Multiple sclerosis: Risk factors in children

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Canadians have one of the highest rates of Multiple Sclerosis (MS) in the world with approximately 1,000 new cases diagnosed each year. Primarily striking in adulthood, physicians and researchers with the Canadian Pediatric Demyelinating Diseases Network (CPDDN), a multi-institutional and multidisciplinary group, have found that MS is being increasingly diagnosed in children. A study by the CPDDN published in the journal *Neurology*, identifies a particular gene involved in the immune response that puts certain children at a higher risk of developing MS.

In children, an initial attack of demyelination (acquired demyelinating syndrome [ADS] in the central nervous system) often remains a single, isolated episode. However, in at least 20 % of children it represents the first clinical attack of MS. This contrasts with adult-onset MS, where most individuals presenting with acute demyelination are subsequently diagnosed with MS. Demyelination is the destructive loss of myelin - the protective covering that insulates and supports nerve cells - damaging the cells' ability to receive and transmit signals in the body.

"The uncertainty of the diagnosis understandably creates a lot of anxiety for children and their families," says Dr. Amit Bar-Or, neurologist and lead investigator at The Montreal Neurological Institute and Hospital - The Neuro, McGill University. "Having the tools to distinguish ADS and MS is important." Researchers at The Neuro in collaboration with researchers at the SickKids in Toronto and international colleagues therefore wanted to identify the risk factors in the 20% of children who go on to develop MS, and to investigate if the risk factors and the disease

biology are the same in both children and adults.

In adults, complex interactions between genetic and environmental factors contribute to risk and the best established genetic susceptibility marker has been identified in the alleles of the major histocompatability complex, a family of genes that play an important role in the immune system and autoimmunity. Specifically, the genetic risk factor for adults of northern European origins is localized to a form of the gene known as the HLA-DRB1 allele. The researchers wanted to verify if this allele predicts MS in at-risk children with ADS. Children, aged 16 or younger (266 children with ADS and 196 healthy controls) provided blood samples for genetic analysis.

"What we found is that there is a higher frequency of HLA-DRB1 in children that would later be diagnosed with MS, but not in children presenting with a single episode of ADS. This indicates that this gene is a risk factor in pediatric-onset MS." Children with ADS that do not go on to develop MS had no difference in HLA gene expression from controls indicating that the gene confers an increased risk for pediatric-onset MS, but not for acquired demyelination in general.

This is one of several studies investigating pediatric MS as part of the CPDDN. As children with pediatric MS are closer to the early mechanisms and biology of the disease, they can also provide insights into factors that represent causes versus consequences of the disease. One in 20 adults with MS can trace the disease back to a pediatric event, and therefore have had the disease for many years. This study reveals a fundamental similarity in genetic contribution to MS risk in both pediatric and adult-onset disease and underscores the importance of understanding the etiology of MS in children providing the possibility for earlier diagnoses and intervention and hopefully new therapies for MS.