NEWS

Autism’s social problems may stem from sense of touch

BY **JESSICA WRIGHT**

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The anxiety and trouble with social skills seen in people with autism stem largely from neurons outside the brain that govern touch, suggests a mouse study published today in *Cell*[1].

Mice lacking the autism-linked gene **MeCP2** in only these touch neurons develop anxiety and social deficits later in life, the researchers found. Conversely, mice that lack MeCP2 in all of their cells except for these neurons show mostly normal social behavior and no signs of anxiety.

“This was remarkable to us,” says **David Ginty**, professor of neurobiology at Harvard University. “It suggests an interesting relationship between normal sense of touch and these more complex behaviors that manifest as anxiety and social interactions.”

Many people with autism report **heightened sensory perception**. They may be acutely aware of sounds or of people or objects touching their skin. Researchers have theorized that this feeling of sensory overload might **make social situations overwhelming** and challenging to navigate.

The new study supports this thinking and suggests that **sensory sensitivity** directly drives social difficulties, at least in some mice. It also hints that treatments aimed at the peripheral nervous system — the set of neurons that connect the brain and spinal cord to limbs and organs — could ease this sensitivity and possibly even social problems and anxiety.

The findings are also an important reminder that the nervous system doesn’t end where the neck begins. “As a scientific community, we have become very obsessed with the brain and not with the parts of the human that interact with their environment,” says **David Moore**, senior lecturer in psychology at Liverpool John Moores University in the United Kingdom, who was not involved in the study.

Touch and go:

Ginty, an expert on the neural circuits that underlie touch, is not an autism researcher. But for several years he had heard reports from colleagues of heightened touch perception in people with autism. “I started thinking that we might be able to make a contribution,” he says.

Ginty and his team assembled mice that carry mutations in various autism-linked genes, including **SHANK3**, **FMR1**, GABRB3 and MeCP2, the gene mutated in the autism-related Rett syndrome.

The researchers found that all of these mutant strains have trouble distinguishing objects by their texture, but can discern them by color or shape. They also jump more readily than controls do in response to a puff of air that tickles the hairs on their back.

The findings suggest that hypersensitivity to touch, which can also make it difficult to discriminate between textures, is a common feature in different forms of autism.

To find the roots of this sensory glitch, the researchers focused on mice lacking MeCP2, which is known to function in all the cells in the body. The researchers engineered two sets of mice that lack MeCP2. In one set, they removed the gene solely from some neurons in the brain and in the other, only from peripheral neurons that relay touch signals.

Only the latter mice are hypersensitive to touch, the study found. These mice are also anxious: They avoid the open arms of a maze raised off the floor (rather than exploring them) and do not adapt to a loud noise. Like mice missing MeCP2 throughout the body, they don’t prefer to interact with another mouse over an object, or with a new mouse over a familiar one. They also do a poor job of building nests for their young.

Sensory overload:

By contrast, mice lacking MeCP2 everywhere except the peripheral neurons show many of the features of Rett syndrome, including a reduced lifespan, breathing difficulties, small brains and motor problems. But they respond normally to touch and show no signs of anxiety and few social problems.

The results suggest that an aberrant sense of touch largely underlies the core social problems associated with autism.

“It’s now an open question whether sensory processing deficits are driving a lot of the symptoms in autism,” says **Mark Zylka**, professor of cell biology and physiology at the University of North Carolina at Chapel Hill, who was not involved in the study.

The researchers found similar results in mice lacking GABRB3 — an autism-linked protein that

helps to dampen signals at neuronal junctions. Mice lacking GABRB3 in their peripheral neurons are also hypersensitive to touch, anxious and have social deficits.

In mice lacking either MeCP2 or GABRB3 in peripheral neurons, the researchers found that signals from the neurons to the spinal cord may run unchecked.

Social cure:

The study hints that sensory problems lead to social deficits only if present early in life. Mice that lose MeCP2 from sensory neurons only in adulthood are hypersensitive to touch, but they are not anxious and for the most part behave typically in social settings.

Likewise, children who cannot distinguish positive touch from negative might have unusual reactions to social contact. “An altered ability to perceive touch will have a huge effect on the development of a child,” Moore says.

Treating sensory sensitivities early in these children may help them better navigate social milestones. The new findings also open the door to drug treatments that act on peripheral neurons even if they cannot breach the blood-brain barrier, which blocks most compounds from entering the brain.

Ginty and his team are trying to pin down the timing of optimal treatment, which may reveal at what age touch perception is most crucial for social development. They are also testing other autism candidates, such as FMR1, SHANK3, **NLGN2** and **NLGN4**, to see whether the importance of peripheral neurons extends to other forms of autism.

“The big, big question that’s going to take a while to unravel is: Why is it that hypersensitivity to light touch leads to alterations in complex cognitive and social interactions?” says Ginty. “There is a lot of space in between there.”

REFERENCES:

1. Orefice L. *et al. Cell* Epub ahead of print (2016) **abstract**