NEWS

Fragile X mice marked by immature synapses

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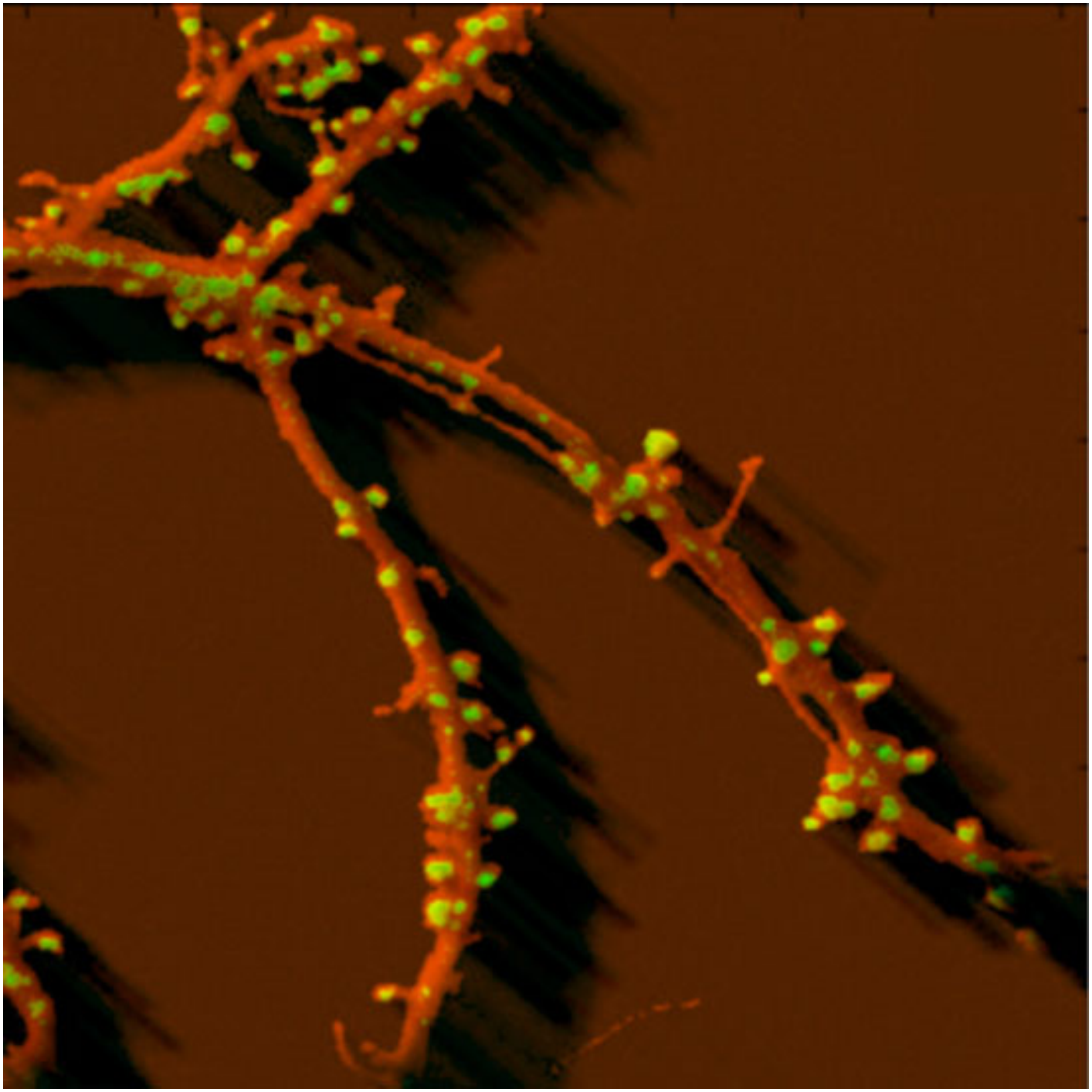

