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Reproductive factors and hormone use and risk of adult gliomas

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Abstract Previous research suggests there may be a hormonal influence on glioma risk as evidenced by lower rates in females, change in incidence rates around ages at menarche and menopause, and presence of hormone receptors in glial tumors. Using the large San Francisco Bay Area Adult Glioma Study, we investigated whether reported reproductive factors and hormone use were associated with gliomas overall or with histologic subtypes among female cases ($n = 619$) and controls ($n = 650$). We found that reproductive factors were generally not associated with gliomas. Weak to moderately elevated odds ratios were observed for self-reported later age at menarche (14+ vs. 12–13 years old: adjusted odds ratio (AOR) = 1.39, 95% confidence interval (CI): 1.02–1.89), particularly for non-glioblastoma histologies (AOR = 1.64, 95% CI: 1.11–2.43). Inverse associations were observed for ever self-reported use of exogenous hormones (oral contraceptive use: AOR = 0.72, 95% CI: 0.53–0.99; postmenopausal hormone use: AOR = 0.56, CI: 0.37–0.84). However, cumulative hormone exposure defined multiple ways demonstrated no clear pattern of association. The results of this study suggest that any protective effect of hormones on gliomas may be limited to exogenous hormones, but a more detailed history of exogenous hormone use is needed to confirm findings.

Keywords Reproductive factors · Gliomas · Case–control study · Exogenous hormone use

Abbreviations
GBM Glioblastoma
OR Odds ratio

Introduction

Hormones play a critical role during brain development in-utero [1, 2], appear to work as a neuroprotectant via estrogen-receptor independent pathways in brain degeneration [3], and may reduce the risk of death and degree of disability in cases of traumatic brain injury [4]. Whether similar hormonal pathways are involved in the etiology or progression of brain cancers is unknown, but cell cultures and animal studies demonstrate evidence of estrogen directly killing glioma cells [5] and inhibiting the growth of gliomas [6, 7], the most common and deadly brain tumor. Plausible mechanisms by which sex hormones may play a role in gliomagenesis have been postulated. For example, estrogen can inhibit cell cycle entry by increasing mitogen-activated protein kinase (MAPK) levels in astrocytes and stimulating the AKT/PIP pathway to assist in cell cycle control [8]. Other plausible mechanisms include an estrogen–astrocyte–TGF-β1 pathway [9] and melatonin-driven neuroprotection via aromatase [10, 11].

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