ADHD and Environmental Risk Factors, with Susan Schantz

Ashley Ahearn

Attention deficit/hyperactivity disorder, or ADHD, is one of the most frequently diagnosed neurobehavioral problems in children and is thought to be largely hereditary. But only a small number of cases have been linked to specific genes, leading many researchers to explore the impact of environmental exposures. In this podcast, Susan Schantz discusses how the neurologic effects of lead and polychlorinated biphenyls compare with symptoms of ADHD and what environmental health researchers can learn from those similarities and differences. Schantz is a professor of veterinary biosciences at the University of Illinois at Urbana–Champaign.

AHEARN: It's *The Researcher's Perspective*, I'm Ashley Ahearn.

Attention deficit/hyperactivity disorder, or ADHD, is one of the most frequently diagnosed neurobehavioral problems in children,[1] and yet the causes of ADHD remain a mystery.

ADHD is thought to be largely hereditary,[1] but only a very small percentage of cases have been linked to specific genes,[2] leading more and more researchers to question whether environmental exposures may be at play.

Dr. Susan Schantz recently published two reviews in *EHP* about ADHD,[3,4] one of which explores the possible role of environmental exposures such as lead and polychlorinated biphenyls, or PCBs.

She's a professor of veterinary biosciences at the University of Illinois at Urbana–Champaign.

Dr. Schantz, great to have you with us.

SCHANTZ: Thank you, Ashley.

AHEARN: So attention deficit/hyperactivity disorder, as it turns out, involves a lot more than just what the name suggests. You know, this isn't just about being hyper and having a hard time paying attention.

SCHANTZ: Yes, people know it best as affecting attention, but kids that have ADHD actually have a lot of trouble with what we call "executive functions" as well. And executive functions include things like working memory, planning ability, cognitive flexibility, and response inhibition.

AHEARN: Your expertise is in chemical exposures and how they affect neurodevelopment in animals. So now you're looking at ADHD, and I'm wondering, how did you get from animals to kids?

SCHANTZ: (laughs) Good question. Yes, I've done a lot of work in animals, and I guess the thing that got me interested in ADHD in the first place is all of the work that I've done looking at the cognitive effects of polychlorinated biphenyls, or PCBs, in animal models, because what we found over time, the more work we did, was that PCBs really seemed to be affecting executive function. When we looked at the pattern of the kinds of problems that rats especially were having after early developmental exposure to PCBs, we saw a lot of parallels with the problems that ADHD kids have.

And one of the things that we saw very clearly was that the PCB-exposed rats had trouble on different kinds of learning tests that required them to have good inhibitory control, so they had to be able to refrain from responding when it wasn't appropriate, so to speak. And we could see that pattern emerging in a number of different contexts—and of course, ADHD kids are impulsive, so that was a very clear kind of parallel that we saw.

AHEARN: How about short-term memory or prioritizing of tasks?

SCHANTZ: Yeah, we've used a test we call "delayed alternation," and it's a spatial working memory task that we've done in both monkeys and rats that have had—well, in our case, early developmental PCB exposure, but other people have done similar studies using lead. What I mean by "working memory" is just the ability to keep something in mind for a very brief period in order to use the information to perform a task.

So for example, in this test the rats have to alternate between two levers, and if they press, say, the left lever first, then the levers retract, and they have to wait for just a few seconds during a delay period, and then the levers come back out, and what they need to do then is press the other lever, the right lever. And if they do that—if they alternate—then they'll receive a food reward. So during that short delay period, which is only a few seconds, they have to remember which lever they just pressed. So that's working memory.

And we found that test to be very sensitive to both lead and PCBs. And in ADHD kids they don't use the exact same test, of course, but they've found that over a number of studies and lots of different kinds of tasks that they've employed that ADHD kids also have trouble with working memory and especially working memory in the spatial domain.

AHEARN: I was really interested in the differences between boys and girls—and it seems that, you know, just as some people might be more genetically susceptible to ADHD, boys may be more vulnerable than girls here. Is that correct?