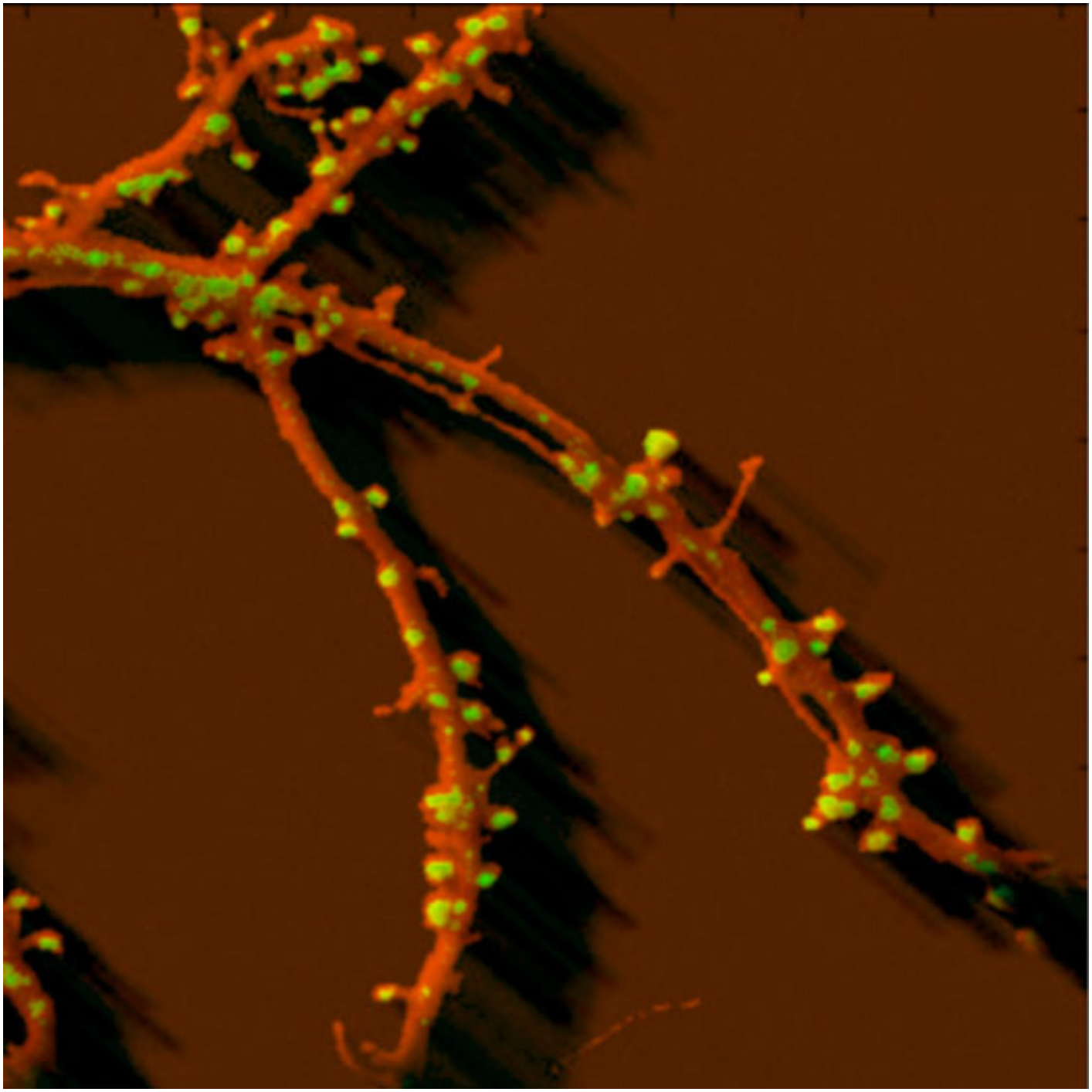

E. Korkotian and M. Segal, The Weizmann Institute

Young mice that mimic fragile X syndrome — an inherited form of mental retardation often accompanied by autism — have immature and unstable dendritic spines, the neuronal branches that receive signals from other cells, according to unpublished research presented Tuesday at the **Society for Neuroscience meeting** in Chicago.

Because these defects are seen during a critical period of learning, they could prevent developing brain cells from linking up to appropriate brain circuits, says lead investigator **Carlos Portera-Cailliau**, assistant professor of neurology and neurobiology at the University of California, Los Angeles. "This presumably has serious consequences for the ability of these mice to learn," he says.

Postmortem brains of adults with fragile X syndrome[1] and adult mouse models of the syndrome[2] have shown longer and more dense dendritic spines.

The new work is the first to look at dynamic changes of the spines *in vivo*, when brain circuits are still intact. It's also the first to look in young animals. As with autism and other forms of mental retardation, symptoms of fragile X syndrome appear early in childhood. "It would be nice to know when the first defect occurs," Portera-Cailliau notes.

In the developing brain, dendrites are constantly reaching out to form connections with other nearby cells.

"Those connections are often very unstable — they appear and reappear, and there's a fine-tuning of that connection until a mature synapse happens," Portera-Cailliau explains.

Using high-resolution two-photon imaging in anesthetized mice that lack the FMR1 gene, the researchers tracked the development of dendritic spines in the mouse brains for the first two to three weeks of their life.

In contrast to previous studies, his team did not find an increase in spine density in these young mice. But dendrites in these mice turn over more rapidly than in controls, preventing them from making as many mature connections.

Because researchers have identified spine defects in various disorders including autism, "this is potentially a final common pathway," Portera-Cailliau says. "Understanding this defect in fragile X syndrome may help understand a variety of other similar disorders."

References:

1.

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2.

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