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Original article

Respiratory and autonomic dysfunction in children with autism spectrum disorders

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Abstract

Introduction: Cardiac parasympathetic hypofunction has been reported in autism spectrum disorders (ASD). This usually is linked to respiratory dysrhythmia which has been documented in some children with ASD.

Objectives: This study evaluated the cardiorespiratory functions in ASD to elucidate the physiologic basis of behaviors.

Methods: Nineteen children with ASD and 18 age matched controls underwent autonomic function monitoring at a defined resting state using the NeuroScope. The non-invasive real time beat-to-beat blood pressure was measured by Portapres and fed into the NeuroScope where heart rate, cardiac vagal tone and cardiac sensitivity to baroreceptor were derived from the EKG and blood pressure waveforms using the Vagosoft software; and respiratory rate and rhythm were measured simultaneously by plethysmograph. Respiration was analyzed breath by breath using our prior published methods.

Results: Various respiratory dysrhythmias, particularly Biot's and Cheyne–Stokes respiration, were detected in children with ASD, who also exhibited greater variability in respiratory rhythm and amplitudes than controls. The respiratory dysrhythmia in children with ASD was associated with a lower cardiac vagal activity.

Conclusion: The Biot's breathing and Cheyne–Stokes respiration coupled with cardiac vagal hypofunction in ASD suggest a brainstem dysfunction consistent with our previous findings. The low parasympathetic activity could explain in part the chronic sensory hyperarousal state in children with ASD.

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Keywords: Respiratory dysrhythmia; Biot's breathing; Cheyne–Stokes respiration; Autonomic dysfunction; Autism spectrum disorders

1. Introduction

Autonomic dysfunction or dysautonomia has increasingly been recognized in autism spectrum disorders (ASD) [1, see review 2]. Children with ASD exhibit symptoms and signs of hyperarousal state, such as anxiety, instantaneous rage that is often inappropriate,

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mood swings, or heightened reactivity to sensory stimuli sometimes referred to as sensory disintegration in the new Diagnostic and Statistical Manual (DSM-V). Chronic frequent hyperarousal state or heightened reactivity suggests unrestrained sympathetic activity. Physiological signs of heightened defensive responses have been reported in ASD by Hutt and colleagues [3] and they described these as being in a chronic state of hyperarousal. Reduced cardiac parasympathetic activity has been reported too [1], which is a good proof of poor sympathetic restraint in the ASD. The high heart rate (HR) reported in ASD also suggests heightened defensive responsiveness [1,2].

It has been suggested that the autonomic nervous system (ANS) is responsible for the atypical behavioral responses to sensation in children with sensory processing disorders [4]. Recent studies also indicate a similar link between dysautonomia and sensory disintegration in children with ASD [5]. Sensory disintegration is frequently reported as a symptom in ASD, often manifesting as atypical responses to sensation [6,7]. According to Diagnostic and Statistical Manual of Mental Disorders (DSM)-V, the diagnostic criteria for ASD include hypo- or hyper-responsivity to sensory input or unusual sensory interest as one criterion fulfilling the restricted or repetitive pattern of behavior. This suggests that sensory disintegration is prevalent in individuals with ASD. Other conditions or disorders associated with autonomic disorders [8] like insomnia, attention deficit hyperactivity disorder (ADHD), anxiety, obsessive compulsive behaviors, mood disorders, aggression and irritability all have been reported in children with ASD [9]. There is direct evidence of dysautonomia in children with ASD [1,2]. Toichi and Kamio [10] found that the mean resting parasympathetic activity in the heart was significantly lower in adolescents with ASD compared to age matched controls suggesting sympatho-vagal imbalance in ASD. In a previous publication we reported significantly lower resting parasympathetic nervous system (PNS) activity and significantly higher sympathetic nervous system (SNS) activity in children with ASD compared with typically developing controls confirming sympatho-vagal imbalance and therefore dysautonomia in ASD [1].

The ANS integrates cardiorespiratory functions. Respiratory sinus arrhythmia, a phenomenon where the heart rate varies in synchrony with inspirations and expirations is measured from the heart periods observed as electrocardiographic R–R intervals modified by respiratory rhythm. It is a good physiological example of such integration. Thus, dysfunction of the ANS affecting the cardiac autonomic innervation may impact on respiratory function. Cardiorespiratory dysfunction is well established in Rett's syndrome [11], a neurodevelopmental disorder sometimes misdiagnosed as ASD. Clinical observation shows that some children with ASD also have irregular breathing patterns. So far to date studies of autonomic dysfunction in ASD have focused on cardiac autonomic indices, skin galvanic conductance, or pupillary reflexes. We hypothesize that the dysautonomia in ASD also affects the breathing pattern. The purpose of this study is to analyze the resting state cardiorespiratory indices including the breathing pattern in children with ASD and age-matched controls.

2. Methods

2.1. Subjects

Children with ASD from The Autism Center and age matched healthy typically developed children as controls from the Pediatric Ambulatory Service, of Rutgers New Jersey Medical School, Newark, NJ were recruited. Children with ASD with double syndrome were excluded from the study. The diagnosis of ASD was made according to the criteria established by the DSM IV-TR, and Autism Diagnostic Observational Schedule-Generic and/or Autism Diagnostic Interview-Revised. Children who took medications known to affect ANS within 48 h of the study were excluded from the final data analysis. These medications were clonidine, resperidone, cough medications, amphetamines, and psychostimulants. All the subjects were screened on the day of the study for acute illnesses such as upper respiratory infection, and physical and emotional stress. Those subjects with any of the above confounding factors including those with more than the child's usual baseline sleep disturbance had their studies rescheduled for another suitable day.

Seventy-six children with idiopathic ASD and 24 controls were sequentially offered to participate in this study. A total of 68 (21 of whom were controls) subjects agreed to participate and were studied. Twenty-eight children with ASD and all 21 controls were able to reach the defined resting state during recording and completed the autonomic study. Only 37 of the 49 subjects had at least 20 min of satisfactory continuous respiratory recordings that were included in data analysis. The 20 min of continuous resting respiratory recording were necessary to ensure a sufficient sampling of the respiratory patterns. The total duration of the autonomic monitoring was at least one hour in each subject.

The subjects consisted of children with all ethnic backgrounds including Caucasian, African American, Asian and Hispanic. There was, however, a skewed representation of male subjects, which reflects the male predominance in this disorder. Table 1 shows the demographic characteristics of the two groups included in data analysis.

The Institutional Review Board of Rutgers – New Jersey Medical School, approved the study protocol.