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PRESS RELEASE (2026/01/15)

New synaptic formation in adolescence challenges conventional views of brain development

Findings may offer new hope for understanding the biological basis of schizophrenia and other neurodevelopmental conditions

Fukuoka, Japan—Adolescence marks an important transition not just socially and physically, but neurologically. During this period, higher cognitive functions such as planning, problem-solving, and decision-making gradually mature. Yet, the underlying mechanisms of neural circuit development remain poorly understood.

Key to this process are synapses—the functional connections between neurons allow information to flow through the brain. Previously, it has long been hypothesized that synapse numbers increase during childhood and then decrease during adolescence. It has also been proposed that excessive "synaptic pruning," a process that refines neural circuits by eliminating unused or weak connections, may lead to neuropsychiatric disorders. One example is schizophrenia, a condition characterized by hallucinations, delusions, or disorganized thinking.

A research team from Kyushu University now challenges this long-held view. In a study published in *Science Advances* on January 14, the researchers found that rather than simply cutting back, the brain also forms new, high-density clusters of synapses on specific segments of dendrites during adolescence.

"We did not set out to study brain disorders," says Professor Takeshi Imai at Kyushu University's Faculty of Medical Sciences.

"After developing a high-resolution tool for synaptic analysis in 2016, we looked at the mouse cerebral cortex out of curiosity. Beyond seeing the beauty of the neuronal structure, we were surprised to discover a previously unknown high-density hotspot of dendritic spines, the tiny protrusions in dendrites where excitatory synapses are formed."

The cerebral cortex is composed of six distinct layers that form highly complex neural circuits. Imai and his team focused on Layer 5 neurons, which integrate diverse inputs and transmit the final cortex output, serving as a key gatekeeper of cortical processing.

Using SeeDB2—the tissue clearing agent Imai's team developed—together with super-resolution microscopy, the researchers looked deep into transparent brain samples. For the first time, they comprehensively mapped the distribution of dendritic spines across entire Layer 5 cortical neurons.

This analysis revealed an unusually high-density "hotspot" within a specific region of the dendrite, known as the apical dendrite of Layer 5 neurons. Developmental analyses further showed that this spine hotspot is absent during early life and emerges during adolescence.

To further study when this spine density hotspot forms during development, the researchers tracked the dendritic spine distribution across developmental stages. In two-week-old mice, before weaning, spines were distributed relatively uniformly across the dendrites. In contrast, between three and eight weeks of age, spanning early childhood to adolescence, spine density increased selectively in a specific region of the apical dendrite, ultimately leading to the formation of a high-density hotspot.

“These findings suggest that the well-established ‘adolescent synaptic pruning’ hypothesis needs to be reconsidered,” says Imai.

“While synaptic pruning occurs broadly across dendrites, synapse formation also takes place in specific dendritic compartments during adolescent cortical development. Disruption of this process may be the key factor in at least some types of schizophrenia,” says Ryo Egashira, the study’s first author and a graduate student at Kyushu University's Graduate school of Medical Sciences when the research was conducted.

To explore this possibility, the team examined mice carrying mutations in genes linked to schizophrenia, such as *Setd1a*, *Hivep2*, and *Grin1*. While dendritic spine density remained normal until two to three weeks after birth, spine formation during adolescence was markedly impaired by the mutations of these genes, resulting in the failure of proper hotspot formation.

For many years, the disorder has been linked primarily to excessive pruning of dendritic spines. The new findings offer a new perspective on schizophrenia's origins or pathology, suggesting that impaired synapse formation during adolescence may be a key. However, it should be noted that the study examined the developmental process only in mice, and it remains unclear if similar mechanisms are at work in primates and humans.

“Moving forward, we hope to identify which brain regions are forming these new synaptic connections during adolescence,” says Imai. “That will tell us what circuits are actually being built during this developmental window. Understanding how and when these connections form can advance our knowledge of both brain development and the mechanisms underlying neuropsychiatric disorders.”

