NEWS

Amygdala, the brain’s threat detector, has broad roles in autism

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The amygdala is a deep brain structure about the size and shape of an almond — from which it gets its name. It is commonly described as a center for detecting threats in the environment and for processing fear and other emotions.

Researchers who study the region argue that its function is broader — and that it plays a crucial role in autism.

“Emotion is such a big part in social function,” says **Wei Gao**, associate professor of biomedical sciences at Cedars-Sinai Medical Center in Los Angeles, California. “So I think the amygdala has got to have a big role in the emergence or development of autism-related traits.”

The amygdala is the brain’s surveillance hub: involved in recognizing when someone with an angry face and hostile body language gets closer, tamping down alarm when a honeybee buzzes past, and paying attention when your mother teaches you how to cross the street safely and points out which direction traffic will be coming from — in other words, things people should run away from, but also those they should look toward, attend to and remember.

In that sense, researchers say, this little knot of brain tissue shows just how tangled up emotion and social behavior are for humans. “Important events tend to be emotional in nature,” as do most aspects of social behavior, says **John Herrington**, assistant professor of psychiatry at the Children’s Hospital of Philadelphia in Pennsylvania.

As a result, the amygdala has long been a focus of autism research, but its exact role in the

condition is still unclear.

To understand how this small structure contributes to autism, researchers may need to take a broad look — at how the amygdala develops over time; its connections to larger brain networks; and its role in other conditions, especially **anxiety**, that often accompany autism.

Altered path:

As far back as the 1950s, studies in primates suggested that the amygdala is a key player in social behavior. If the most dominant monkey in a social group sustains damage to its amygdala, its position in the hierarchy soon plummets.

People who sustain damage to the amygdala have social behaviors reminiscent of autism, such as avoiding eye contact and having difficulty judging facial expressions, but they **do not meet diagnostic criteria** for the condition. Altered amygdala structure or function has been linked to nearly every neuropsychiatric condition, from anxiety and bipolar disorder to **schizophrenia**, making it difficult to say how the region might uniquely explain autism traits.

Beginning in the 2000s, postmortem studies of autism showed that autistic people have fewer neurons in their amygdala than controls do[1]. And some imaging studies have suggested that the structure is unusually small in autistic people's brains[2]. But others suggest that children with the condition often have an enlarged amygdala[3].

These seemingly contradictory findings may be due to differences in the study participants' ages.

"A lot of the structural imaging studies show amygdala enlargement in young kids but not in older kids," says **Christine Wu Nordahl**, associate professor of psychiatry and behavioral sciences at the University of California, Davis MIND Institute.

In typical people, the amygdala continues to grow for longer into adulthood than other brain regions do. In people with autism, by contrast, it grows faster than normal in early childhood, up until around age 12, and then tapers off, and it may even shrink.

"It's not necessarily a single time point that's different in people with autism; it's really more of the growth trajectory," says **Cynthia Schumann**, associate professor of psychiatry at the University of California, Davis.

Schumann's studies of postmortem brain tissue show the same pattern: In young autistic children, the amygdala **contains more neurons** that make more connections than those of controls do; this excess disappears in older children.

Emotion attention:

In 2000, British researcher **Simon Baron-Cohen** published an influential paper detailing his 'amygdala theory of autism.' He argued that diminished amygdala function hinders autistic people's ability to pay attention to and interpret social information[4].

But the picture soon grew more complex. For example, one 2005 study showed that when evaluating facial expressions, autistic people show less activation in their amygdala than controls do. However, when they look at the eye region of a face, their amygdala lights up more strongly than that of controls. In fact, there is some evidence that their difficulty interpreting emotions may result from **excessive activation of the amygdala**.

The amygdala is not the sole center of emotion processing, however. "More and more evidence suggests that it's not working alone; it's actually working as a hub of a big distributed network," Gao says.

