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Editorial

A New Strategy for the Diagnostics and Management of Dysautonomia in Childhood

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According to latest clinical research, children with health problems due to the COVID-19 disease have autonomic dysfunction.[1] First, dysautonomia in childhood is a chronic disease that requires comprehensive treatment. Second, patients with dysautonomia present with varying degrees of social and behavioral impairment. Its treatment must be individualized, according to social function and the specific needs that correspond to the child's age.[2] The treatment of dysautonomia requires a multidisciplinary approach that leverages the child's strengths to address the deficits.[3] Finally, there are differences in treatment modalities in different geographical areas. Compared to the commonly used cardiovascular medication, Chinese experts have proposed the identification of the disease from the internal organs, considering that the disease is closely correlated to the spleen and kidneys, and that there is a distinction between deficiency and actuality in its pathogenesis.[4] Therefore, the diagnosis and management of dysautonomia in childhood remains challenging, and has become a hotspot in research. Due to the global outbreak of coronavirus disease 19 (COVID-19), there have been increasing reports of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) neurological involvement, including autonomic dysautonomia, which has been reported mostly in critically-ill patients, or in the long-COVID syndrome.[5]

Recently, the macro and micro effects of nutrition on heart rate was investigated by Dr. Buchhorn[6] to gain a more comprehensive understanding of autonomic disorders in children with disorders, such as anorexia nervosa, obesity, attention deficit disorder, and heart-brain interactions. This author perceptively identified the further increase in the number of autism cases in children and adults during the COVID-19 pandemic, considering that this may be correlated to the decrease in autoimmunity in adults and children infected with SARS-CoV-2. The following seemingly unrelated keywords were identified to be inextricably linked in a very novel manner: COVID-19, children, and autonomic dysfunction.

Simone *et al*.[7] described the prevalence of autonomic dysfunction in 20 non-critically-ill COVID-19 patients (these patients were not critically ill [COVID + group] during the acute phase of the disease) through a composite instrumental evaluation that comprised of Sudoscan, automated pupillometry, heart rate variability (HRV), and pulse transit time, choosing indicators that are similar to those chosen for the assessment conducted in the present study. In the present observational, cross-sectional study, the development of autonomic dysfunction was observed early in the disease. Furthermore, the present study revealed that autonomic dysfunction can be used as a diagnostic tool to help treat various psychosomatic and COVID-19-related illnesses in children and adults, based on regular clinical data.[8] However, more objective diagnoses and treatments of ill-defined psychosomatic disorders, such as long-term COVID, through a two-way interaction between heart rate and mood, are needed. Physicians may employ these techniques more frequently in clinical settings, in order to provide reference for its clinical diagnosis.

The study conducted by Berger *et al*.[9] investigated the clinical data that comprised of 51 long-term childhood cancer survivors diagnosed before age 15, between 1987 and 1992, in a prospective study. In that study, the main cofactor drugs for autonomic dysfunction were discussed. However, the expected results were not reached due to the small sample size. These drugs were similar to the following clinically common cardiovascular drugs: propranolol, ivabradine, and omega-3-fatty acids (O3-FA) supplements. Furthermore, the author enriched the reliability of that study by conducting a special analysis of four clinical cases. Future research is needed to elucidate the effects of autoimmunity on autonomic dysfunction, and improve the persistent symptoms that could not be improved by cardiovascular drugs.

The above results were combined with a study[6] to confirm the objective diagnosis of autonomic dysfunction in children using the 24-hour heart rate and ambulatory electrocardiogram (ECG). According to the HRV analysis, compared to patients with inappropriate sinus tachycardia and patients with postural orthostatic tachycardia only in the upright position, patients with autonomic dysfunction have a vagal weakness. Autoantibodies against the G protein-coupled receptors of the autonomic nervous system have also been linked to autonomic dysfunction in some children. Therefore, it needs to be considered that the clinical application of HRV is different from other indicators, such as blood pressure. Furthermore, for people of

Keywords: COVID-19; Heart rate variability; Dysautonomia; Clinical entities; Children.

Abbreviations: COVID-19, coronavirus disease 2019; ECG, electrocardiogram; HRV, heart rate variability; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; O3-FA, omega-3-fatty acids.

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the same age and gender, the normal value of HRV significantly varies, and the normal change in HRV value also significantly varies with age. A retrospective analysis of existing studies on short-term HRV normal values revealed the wide variation in HRV normal values.[10] The supplementation of O3-FA can reduce the heart rate during standing only, and this has a significant effect on the heart rate during the day and night, and on the global HRV in the 24-hour ambulatory ECG. The testing of these dynamic indicators would make the study more reliable and convincing.

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Conflict of interest

The authors have no conflicts of interest related to this publication.

Author contributions

YL and ZZJ proposed the main opinions and wrote the manuscript. All authors made a significant contribution to the study, and approved the final manuscript.

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