SCHANTZ: Yes, and that's true of several neurodevelopmental disorders, autism as well, but boys are quite a bit more likely to be diagnosed with ADHD. An interesting parallel actually is that in our PCB studies, for a lot of the types of tasks that we're looking at, we're also seeing that the males seem to be more affected, so this greater sensitivity of the males seems to be another aspect that parallels what you see in ADHD kids.

AHEARN: So, there are different subtypes of ADHD, and I'm wondering, could environmental exposures influence the type of ADHD that someone might have, and could you talk a little bit about those different subtypes?

SCHANTZ: Yeah, that's a really good question, actually, and something that I think will be a really interesting area for research in the future. So, there are three subtypes of ADHD that have been identified—first what's called the "combined type" is children that are both inattentive and impulsive, and the majority fall into that category; but there's two other subtypes that have been identified, one that's primarily inattentive and not so much impulsive, and one that's primarily impulsive. And that differs a little between boys and girls, too. Girls are more likely to have the inattentive type, whereas boys are more likely to have the combined type or the impulsive type.

And when you look at the different cognitive functions or executive functions that are affected with, for example, lead and PCBs, there are some differences between the two chemicals. So it's interesting to speculate that if chemicals are involved in ADHD that maybe some of the heterogeneity you see in kids is because of different chemical exposures.

AHEARN: So, what are the mechanisms here? You know, when you're exposed to lead or PCBs, what happens, and how are those results similar to the problems we're seeing in children with ADHD?

SCHANTZ: Well, we don't know everything about the mechanism of action by any means for these chemicals, but one thing that lead and PCBs share in common is that they both affect catecholamine systems in the brain, especially the dopamine neurotransmitter system, and they reduce the activity or function of that system, and that parallels what seems to be going on with ADHD. We also don't understand completely the underlying neurochemistry that causes ADHD, but two of the drugs that are most effective in treating ADHD are methylphenidate and amphetamine, and these are both drugs that increase the release of dopamine, and in doing so they help to alleviate the symptoms of

ADHD. So, the dominant hypothesis is that it's a problem of hypodopamine[5] function in the brain, very similar to what's occurring with these chemical exposures.

AHEARN: How is your research being received by experts in the ADHD community? I would think that comparing kids with ADHD to rats that have been exposed to chemicals could be kind of touchy.

SCHANTZ: (laughs) I think that our research is generating more interest actually among people that are looking at effects of environmental exposures in children. And the fact that we're seeing these parallels in animal models has caused people that have human cohorts where they're looking at exposure to PCBs or lead or other contaminants now like pesticides and phthalates are thinking, you know, "We need to look and see if these exposures are increasing the risk for ADHD or are causing the children to have a behavioral profile more like ADHD with attention problems and executive function problems."

AHEARN: Dr. Schantz, thanks so much for being here.

SCHANTZ: Thank you, Ashley. It was a pleasure to do this.

AHEARN: Dr. Susan Schantz is a professor of veterinary biosciences at the University of Illinois at Urbana–Champaign.

And that's *The Researcher's Perspective*. I'm Ashley Ahearn. Thanks for downloading!

References and Notes

[1] NIMH. Attention Deficit Hyperactivity Disorder [website]. Updated 27 Sep 2010. Bethesda, MD:National Institute of Mental Health. Available: http://tinyurl.com/asvh7f [accessed 3 Nov 2010].

[2] Faraone SV, et al. Biol Psychiatry 57(11):1313–1323 (2005); doi:10.1016/j.biopsych.2004.11.024.

[3] Eubig PA, et al. Environ Health Perspect 118(12):1654–1667 (2010); doi:10.1289/ehp.0901852.

[4] Aguiar A, et al. Environ Health Perspect 118(12):1646–1653 (2010); doi:10.1289/ehp.1002326.

[5] That is, dopamine is either decreased in amount or is not functioning properly.

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