



NYU



Prognostic Tool for Risk Stratifying Patients with Epilepsy to Improve Clinical Outcomes

Earlier and more accurate methods to diagnose and treat Status Epilepticus (SE) and New-Onset Refractory Status Epilepticus (NORSE).

Technology

The NYU research team has developed a prognostic tool for risk stratifying epileptic patients based on their gastrointestinal (GI) microbiome signatures to improve patient survival outcomes by predicting disease progression and treatment responsiveness. As described in unpublished work, statistical analysis of clinical fecal samples from epileptic patients revealed that their GI microbiome composition varies after a seizure depending upon the seizure type. Specifically, shotgun metagenomics identified species-level and functional-level differences in microbiome features between the chronic epilepsy control group and the status epilepticus (SE) or new-onset refractory status epilepticus (NORSE) cohorts. The SE cohort showed an enrichment of *Fusicatenibacter saccharivorans*, *Clostridium leptum*, *Lacticaseibacillus rhamnosus*, *Streptococcus anginosus*, and *Roseburia hominis*, while the NORSE cohort exhibited an enrichment of *Enterocloster bolteae*, *Nakaseomyces glabratus*, and *Marasmius oreades*. Further statistical analysis of hospitalization records for SE and NORSE patients revealed that surviving patients exhibited higher bacterial alpha diversity, with distinct microbial communities differentiating survivors from non-survivors, suggesting that specific microbiome profiles could predict mortality risk in SE and NORSE patients. Further, altered microbiota taxa in SE and NORSE were correlated with the upregulation of specific pro-inflammatory cytokines, such as IL-6, TNF- α , IL-10, CCL2, MIP-1 α , and IL12p70. By exploiting this newly discovered relationship between the GI microbiota, their pro-inflammatory cytokines, and mortality risk in epilepsy subtypes, the NYU research team hypothesizes that the use of treatments such as antibiotics, antifungals, probiotics, or cytokine inhibitors would restore gut microbiota levels and reduce recovery-hindering inflammation. This innovative approach paves the way for more accurate prognostic strategies based on individual microbiome signatures, which could ultimately lead to improved clinical outcomes.

Background

Status epilepticus (SE) is a condition in which patients suddenly experience continuous seizures or very frequent seizures that do not respond to standard anti-seizure medications. Seizures are thought to be provoked due to a surplus of pro-inflammatory molecules in the brain, possibly triggered by a simple viral infection, although the underlying mechanism remains unclear. New-onset refractory status epilepticus (NORSE) is a clinical presentation of refractory SE without an obvious cause. Despite its low incidence (approximately 3,200 cases per year in the US), the mortality of NORSE is high, with approximately 20% of patients dying during an acute episode. Among those who survive, half suffer disabling neuropsychological symptoms and continue to experience consistent seizures despite medication. Since the cause of NORSE is unknown, no effective and specific diagnostic tests or therapeutic interventions are available to test or treat NORSE, respectively. Current standard of care treatments for NORSE and SE are anti-seizure medications and coma-induced drugs, but these options are not effective for all

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patients and require intense hospitalization. Given the lack of efficacious diagnostic and therapeutic interventions for NORSE and SE, there is a critical need for new prognostic tools to predict disease outcomes and inform clinical intervention strategies, with the overall goal of improving patient quality of life and reducing mortality. therapeutic interventions for NORSE and SE, there is a critical need for new prognostic tools to predict disease outcomes and inform clinical intervention strategies, with the overall goal of improving patient quality of life and reducing mortality.

Development Status

The NYU research team is developing diagnostic and predictive tools for microbiome measurements in patients with NORSE. Microbiome signatures will be correlated with the effectiveness of various therapies in a large repository of patients.

Applications

- **Risk stratification:** Predict the likely clinical outcomes for SE and NORSE patients.
- **Clinical intervention:** Inform treatment regimen selection based on risk stratification.

Advantages

- **Personalized Tool:** Distinct microbiome signatures and their cytokine profiles can inform patient-specific clinical interventions.
- **Risk stratification:** Can predict severe outcomes, including mortality.
- **Potential integration with other biomarkers:** Could be incorporated with other biomarkers (genetic, proteomic, metabolic) to create more accurate prognostic tools.

Intellectual Property

NYU has filed a U.S. non-provisional patent application covering the method of diagnosing SE and NORSE, and the method of determining mortality risk based on mammalian GI microbiota. The application also covers the treatment of SE and/or NORSE via use of probiotics, prebiotics, and other compositions for modulating bacteria and fungus growth, and cytokine regulation in the GI microbiota.