

## **Cognition: how can we help?**

Workshop Facilitator: Dr. Maria Pia Amato,

Members        Dr. Lauren Krupp  
                    Dr. Maria Pia Amato  
                    Dr. Joy Parrish  
                    Dr. Leigh Charvet  
                    Dr. E. Portaccio  
                    Dr. Michael Absoud  
                    Dr. Iris Penner  
                    Dr. Shay Menascu,  
                    Dr. Bianca Weinstock-Guttman

Multiple sclerosis (MS) is a chronic demyelinating disease of the central nervous system in which cognitive dysfunction, major depression, and fatigue are common. While these problems are well documented in adults with MS, they are less investigated in children and adolescents with the disease. Children and adolescents can be particularly vulnerable to MS-related cognitive issues as the disease occurs during key periods of age-expected brain growth, active myelination, and maturation of neural networks, moreover during the learning curve and key formative years in the academic career. It should also be considered that disease activity (clinical and magnetic resonance imaging [MRI]) is higher than in adults with MS, while, on the other hand, brain plasticity and ability for compensation is deemed to be more efficient in this age range.

This workshop provides a comprehensive and updated overview of available evidence on cognitive and psychosocial issues in the pediatric MS population and highlights the challenges and needs for future research in this field.

Similar to their adult counterparts, pediatric patients with MS are often cognitively impaired, with estimated figures around 30 % of the cases. The pattern of cognitive dysfunction largely overlaps with that described in adult-MS. However, beyond deficits of information processing speed, memory and executive functions, one peculiar aspect in a few studies is involvement of language, usually spared in the adults. It is noteworthy that even mild linguistic deficits can have great functional impact and may negatively affect present and future academic achievements. Impact on general cognitive faculties and intelligence quotient has also been reported in children who are younger at the disease onset, suggesting a special vulnerability of this subgroup. The study of large cohorts of patients is needed in the future to clarify whether the pattern of cognitive dysfunction in this population of patients may differ reflecting different developmental trajectories and depend on different classes of age and age at disease onset.

Current evidence also indicates an apparent dissociation between the physical dimension and the cognitive dimension of MS-related disability in this patient population. As compared with adult patients, in fact, in children and adolescents, accrual of irreversible disability on the Expanded Disability Status Scale (EDSS) takes longer time. Cognitive dysfunction in children has been

documented in clinically isolated syndromes and may progress in the absence of any significant physical disability. The evolution of cognitive dysfunction is heterogeneous, with overall stability, improvement but also deterioration in a sizeable proportion of subjects documented in different studies. Male gender, younger age at MS onset and lower educational level represented risk factors for a worse cognitive outcome in one study. Clearly, longer-term studies on larger patient populations are needed to assess the definitive cognitive outcome as well as potential risk factors or protective factors. It has been consistently reported that cognitive dysfunction can have a negative impact on academic performance and lifestyle. Although neurologists may not be directly involved in interventions for psychosocial issues, sensitivity to such issues is important so that appropriate referral for assessment and treatment can be made. Therefore, addressing cognitive issues beyond disease duration, relapses and physical disability appears to be of critical importance for patient counseling, rehabilitation, and therapeutic decision making. To this aim, there is a critical, unmet need for the development of valid and brief assessment tools that can be used in everyday practice, to screen for cognitive difficulties. As for psychosocial issues, fatigue is reported in 20 to 50% of the MS children, whereas the prevalence of depression varies from 6 to 46%. As in adults, fatigue and depression can interfere with the child's daily functioning and quality of life. Also in this case, systematic evaluation of fatigue and depression by means of validated instruments appears to be mandatory in routine follow-up care for all young patients.

Early identification of these cognitive and psychosocial issues is critical so that special accommodations can be implemented at home and at school. Whether early initiation of MS therapies can help in improving cognitive function by confining the burden of the disease in the brain remains unclear and should also be addressed by future research. The development of cognitive rehabilitation techniques tailored to the needs of this population is another major undertaking. Finally, MRI research in this field is still in its early days. Cognitive dysfunction has been consistently associated with lesion load in the brain, corpus callosum and thalamic atrophy. Functional MRI studies may shed some light on adaptive and compensatory mechanisms and help measuring the effectiveness of therapeutic strategies based on cognitive rehabilitation.