encountered this combination in a cohort of fetuses with IVH,[5] and believe it is actually not so rare.

We propose that to gain a deeper understanding of cerebellar hemorrhage in the context of GM-IVH, it is valuable to explore its occurrence and pathogenesis during fetal life. The risk factors in utero differ, as the immature brain is not yet exposed to the systemic hemodynamic stressors brought on by preterm birth and the extrauterine environment.

Recent advances in prenatal neurosonography and the increased use of brain MRI have contributed to a rise in the prenatal diagnosis of GM-IVH. However, the association between GM-IVH and cerebellar hemorrhage in fetuses has been scarcely documented despite the frequent association between cerebellar bleeding and unilateral cerebellar hypoplasia. The aetiology of isolated antenatal cerebellar hemorrhage has been attributed to maternal factors, such as trauma, placental insufficiency, seizures, and certain medications, or fetal factors, including vascular malformations, congenital infections, and thrombocytopenia and not to concurrent GM-IVH.

We suggest that an international multicenter study on fetal GM-IVH with cerebellar hemorrhage and postnatal outcome would complement the important study by Buchmayer et al.[3] Such a study should incorporate the new parameters presented by Hadi et al.[5] for the evaluation of fetal IVH, including the involvement of the posterior fossa and focusing on imaging patterns, underlying aetiologies, and predictors that influence clinical outcome.

DATA AVAILABILITY STATEMENT

Not required.

ORCID

Tally Lerman-Sagie https://orcid.org/0000-0001-6641-6875

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Generalized estimating equations for developmental medicine and child neurology

Camille Dieu | **Giovanni Briganti**

Department of Computational Medicine and Neuropsychiatry, Faculty of Medicine, Pharmacy and Biomedical Sciences, University of Mons, Mons, Belgium

Generalized estimating equations (GEEs) are a statistical method for analyzing correlated data, which is common in many applied fields such as longitudinal studies, clustered designs, and repeated measures experiments. The use of GEEs is particularly relevant when the aim is to estimate population-average effects (the average effect of predictors on the population rather than on individuals) rather than subject-specific effects (effects that vary between individuals). GEEs are therefore particularly well-suited to specific research models[1] in developmental medicine and child neurology.

GEEs extend the framework of generalized linear models to accommodate correlation structures within data while remaining robust to certain model assumptions.[2] The robustness of GEEs stems from the fact that they are essentially moment-based methods (methods that rely on the moments of the distribution, such as the mean and variance), relying on the specification of the first two moments (the mean and variance), rather than a fully parametric distribution.[3] GEEs are thus semi-parametric (a type of statistical model that incorporates both parametric and non-parametric components) and model the mean of the response variable (the outcome being studied) as a function of the covariates (independent variables or predictors), similar to generalized linear models, but also account for the correlation within clusters or subjects through a working correlation matrix (an assumed structure that describes how observations within a cluster are correlated). The structure of this correlation matrix is specified a priori and can take several forms, such

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as independence (assuming no correlation between observations), exchangeable (or compound symmetry, assuming a constant correlation between all pairs of observations), autoregressive (assuming the correlation diminishes with time or distance), or unstructured (allowing each pair of observations to have its own correlation). The working correlation matrix serves as an approximation that helps improve the efficiency of parameter estimates (improving precision), but it does not need to be precisely accurate. This flexibility allows GEEs to remain consistent (providing unbiased estimates of the parameters) even if the correlation structure is misspecified, provided the mean model (the relationship between the response and predictors) is correctly specified.

Frazier et al.[4] used GEE in their recent study with individuals with different genetic neurodevelopmental syndromes. In this study, they compared individuals with different genetic neurodevelopmental syndromes with neurotypical individuals and individuals with idiopathic neurodevelopmental disorders (including autism spectrum disorder, attention-deficit/hyperactivity disorder, anxiety, and mood disorder diagnoses). The main aim of their study was to assess neurobehavioral outcomes in genetic neurodevelopmental syndromes via an online assessment tool, the Neurobehavioral Evaluation Tool (NET), across time, and more specifically at three different time points (baseline, 1 month later, and 4 months later). Outcomes are NET's six symptom scales and five skills and functioning scales.

Due to the longitudinal nature of the data and the within-subjects design of the study, a series of GEEs was used. The authors assessed group differences in standardized NET scale and subscale scores using a series of GEE models, calculated with study group, time, and their interaction as fixed-effect factors and across analysis sets (age, estimated cognitive level, speech level, and autism spectrum disorder status).

For clinicians and researchers interested in replicating these methods, R software offers a robust environment for implementing GEEs via the geepack package,[5] as well as packages offering specialized models (for multinomial or ordinal results) such as gee and multgee.

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ORCID
Giovanni Briganti https://orcid.org/0000-0002-4038-3363

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Moving the use of OMICS technologies from research to practice

Shaun Sutehall

Clinical Research Division, Alder Hey Children's NHS Foundation Trust, Liverpool, UK

There has been a growing interest in the application of OMICS technologies into routine clinical and physiology testing for many years. Despite demonstrating significant advancement in both OMICS technology and analytical techniques in recent years (e.g. in transcriptomics[1]), there has been a continual struggle to translate research advancements into a widely used and approachable tool for clinical or practical use.

In this regard, the paper by Hanaoka et al.[2] demonstrates that the development of applied metabolomics is progressing, highlighting the potential of integrating metabolomics into clinical practice. Specifically, this study investigates the association between functional capacity and abundance of metabolites in individuals with typical development and individuals with cerebral palsy (CP). In addition to increasing the understanding of the mechanisms that underpin CP, the

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