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## **Glioma-related epilepsy**

Glioma-related epilepsy (GRE) is defined as symptomatic epileptic seizures secondary to gliomas, occurring in nearly 50% of high-grade glioma (HGG) patients and up to 90% in patients with low-grade glioma (LGG). Uncontrolled seizures, which have a major impact on patients' quality of life, are caused by multiple factors.

Glioma-related epilepsy (GRE) is a common symptom in patients with prefrontal glioma. Epilepsy onset is associated with functional network alterations.

Patients with diffuse high-grade gliomas (DHGGs), who received prophylactic anti-epileptic drugs (AEDs) for three months following surgery, were enrolled into the study. The patients were assigned randomly into training (n=166) and validation (n=42) cohorts. Differentially expressed genes (DEGs) were identified based on preoperative glioma-related epilepsy (GRE) history. Least absolute shrinkage and selection operator (LASSO) logistic regression analysis was used to construct a predictive gene-signature for the occurrence of postoperative seizures. The final integrated prediction model was generated using the gene-signature and clinical data. Receiver operating characteristic analysis and calibration curve method were used to evaluate the accuracy of the gene-signature and prediction model using the training and validation cohorts.

A seven-gene signature for predicting the occurrence of postoperative seizures was developed using LASSO logistic regression analysis of 623 DEGs. The gene-signature showed satisfactory predictive capacity in the training cohort [area under the curve (AUC) = 0.842] and validation cohort (AUC = 0.751). The final integrated prediction model included age, temporal lobe involvement, preoperative GRE history, and gene-signature-derived risk score. The AUCs of the integrated prediction model were 0.878 and 0.845 for the training and validation cohorts, respectively.

They developed an integrated prediction model for the occurrence of postoperative seizures in patients with DHGG using clinical and RNA-Seq data. The findings of this study may contribute to the development of personalized management strategies for patients with DHGGs and improve our understanding of the mechanisms underlying GRE in these patients <sup>1)</sup>.

This study investigated alterations of functional networks in patients with prefrontal glioma and GRE.

Sixty-five patients with prefrontal lobe gliomas were retrospectively assessed and classified into GRE and non-GRE groups. Additionally, 25 healthy participants were enrolled after matching for general information. Imaging data were acquired within 72 h in pre-operation. The sensorimotor network was used to delineate alterations in functional connectivity (FC) and topological properties. One-way analysis of variance and post-hoc analysis with Bonferroni correction were used to calculate differences of FC and topological properties.

All significant alterations were solely found in the sensorimotor network. Irrespective of gliomas located in the left or right prefrontal lobes, the edge between medial Brodmann area 6 and caudal ventrolateral Brodmann area 6 decreased FC in the GRE group compared with the non-GRE group [p

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< 0.0001 (left glioma), p = 0.0002 (right glioma)]. Moreover, the shortest path length decrease was found in the GRE group compared with the non-GRE group [p = 0.0292 (left glioma) and p = 0.0129 (right glioma)].

Conclusions: The reduction of FC between the medial BA 6 (supplementary motor area) and caudal ventrolateral BA 6 in the ipsilateral hemisphere and the shortening of the path length of the sensorimotor network were characteristics alterations in patients with GRE onset. These findings fill in the gap which is the relationship between GRE onset and the alterations of functional networks in patients with prefrontal glioma.

Significance statement: Glioma related epilepsy is the most common symptom of prefrontal glioma. It is important to identify characteristic alterations in functional networks in patients with GRE. We found that all significant alterations occurred in the sensorimotor network. Moreover, a decreased FC in the supplementary motor area and a shortening of the path's length are additional characteristics of glioma-related epilepsy. We believe that our findings indicate new directions of research that will contribute to future investigations of glioma-related epilepsy onset <sup>2)</sup>.

Seizures are common in patients with gliomas; however, the mechanisms of epileptogenesis in gliomas have not been fully understood. A study hypothesized that analyzing quantified metabolites using magnetic resonance spectroscopy (MRS) might provide novel insights to better understand the epileptogenesis in gliomas, and specific metabolites might be indicators of preoperative seizures in gliomas. Nakae et al. retrospectively investigated patient information (gender, age at diagnosis of tumor, their survival time) and tumor information (location, histology, genetic features, and metabolites according to MRS) in patients with gliomas. The data were correlated with the incidence of seizure and analyzed statistically. Of 146 adult supratentorial gliomas, isocitrate dehydrogenase (IDH) mutant tumors significantly indicated a higher incidence of preoperative seizures than IDHwildtype gliomas. However, the MRS study indicated that glutamate concentration in IDH-wildtype gliomas was higher than that in IDH mutant gliomas. Glutamate was not associated with a high frequency of preoperative seizures in patients with gliomas. Instead, increased total N-Acetylaspartic acid (tNAA) was significantly associated with them. Moreover, the multivariable analysis indicated that an increased level of tNAA was an independent predictor of preoperative seizures. According to MRS analysis, tNAA, rather than glutamate, might be useful to detect preoperative seizures in a patient with supratentorial gliomas 3).

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