Anti-anxiety drug may improve brain cancer survival chances

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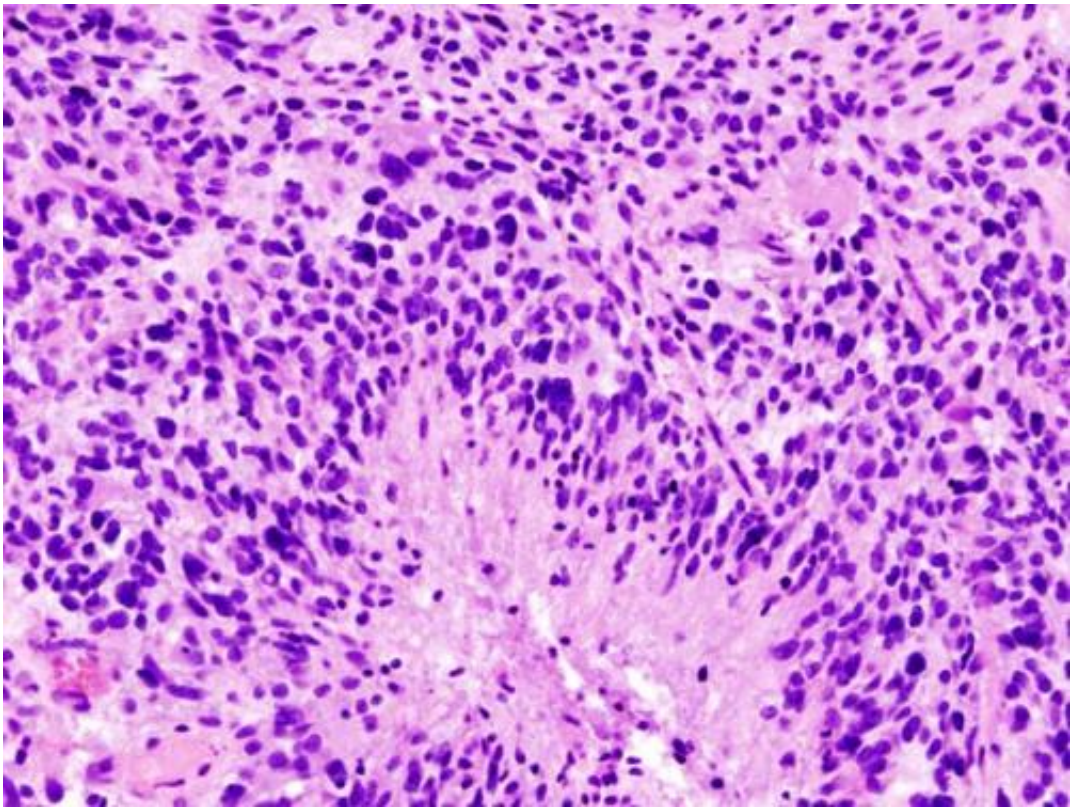

Glioblastoma (histology slide). Credit: Wikipedia/CC BY-SA 3.0

A new study shows that cerebrospinal fluid reduces current treatment efficacy in brain cancer and identifies new therapeutic opportunities.

Cerebrospinal fluid, the clear colorless liquid that protects the brain, also may be a factor that makes brain cancers resistant to treatment,

Australian researchers led by Associate Professor Cedric Bardy at the South Austraila Health and Medical Research Institute (SAHMRI) and Flinders University reveal in the journal Science Advances.

Reporting how this occurs, the study, titled "Human cerebrospinal fluid affects chemoradiotherapy sensitivities in tumor cells from patients with glioblastoma," in *Science Advances* shows that a decades-old anti-anxiety drug can improve the effectiveness of chemo-radiotherapy towards glioblastoma, or GBM, the most common and lethal brain cancer.

Brain cancers kill more children and adults under 40 than any other cancer. They are resistant to therapies that kill cancers elsewhere in the body. The study team speculates that unique brain features might contribute to this.

The collaborative Australian team of neurobiologists, neurosurgeons and oncologists tested the effect of the precious resource of human cerebrospinal fluid on the growth of tumor cells collected from 25 local patients with glioblastoma.

Among their findings, the tumor cells quickly changed their identity and became more resistant to radiation and the drug temozolomide, which are mainstays of glioblastoma therapy.

Associate Professor Cedric Bardy says, "Glioblastoma kills so many people who are otherwise fit, healthy and young, within months. This is a horrible disease, and the treatments available are just not effective enough despite serious side effects.

"This study helps us understand the limitations of the current chemotherapies and provides new hope for repurposing a class of drugs that could be added to the standard of care. We are working hard now to try this on patients in a clinical trial."

Investigating the molecular basis for these changes, the team found glioblastoma cells exposed to cerebrospinal fluid were more resistant to ferroptosis, a form of therapy-induced cell death.

Importantly, they showed that trifluoperazine, an anti-anxiety drug used since the 1950s, could re-sensitize glioblastoma cells to both therapies. In contrast, trifluoperazine was found not to harm healthy brain cells. The researchers concluded that combining trifluoperazine with standard care may improve GBM patient survival.

More information: Brett Stringer et al, Human cerebrospinal fluid impacts chemoradiotherapy sensitivities in tumour cells from glioblastoma patients, *Science Advances* (2023). DOI: 10.1126/sciadv.adf1332. www.science.org/doi/10.1126/sciadv.adf1332

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