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## Effects of N-6 essential fatty acids on glioma invasion and growth: experimental studies with glioma spheroids in collagen gels.

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### Abstract

**OBJECT:** Intracranial infusions of gamma-linolenic acid (GLA), an essential fatty acid, have been used as an adjuvant therapy following malignant glioma resection; however, little is known about the dose response of glioma cells to this therapy. In this in vitro study the authors address this important pharmacological question.

**METHODS:** Glioma spheroids derived from U87, U373, MOG-G-CCM, and C6 cell lines were grown in collagen gel and exposed to a range of GLA concentrations (0-1 mM) for 5 days. The diameter of glioma spheroids was measured, the apoptotic index was assessed using both the terminal deoxynucleotidyl transferase-mediated deoxyuridine triphosphate nick-end labeling technique and cell morphological testing, and the levels of proliferating cell nuclear antigen were also measured.

**CONCLUSIONS:** The dose-response patterns were similar for all four glioma spheroids. Low concentrations of GLA (<100 microM) increased both apoptosis and proliferation with a net increase in tumor growth and invasion, whereas high-dose GLA (>100 microM) significantly impaired spheroid cell growth. The proliferative effects of low-dose GLA could be a hazard in the clinical treatment of malignant glioma; however, because of the low toxicity of GLA against normal cells, local delivery of millimolar doses of GLA could significantly reduce tumor size.

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