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Neuro-Immune Abnormalities in Autism

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Editorial Note

Autism spectrum disorder (ASD) is a heterogeneous condition affecting an individual's ability to communicate and socialize and often presents with repetitive movements or behaviors. It tends to be severe with less than 10% achieving independent living with a marked variation in the progression of the condition. To date, the literature supports a multifactorial model with the largest, most detailed twin study demonstrating strong environmental contribution to the development of the condition.

Autism spectrum disorder

Neurodevelopmental disorder of unknown etiology. Recent evidence suggests a strong environmental component and persistent neuroinflammation. Within the phenology of ASD and associated disorders, the subjectivity involved in attributing an infant or toddler with introversion (or being in one's own world, autism) is fraught with difficulty. The difficulty is not whether such behavioral abnormalities represent a neurobiological illness – consensus is for an organic brain disorder – the challenge stems from the wide-ranging possibilities underlying the visible disease. A secondary obstacle to the adequate identification of disease process in ASD patients pertains to scientific disparity.

Epidemiology: Autism spectrum disorder was first identified by Kanner in 1938. Over the subsequent 10 years, Kanner discovered 50 further cases . Kanner subsequently reviewed the first 11 patients at 30-year follow- up. Only one known patient achieved employment. More recent evidence also suggests a high level of disability in affected individuals, with 60–75% achieving poor or very poor outcomes in adulthood.

Morbidity and mortality

Shavelle et al. investigated the mortality rate of ASD in over 13,000 patients between 1983 and 1997 and found it to be more than twice that of neurotypical peers. Standardized mortality ratio (SMR) was estimated as 2.4. Certain causes carried significantly higher SMR. Similar mortality rates have been reported in other studies with a consistent increased mortality rate for ASD, and a substantially greater risk in female ASD patients. Whilst mental retardation predicted risk of early demise, those without mental retardation also had increased risk.

Immune Abnormalities and Neuroinflammation in ASD

Perhaps one of the most substantive studies in the last decade was conducted at the John Hopkins Institute, and involved an analysis of autopsy specimens and cerebrospinal fluid (CSF) samples from affected individuals and controls. The results indicated a neuroinflammatory response, regardless of age (in patients between 5 and 46 years of age), involving excess microglial activation and increased pro-inflammatory cytokine profiles. The study carries high statistical significance.

Neurological abnormalities in ASD

With the exception of neuroinflammatory changes, most reported neurobiological abnormalities in ASD are inconsistent.Structurally, abnormalities have been described in the cerebellum, hippocampus, amygdala, and insular cortex. Abnormal brain volume has also been identified. A meta-analysis reported on an average of 13% smaller brain volume at birth, an average of 10% larger brain volume at 1 year of age than controls, and 2% larger in adolescence. An increase in gray matter with a reduced unit density has been quite reliably identified in this cohort. CSF volume has also been reported to be increased with enlarged ventricles and mini-columnar size is decreased

Autonomic Dysfunction

Autonomic involvement in ASD has been widely reported for over 30 years A recent controlled trial explored in detail the nature and type of autonomic involvement. Real-time variability together with continuous monitoring of blood pressure and breathing rhythms were assessed in an ASD cohort versus controls. Over 80% of the ASD cohorts were found to have a reduced vagal tone, highly suggestive of low central parasympathetic activity and, significantly, in a separate study, vagal tone in the neonate was found to predict neurodevelopmental outcome more accurately than birth weight, socio-economic status, or co-morbid medical conditions.

Autism spectrum disorder is a severe neurological condition with variable presentation, disease evolution, and variable, albeit generally poor, functional outcomes. Patients with ASD have greater risk of physical and mental health complications, and also a greater mortality. Neuroinflammation, peripheral immune abnormalities, and environmental factors have consistently been identified, further supporting the need for research that prioritizes disease prevention and harm reduction.

Heterogeneity has been a significant barrier to successful intervention in ASD. It may be that the commonality of impaired social integration represents dysfunction of a wide variety of systems and faculties during a crucial developmental period required for the complexities of social integration and as such the commonality is merely etiological.