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Increased neural excitability and glioma synaptic activity drives glioma proliferation in human cortex

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Abstract

Adult gliomas are incurable primary brain cancers that infiltrate healthy brain and incorporate into neural networks. Gliomas can be classified as low grade or high grade based on histopathological and molecular features, which broadly predicts their aggressiveness. Here we performed patch-clamp electrophysiological recordings from pyramidal neurons and glioma cells from individuals with either low- or high-grade glioma. We find that the biophysical properties of human pyramidal neurons within glioma-infiltrated cortex differ according to tumor grade, with neurons from high-grade glioma being more excitable than those from low-grade glioma. Additionally, glioma cells within high-grade tumors have smaller, longer synaptic responses. Increased neuron-glioma network activity within human high-grade tumor tissue leads to increased glioma proliferation, suggesting that the hyperexcitability of pyramidal neurons in human high-grade glioma may drive tumor growth. Combined, our findings illustrate that high- and low-grade glioma differentially hijack neural networks.