

## Session 1

Adam Lake: How does this "brain switch" conceptual model mesh with the spectrum of illness where a good number of people with milder use disorders aren't irreversibly "broken"?

- Dr. Levounis: Excellent point--especially for alcohol. Most likely the "classic brain switch" has not been flipped on for people with milder conditions.

Adam Lake: Is it still best understood as a "switch" as opposed to a related spectrum? I understand the finality of a "switch" in someone with very severe disease

- Dr. Levounis: Adam, there is evidence of some discontinuity, maybe not as strong as once thought, but still some "genou" in the hypothetical continuum. In clinical practice, this translates into the long-term increased vulnerability to relapse.

Bruce Burns: Does insula help more to suppress or promote the priorities from the different signals?

- Dr. Levounis: Bruce, both. It "decides" what's "worth" going through and perhaps promoting.

Yngvild Olsen: I have wondered whether part of the vulnerability to addiction may involve people whose antireward circuits are heightened at baseline, even before exposure to substances, such that the substances don't activate the reward circuits to the same extent as in people without that vulnerability but perhaps "normalize" the overall system - I've had so many patients tell me that they didn't feel "normal" or "right in their skin" until the first time they used a substance. Thoughts?

- Yngvild Olsen: The hyperkatefeia concept really makes the case for more prevention
- Adam Lake: I definitely hear the same thing! (then I hear it again when people who use opioids start buprenorphine). It makes me recall the "rat park" experiments
- Dr. Levounis: Hi Yngvild! Yes, this is exactly the whole point of George Koob's "hyperkatefeia."
- Yngvild, it also relates very well to the Self-Medication theory of addiction, see Ed Khantzian's work.

Bezalel Dantz, MD: can you talk more about the antireward system of the brain and how it evolves during the course of addiction