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The chemical exposome in brain cancer: an exploratory study

Gil-Solsona R.[1], Pons-Escoda A.[2], Díez S. [1], Gutiérrez-Martín D.[1,3], Vidal-Sarro N[2], Bruna J[2], Dadvand P.[4], Majós C.[2], Gago-Ferrero P[1,*]

[1]Institute of Environmental Assessment and Water Research (IDAEA-CSIC), Barcelona, Spain.
[2]Bellvitge University Hospital - Bellvitge Biomedical Research Institute (HUB-IDIBELL), Barcelona, Spain.
[3]Institute of Sustainable Processes (ISP) & Faculty of Sciences, University of Valladolid, Valladolid, Spain.
[4]Barcelona Institute for Global Health (ISGlobal), Barcelona, Spain*corresponding author:
e-mail: pablo.gago@idaea.csic.es

Abstract. Diffuse gliomas are a highly heterogeneous and aggressive brain tumours with poor prognosis and survival and few established risk factors. Environmental exposures are suspected in the pathogenesis of these tumours; however, results of existing studies are limited and inconsistent, particularly for exogenous organic chemicals, with no available characterization of the chemical exposome of these tumours. Also, better understanding of phenotypic differences in tumour types is needed in order to improve clinical decision making and provision of personalised treatment recommendations. In this proof-of-concept study we analysed 33 glioblastoma samples (Bellvitge Glioma Cohort (BGC), Spain, 2005-present), including 16 methylated and 17 non-methylated tumours combining HRMS-based wide-scope target and suspect strategies. Forty-six exogenous chemicals were identified in the tumour tissue samples (31 confirmed with standard) including a variety of industrial chemicals (e.g. plastic additives or perfluorinated compounds), personal care products and pharmaceuticals. Our findings provide novel evidence on the presence of these chemicals in brain tissue, highlighting the need for comprehensive evaluations of their potential effects in the tumour pathogenesis. Finally, after applying metabolomics methods we observed clear differences in the profiles of endogenous chemicals among the studied glioma subtypes, and identified possible biomarkers. These chemicals have potential to be determined in a non-invasive manner, either by LCHRMS-based blood analysis or using complementary techniques (proton magnetic resonance (1H-MRS)). These are inspiring results since methylation is a strong independent predictor of survival as well as tumour response to chemotherapy for glioblastoma. Indeed, its non-invasive and pre-surgical determination would have a major impact on patient management. Our preliminary data is suggestive for the potential of nontargeted exposome methods to find new valuable biomarkers for diffuse gliomas diagnostic and prognostic stratification.

Keywords: Glioma, Environmental exposure, High resolution mass spectrometry (HRMS), organic chemicals, non-target analysis.

1. Introduction

Diffuse gliomas represent a type of brain tumour characterized by their high heterogeneity and aggressive nature, leading to a poor prognosis and limited survival rates. Unfortunately, there are only a few well-established risk factors known for these tumours. The role of environmental exposures in the development of diffuse gliomas has been suggested, but existing studies have provided limited and inconsistent findings, especially regarding the impact of exogeneous organic chemicals. Furthermore, there is currently no comprehensive understanding of the chemical exposome associated with these tumours. Gaining a better understanding of the phenotypic variations among different tumour types is crucial to enhance clinical decision-making and provide personalized treatment recommendations.

2. Methods

A unique retrospective cohort of 500 patients, including brain tumour sample with high-quality histopathology data (Bellvitge Glioma Cohort, BGC HUB-IDIBELL; 2005-present), as well as non-tumour brain tissue samples from autopsies. In this proof-of-concept study, a total of 33 glioblastoma samples (16 methylated and 17 non-methylated tumours) along with 20 non-tumoural samples were examined combining HRMS-based wide-scope target and suspect strategies. Additionally, metabolomics workflows were employed to identify variations in endogenous chemical profiles among the different glioma subtypes studied.

3. Preliminary results

Forty-six exogenous chemicals, including various industrial chemicals (e.g., plastic additives or perfluorinated compounds), personal care products, and pharmaceuticals, were identified in the tumour tissue samples. Among these, thirty-one were confirmed through standard methods. These findings present novel evidence of the presence of these chemicals in brain tissue, emphasizing the importance of comprehensive evaluations to understand their potential effects on tumour development.

Furthermore, our application of metabolomics methods revealed distinct differences in the profiles of endogenous chemicals among the different subtypes of glioma studied, along with the identification of potential biomarkers. These chemicals show promise for non-invasive detection, either through LC-HRMS-based blood analysis or complementary techniques such as proton magnetic resonance (1H-MRS). These results are particularly significant considering that methylation is a strong independent predictor of survival as well as tumour response to chemotherapy for glioblastoma. methylation serves as a robust independent predictor of survival and tumour response to chemotherapy in glioblastoma. Indeed, non-invasive and pre-surgical determination of methylation status would greatly impact patient management.

Our preliminary data suggests the potential of non-targeted exposome methods to discover new valuable biomarkers for diagnosing and prognosticating diffuse gliomas.

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