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# Researchers find link between nicotine addiction and autism

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Scientists have identified a relationship between two proteins in the brain that has links to both nicotine addiction and autism. The finding has led to speculation that existing drugs used to curb nicotine addiction might serve as the basis for potential therapies to alleviate the symptoms of autism.

The discovery identified a defining role for a protein made by the neurexin-1 gene, which is located in brain cells and assists in connecting neurons as part of the brain's chemical communication system. The neurexin-1 beta protein's job is to lure another protein, a specific type of nicotinic acetylcholine receptor, to the synapses, where the receptor then has a role in helping neurons communicate signals among themselves and to the rest of the body.

This function is important in autism because previous research has shown that people with autism have a shortage of these nicotinic receptors in their brains. Meanwhile, scientists also know that people who are addicted to nicotine have too many of these receptors in their brains.

"If we were to use drugs that mimic the actions of nicotine at an early time in human brain development, would we begin to help those and other circuits develop properly and thus significantly mitigate the deficits in autism? This is a novel way of thinking about how we might be able to use drugs to approach autism treatment," said Rene Anand, associate professor of pharmacology in Ohio State University's College

of Medicine and principal investigator of the research.

"It would not be a complete cure, but right now we know very little and have no drugs that tackle the primary causes of autism."

The drugs in question are known as cholinergic agents, which interact with the brain to counter nicotine addiction. Anand said the medications could be retailored for use in children in an effort to increase the level of neurexin-1 beta protein in the brains of people with autism.

More neurexin would in turn not only enhance the presence of nicotinic acetylcholine receptors, but also a host of other proteins that are important for the proper formation and maturation of synapses. Proper synapse function is critical to the nervous system's ability to connect to and control other systems of the body.

"Now that these associations have been made, we believe that nicotine in smokers' brains possibly increases the level of neurexin-1 and, as a consequence, helps bring more receptors to the synapses and makes those circuits highly efficient, reinforcing the addiction. In autism, we have the opposite problem. We have a lack of these receptors, and we speculate that neurexin levels are lower," he said.

Anand presented the research Monday (11/17) at the Society for Neuroscience meeting in Washington, D.C.

Autism symptoms include impaired social interaction, problems with verbal and nonverbal communication, and repetitive or severely limited activities and interests. An estimated three to six of every 1,000 children are diagnosed with autism, and boys are four times more likely than girls to have the disorder, according to the National Institute of Neurological Disorders and Stroke.

Anand and colleagues were studying drug abuse and addiction when they discovered the neurexin-1 beta protein's relationship to a certain type of nicotinic receptor. The timing of the discovery was key, as it built upon two other research groups' previous observations: The brains of people with autism and other neurological disorders that were examined after their death showed a 60-percent to 70-percent decrease in specific nicotinic receptors, and some patients with autism have mutations in the neurexin-1 gene that suggest the gene's improper functions could play a role in the disorder.

"These have all been 'association studies.' None has been able to prove what causes autism," Anand said. "And then we accidentally discovered that neurexin-1 and nicotinic receptors tangle. So we knew that there was a genetic link to the process leading to synapse formation, and we had nicotinic receptors that had disappeared in the brains of autistic patients. Our finding filled a gap by saying there is a physical and functional association between these two things occurring in the brain."

Neurexin has implications for tobacco addicts, as well, Anand said. Yet another group of researchers recently found that people with a mutation in the neurexin-1 gene were more likely to be smokers, meaning changes in the gene's functions that lead to excess levels of the nicotinic receptors might make people more susceptible to nicotine addiction.

"Our research reveals how changes in the functions of neurexin could affect the guidance of nicotinic acetylcholine receptors to their functional destinations in nerve cells, perhaps increasing receptors in tobacco addicts while decreasing them in autistic individuals, thus increasing susceptibility to these devastating neurological disorders," Anand said.

The finding also has implications for nicotine addiction because drugs known to alter neurexin's guidance of nicotinic receptors within nerve

cells could be used to suppress tobacco addiction.

Source: Ohio State University