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Predicting onset and remission of infantile spasms by pairing clinical signs and a disease biomarker CSF-GABA

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Background: Infantile spasms or West Syndrome (WS) represents one of the most devastating seizure disorders of pediatric epilepsy and are more frequently associated with poor intellectual outcomes. Early diagnosis with prompt initiation of treatment is key to effective control of spasms and may improve patient outcomes. Although the onset of WS is known to typically happen between ages 4-8 months, very little is known about the precise neuromechanical triggers or biochemical disease markers that herald its onset or remission. Diagnosis of WS usually involves visual observation of spasms and confirmation of hypsarrhythmia (disorganized wave-pattern) with an Electroencephalogram (EEG). Studies have identified a pre-hypsarrhythmia window of 3-6 weeks characterized by slow spikes that increase in frequency as condition deteriorates. However, the cutoff point to initiate treatment and avert disease could not be concisely defined. Also, decreased levels of brain γ -Amino Butyric Acid (GABA) have been associated with seizures, but exploitation of this knowledge in disease management was limited by several challenges including the absence of a reliable method for measuring GABA.

Method: We postulate that pairing a test for CSF-GABA concentration with clinical signs observed would greatly enhance chances to accurately predict spasms prior to onset. We plan a prospective study of CSF GABA levels as an indicator in the onset/development and remission of WS using our new method.

Findings: Using a novel LC-MS/MS method we recently developed for quantifying GABA in small amounts of CSF, we found that the mean GABA concentration in CSF from infants with seizures (n=16) was significantly lower (P=3.44e-12) compared to their age-matched controls (n=43), suggesting that susceptible infants have significantly lower CSF-GABA for their age during the pre-hypsarrhythmic period.

Significance: This study will offer providers a powerful tool for screening/identification of susceptible individuals during the predictive onset period of infantile spasms.

Biography

Stephenson W Nkinin is an Adjunct Professor of Microbiology at the university of Cincinnati Department of Biology. He is currently pursuing his MPH (Epidemiology) in the department of Environmental Health, University of Cincinnati. Prior to registering in the MPH program, He was a Research Associate Scientist at the Pathology/Clinical Mass Spectrometry Department at Cincinnati Children's Hospital.

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