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For more information about this research, see “Dendritic compartment-specific spine formation in layer 5 neurons underlies cortical circuit maturation during adolescence,” Ryo Egashira, Meng-Tsen Ke, Nao Nakagawa-Tamagawa, Satoshi Fujimoto, Shigenori Inagaki, Tsuyoshi Takagi, Tsuyoshi Miyakawa, Yoshiaki Tagawa, and Takeshi Imai. *Science Advances*, https://10.1126/sciadv.adw8458

About Kyushu University

Founded in 1911, Kyushu University is one of Japan's leading research-oriented institutions of higher education, consistently ranking as one of the top ten Japanese universities in the Times Higher Education World University Rankings and the QS World Rankings. Located in Fukuoka, on the island of Kyushu—the most southwestern of Japan’s four main islands—Kyushu U sits in a coastal metropolis frequently ranked among the world’s most livable cities and historically known as Japan’s gateway to Asia. Its multiple campuses are home to around 19,000 students and 8,000 faculty and staff. Through its VISION 2030, Kyushu U will “drive social change with integrative knowledge.” By fusing the spectrum of knowledge, from the humanities and arts to engineering and medical sciences, Kyushu U will strengthen its research in the key areas of decarbonization, medicine and health, and environment and food, to tackle society’s most pressing issues.

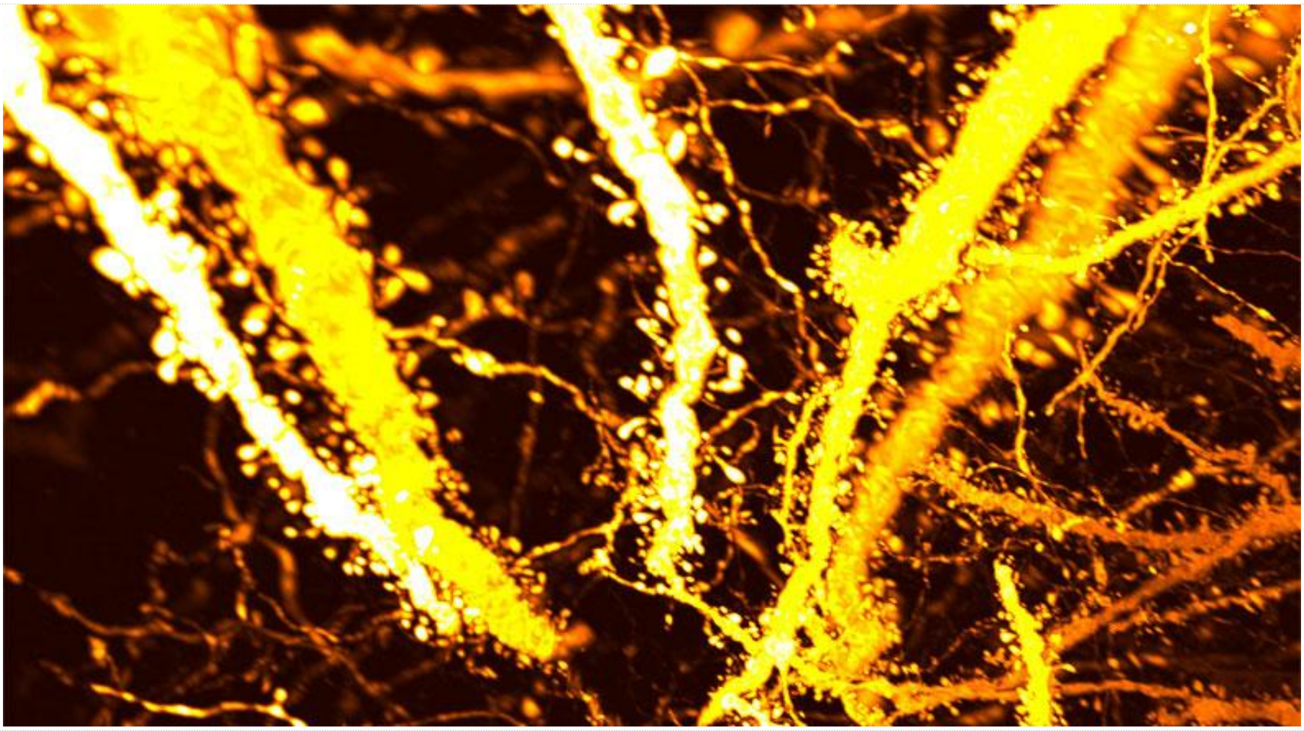

Fig. 1. New synaptic formation in adolescence challenges conventional views of brain development
This image shows densely accumulated dendritic spines. Researchers from Kyushu University discovered a previously unrecognized synaptic "hotspot" that forms during adolescence, challenging the long-held view that adolescent brain development is driven mainly by synaptic pruning.

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