'll be intriguing to find out. And he's the chief of impulse-control disorders at Brown Medical School and Butler Hospital. It gives me great pleasure to introduce Jon. He'll talk on the neurobiology of pathological gambling. And I'm sure Jon will be too humble to mention it, but he's recently published his work with Marc Potenza on pathological gambling, and it's a good read. Jon.

Jon Grant: Thank you. So, in five or ten minutes all that we know about the biology of gambling addiction. I'm happy that it's only a short amount because the key here, I think, is the take-home message: we're learning a lot more about the biology of what makes someone with a gambling addiction different from somebody without. But we don't know the whole picture, and so I'm not here to say, well, this is the cause. But we get little pieces of the puzzle, which I think are important because as we start to know more, we should be able to fill in that puzzle.

And when I talk about biology, I don't mean at all to suggest that all these other events in people's lives aren't important. As a matter of

fact, I think one of the issues that we don't know yet is how all of the other things that go into developing a gambling addiction—one's upbringing, one's development, one's current situation—how that affects biology. I mean, my grandmother, God rest her soul, could tell you if she met a gambling addict. There's something different about that person, and so this is just one piece of that puzzle, which I want to present to you and let you know that people are thinking about it, people are working hard on it, and we are trying to figure it out.

There are chemicals in the brain called neurotransmitters and early on some researchers were thinking that maybe some of these neurotransmitters are different in people who have a gambling addiction. One of the interesting things that we don't know—I think it is going to be very important—is the answer to the question, are these neurotransmitters different because somebody starts having a gambling addiction, or are they different, and that leads someone to having a gambling addiction? That cause and effect is not clear, but we do have little pieces here.

One of them is serotonin. Everybody talks about serotonin. It's a chemical that's all over the brain and all over the body and it's an easy answer to everything. But what's interesting about this is when we've looked at certain studies with MAOB, which is a peripheral marker, and if I check someone's platelets to see how well their serotonin's functioning, this seems to be a little off in people who have a gambling addiction. When we look at serotonin in the cerebral spinal fluid (which bathes the brain and the spine), it is a little different from that of people who don't have a gambling addiction.

The SSRIs [selective serotonin reuptake inhibitors] are medications that affect serotonin, which are most popularly the antidepressants: Prozac, Paxil; we've all heard about them. These have shown benefit in gambling addiction. That perhaps tells us that serotonin may have something going on in gambling addiction, but again, as part of the puzzle. And none of these act alone. They act in concert with each other.

Dopamine is another great chemical that's involved in the brain, and we associate dopamine with rewarding experiences. When people find something very enticing, the dopamine is activated, so it made sense for researchers to start looking at dopamine. When researchers looked again at cerebral spinal fluid, then dopamine seemed to be a little out of whack compared to people who don't have a gambling addiction.

Most interesting is the case of Parkinson's disease, which has gotten a lot of publicity recently. Parkinson's represents depleted dopamine, so when these patients take medications that increase

dopamine, interestingly enough, and neurologists have been noticing this, many of the Parkinson's patients develop a gambling addiction, even people who have never gambled before. An intriguing concept. Why is this? Why does this happen when we put dopamine in people's brains? We have case reports in the literature: it's interesting and it's intriguing.

Bupropion is a medication with a dopamine effect—it's also called Wellbutrin, Zyban—it goes by a lot of names. It's used to treat smoking problems. It has also been shown in some early studies to be effective against gambling addiction.

And then last are endorphins, the opiate part of the brain, which gets revved up and tells us something's pleasurable. You can see how this is yet another thing that might be involved. And it makes sense that it should be involved because people get that rush, that thrill, and they find it pleasurable when they gamble even though afterwards they'll regret it. We've found out that when you look at different parts of the opiate system, metabolites in the cerebral spinal fluid, again, it's a little out of whack in people who have a gambling addiction. And we have used opiate antagonists, the most widely known being Naltrexone, which is a medication to treat alcoholism and the urges of alcoholism, and we've used that in gambling addiction as well. People say that when they are on the medicine they gamble and it isn't any fun any more. They don't get that rush.

We find that different chemicals may be involved. One of the questions is, are all these equally involved? Are they differently involved in different people? We don't know that yet. But we're getting some indications.

Cognitive testing of people with a gambling addiction shows differences in terms of attention. So is that part of the brain that focuses on attention different in people who have a gambling addiction? It appears to be so. We find that when these people perform tests—computer tests, paper and pencil tests—they don't want to delay gratification. They want something right away. They'd rather take a smaller thing right away than even think about something later on. And that inability to delay gratification may also be at play and that would be a part of the brain that's involved in that.

When we look at arousal and we measure people's blood pressure, their sweating and heart rate and all these, people with a gambling addiction tend to have higher physiological responses when they gamble compared to people who don't have a gambling addiction. Again, pieces of the puzzle.

Interesting aspects have come out of our brain-imaging studies. Marc Potenza at Yale has done a couple of imaging studies. And Marc much regrets not being able to be here. When you look at different tests you're looking for two things, I think, in gambling. One, people who have a gambling addiction probably want to gamble more intensely than people who don't, so you look at that urge state. What is it about these folks? Where in the brain would that be where we intensely want to do something? And then, the other part is their inability to stop; they have more of a difficulty in restraining behavior. Restraint is a normal part of our brain function. When we really want to do something, part of our brain says, "Don't do it. Maybe you shouldn't do it." I mean, that's generally speaking, and if it's not harmful, we say, "OK, do a little bit of it." And then part of the brain says, "Don't," and part of it says, "I want to." One theory about gambling addiction asks if it's the part that wants to be more intense, or is the problem with the part that says, "Don't do it," being out the window and not working, or is it an imbalance in these? Other approaches involve using Stroop tests where you're looking at different colors, and you have to match colors with words; this assesses the part of the brain that can control our impulses.