For example, the amygdala links to the hippocampus to mark emotionally important events in the memory, to the brain stem to coordinate fight-or-flight responses to dangerous situations, and to the **prefrontal cortex** to modulate and control emotional responses.

Making connections:

Some studies suggest that weak connections between these regions might explain the social difficulties in autistic people.

In a 2016 paper, for example, Nordahl and her colleagues reported that autistic boys with the weakest connectivity between these regions also have the **most severe autism traits**. In a follow-up study published this year, they showed that altered connectivity of the amygdala is more pronounced in autistic girls than in autistic boys[5].

Connections between the amygdala and the prefrontal cortex, a region involved in orchestrating complex tasks, appear to be especially important for regulating emotions and are weaker in those with autism[6]. **Kevin Pelphrey** and his team are investigating whether cognitive behavioral therapy **strengthens these links**.

Connections between the amygdala and prefrontal cortex are likely to have roots in infancy and toddlerhood. In newborns, the amygdala has strong connections to sensory and motor regions of the brain. That is itself a surprising finding, because relatively few long-range connections exist in the newborn brain, Gao says.

But over the first two years of life, the amygdala's connections to these sensory and motor areas

diminish, and the amygdala forms **connections to the prefrontal cortex** that look similar to the circuits responsible for regulating emotions in adults. “This might be the critical period for such capability emerging,” Gao says. It is also the period during which early autism signs unfold.

Anxiety link:

Some researchers are investigating the links between the amygdala and conditions that often occur along with autism. But the increasing recognition that autism is often **accompanied by anxiety** poses a new conundrum for scientists studying the amygdala: Social difficulties in autistic people are linked to diminished amygdala activity, but anxiety is associated with increased activity in the region.

In a 2016 imaging study, Herrington and his colleagues found that in people with autism, the amygdala seems more involved in anxiety than in social difficulties[7]. The following year, they showed that children who have **both autism and anxiety** have a smaller amygdala than controls do, but that the region is of average size in those with autism alone.

“Maybe the amygdala is doing something different in those kids” who have both conditions, Nordahl says.

Nordahl’s studies suggest that sex may also be a factor. Among 3-year-olds with autism, **girls with anxiety** have an **enlarged right amygdala**, but boys with anxiety do not. (In boys, a portion of the prefrontal cortex appears to be linked to the anxiety.)

Working out the links between autism, anxiety and other emotions may require an even closer look at the amygdala. Though it is a small structure, the amygdala is made up of subunits, each with distinctive cell types, chemistry and connections. “It may well be that there is a part of the amygdala that’s involved in social behavior that’s distinct from a part of the amygdala that’s involved in emotion processes,” Herrington says.

Researchers have been working to develop techniques to **distinguish different parts** of the amygdala in imaging and other studies, which could help tease apart their different functions. One such study suggests that a chunk of the amygdala called the basolateral nucleus may be **linked to anxiety** and **depression** in autistic children.

But parsing these amygdala subunits is difficult, Herrington says: “It’s very challenging, and it’s at the outer limits of what technology can provide for us at this point — which stinks if you’re someone like me.”

REFERENCES:

1. Schumann C.M. and D.G. Amaral *J. Neurosci.* **26**, 7674-7679 (2006) **PubMed**

2. Rojas D.C. *et al. Am. J. Psychiatry* **161**, 2038-2044 (2004) **PubMed**
3. Abell F. *et al. Neuroreport* **10**, 1647-1651 (1999) **PubMed**
4. Baron-Cohen S. *et al. Neurosci. Biobehav. Rev.* **24**, 355-364 (2000) **PubMed**
5. Lee J.K. *et al. Biol. Psychiatry Cogn. Neurosci. Neuroimaging* **5**, 320-329 (2020) **PubMed**
6. Pitskel N.B. *et al. Dev. Cogn. Neurosci.* **10**, 117-128 (2014) **PubMed**
7. Herrington J.D. *et al. Soc. Cogn. Affect. Neurosci.* **11**, 907-914 (2016) **PubMed**