And the upshot of these pictures is that the ventral medial prefrontal cortex, which is the front part of the lower part of the brain, does not seem to be as activated, and this is the part of the brain that would say, "Don't do it. Not a good idea." It seems to be less activated in people who have a gambling addiction compared to people who don't have a gambling addiction. And when you look at, especially the third picture, when you compare gambling addictions to controls, that's the part of the brain that is less activated in people who have a gambling addiction, and that's the part that would tell us not to do something.

People who have manic depression, which is an illness defined by its impulsivity, tend to have the same finding on fMRI [functional magnetic resonance imaging] brain scans. So our brain doesn't understand gambling as opposed to anything else, but it understands impulses, and it understands not being able to control impulses. It's not surprising that the same part of the brain in, say, manic depression that is involved in impulsivity would be involved in gambling impulsivity too. That's not to say that they're the same illness, but perhaps the same part of the brain is involved when someone cannot control impulses. You could look at this in terms of sexual addictions and drug and alcohol addictions, and if you could do the same scan, most likely the same part of the brain would be at work, the part that says, "I can't control myself when I really want to do something." Another of Marc's studies with people turned on to gambling found that the part of the brain that says don't do something tends to be deactivated, and you don't see that when you have people scanning under other conditions.

What we now know from brain scans and from studies of the neurotransmitters is that something is different, and while that may be obvious we have some clues about *what* may be different. I think part of what we're going to have to do in the future is understand how either all these other factors in people's lives create the difference, or the difference creates those other factors: as in which way the arrows go, cause or effect. And then, most importantly for the people who suffer, what the heck can we do about it once we know that the brain is actually different? Can we actually—through treatments, through therapy, and through medication—start making the brain return to how a normal control's brain would look?

Alex Blaszczynski: Thanks very much, Jon. It's an interesting area in terms of neurobiology and its implication with gambling behavior. I'd like to come back to the Parkinson's disease issue because I'm reviewing the literature at the moment. I've seen a case of a 56-year-old, I think it was, a chap with atypical Parkinson's who exhibited the same issues of sudden onset of pathological gambling in relation to medication. But when you analyze it from a clinical perspective, there's a question raised because he was attempting to deal with the implications of his Parkinson's. He had clear ideas that he wanted to be a businessman, and, in his eyes, he was a failure to his wife because he hadn't actually put into effect some of his brilliant ideas. And his gambling was an attempt to get money quickly so that he could then start to advertise or market his particular product. And I raised the question with him, was it the medication and the change, and we started to look at the correlation between medication and behavior change. And that didn't seem to be a one-to-one relationship.

But I'm wondering whether these other particular cases of Parkinson's and gambling are an artifact of the fact that people haven't explored the clear relationship and implications of Parkinson's coping mechanisms and gambling behavior, and as a consequence there is an inconsistent picture.

Jon Grant: I think that may be the case with some folks, of course, because when you read reports that are written largely by neurologists in neurology journals, oftentimes they don't go into incredible detail about understanding how people are coping with their illness. In my personal experience, I've seen folks who have not had a gambling problem. They've been on Parkinson's meds for many years. They've been stable. Their mood has been good. They've been active in the community. And I've had a couple patients whose neurologists changed them over to certain Parkinson's medication, and the patients wanted to go to the casino and start gambling.

Interestingly enough, there are problems not just with gambling. In general, these medications may produce a general lack of impulse control. Some of my patients have started exposing themselves. They've been inappropriately sexual with neighbors. It's not as if it's just going to cause gambling, but it may be more a lack of impulse control. And then it's a question of which target they seem to light on for whatever reason, maybe because they remember having gambled in the past, and they enjoyed it or something such as that. But it seems as if there is a global impulsivity.

Alex Blaszczynski: In terms of the disregulation, what, Jon, is the process by which a gambler gambles for a period of time, possibly on average five to nine years at social levels, and then starts to develop problems? What is it about the neurotransmitter system that becomes disregulated? What's the actual event that causes that, and does it spontaneously correct when the person goes into spontaneous recovery? In a sense, I'm trying to look at the triggering factors that cause the particular pathological process.

Jon Grant: That's a good one too and would be a great research question, which we have to address. We're not sure, for instance, why somebody can go nine years and gamble harmlessly and then suddenly develop an addiction, and somebody else can come in after three months and say, "I'm addicted. This is outta control."

I actually saw somebody the other day who started gambling and within two months was going every single day for 12 hours a day. And I thought, that's intense, and that's quickly intense. Why is that person different—what is going on? Are the neurotransmitters so easily beaten down by those events in that person's brain? Maybe, as we have talked about, for genetic reasons, maybe life events—maybe there have been enough stresses on the human body in that person that, over time, the stress of the financial problems and the anxiety and everything has beat it down more? We don't know yet.

That's a great $10 million question because it would help us know how to get back to interventions. If you know that some people are more at risk for having their transmitters out of whack early, you'd intervene earlier. If you think most people don't have a problem for nine years, your interventions don't have to be as intensive, perhaps, but we don't know any of that yet. That's not satisfying, is it? See, it's not satisfying for me. I'm always happy about where the state of science is today because I think we're much better off than we were five, particularly, ten years ago, but it's still not satisfying in the sense that you get to go home and think, "OK. Yeah. I got the answer. That makes sense."

Alex Blaszczynski: Thanks very much, Jon. Being lucky at Harrah's last night, I won $1 million. I'm going to give it to Jon at

lunchtime, and after lunch I'm going to ask him to apply it to a research methodology or design that would address some of these particular questions.

[End of session.]

For correspondence: grant045@umn.edu

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